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FOREWORD

Alhamdulillah, praised to Allah, Journal *Qanun Medika: Fakultas Kedokteran Universitas Muhammadiyah Surabaya* vol 04 no 01 has been published. It consists of 15 articles including 3 literature reviews, 6 case reports and 6 research articles in medical field. We would like to thanks to our reviewers and editorial board members who helped us in this publication. In order to be internationalized, we only published articles written in English since July 2019. We hope that these articles can be read widely both by domestic and foreign readers.

Thank you,

Yelvi Levani, MD.,M.Sc

Editor in Chief

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Literature Review

Effectiveness of core stability exercise for knee joint osteoarthritis: A review

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ABSTRACT

The knee joint is a weight-bearing support joint that often affected by osteoarthritis. Knee joint osteoarthritis is characterized by pain in a movement that disappears when resting, joint stiffness especially after prolonged resting or waking up, crepitations, and can be accompanied by synovitis with or without joint fuid effusion. If the patient was passive, did not do exercises, muscle atrophy can occur, which will worsen the stability and function of the joint. Other consequences that can disrupt daily activities to the most severe feature, such as an inability to walk. To discuss the role of core stability exercise for pain reduction in osteoarthritis. This type of study is a literature review. The goals of core stability exercise include: increasing muscle strength, improving posture, reducing pain, increasing ability, and functional mobility in patients. The provision of core stability exercise has a relationship between core stability with hip, knee, and ankle. This is because all parts of the body are connected to each other, both directly and indirectly. If the core muscle is strong, the muscles of the hip, knee, and ankle will also be strong. Core stability exercise is potential in the management of knee osteoarthritis

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INTRODUCTION

Osteoarthritis is a chronic joint disease that often occurs in the world, especially in the elderly. The prevalence of osteoarthritis in Indonesia is also quite high as 5% at age > 40 years old, 30% at age 40-60 years old, and 65% at age > 61 years old. This disease is experienced by 10% of men and 13% of women overall aged over 60 years (Zhang & Jordan, 2011). Osteoarthritis mainly attacks the waist and knees in the bones and joints in the area. The cartilages between the joints serve as a cushion when the joint is worn, but because this part is damaged, the bone surfaces in the joints collide with each other so that it causes pain, swelling, and stiffness (Hamijoyo, 2012).

According to the Indonesian Rheumatology Association, Osteoarthritis is defined as a degenerative joint disease that occurs due to chronic inflammatory processes in the joints and bones around the joints. This causes the bones to become brittle and become porous. Some risk factors for OA are trauma, obesity, heredity, and age (Hamijoyo, 2012).

Osteoarthritis (OA) included as a degenerative joint disease with a complex etiology that results in loss of normal joint function due to damage to the articular cartilage (Loeser, Goldring, Scanzello, & Goldring, 2013). The knee joint is a weight-bearing support component which often affected by osteoarthritis. Knee joint osteoarthritis is characterized by pain in a movement that disappears when resting, joint stiffness, especially after prolonged resting or waking up, crepitations, and can be accompanied by synovial inflammation, with or without joint fluid effusion. If the patient only had passive activity, does not want to do training, muscle atrophy can occur, which will worsen the stability and function of the joint. Other consequences that can disrupt daily activities ranging from pain when sitting to the most severe feature like walk difficulty (Valderrabano & Steiger, 2011).

Pain is a clinical symptom that is often found in patients with knee osteoarthritis, especially when doing activities or weight-bearing movement. As a result of knee osteoarthritis is a decrease in functional activity, especially difficulty from getting up to sitting, walking, going up and downstairs, and others (Sharma et al., 2015). Various kinds of treatment can be given in this case, including medical drugs administration, non-steroidal anti-inflammatory drugs, surgery, and physiotherapy. Treatment that is often given is non-steroidal anti-inflammatory drugs (NSAIDs) that are used to treat complaints of pain and inflammation. The use of this drug in the long term can have adverse effects (Steinmeyer et al., 2018).

Core stability exercise describes the ability to control or control the position and central movements of the body. Core stability exercise activities will help maintain good posture in motion and be the basis for all movements of the arms and legs. This shows that with optimal posture stability (activation of the Core Stability muscles), mobility in the upper and lower limbs can be done efficiently (Yu & Park, 2013). The purpose of this study was to review the role of core stability exercise in the management of knee osteoarthritis

LITERATURE REVIEW

OSTEOARTHRITIS (OA)

Osteoarthritis is a non-inflammatory degenerative joint disease that mainly occurs in older people, characterized by degeneration of joint cartilage, bone hypertrophy at the edges, and changes in the synovial membrane (Li et al., 2013). Secondary osteoarthritis experienced before the age of 45 years is usually caused by trauma (instability) that causes injuries to the joints (e.g., broken joint surfaces) due to loose joints and surgery on the joints. Other causes of osteoarthritis are genetic factors and metabolic diseases (Yucesoy et al., 2015). Pain is the most common complaint submitted by sufferers of

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OA patient, especially in joints supporting weight, pain when walking, especially when going up and downstairs, pain when not doing activities, mainly at night often occurs in patients with OA, but the more severe the disease, the pain will appear only with minimal joint movement, even when resting (Hunter et al., 2008). Clinically OA is manifest into various levels such as subclinical, with no clinical signs found. Only pathologically can be found an increase in the amount of cartilage tearing, the formation of bull/blister and fbrillation fbers of collagen connective tissue in joint cartilage (Man & Mologhianu, 2014), whereas in the subchondral bone sclerosis occurs. According to the aferent theory consists of 2 groups of fbers namely large fbers (A-Beta) and small fbers (A-delta and C). The mechanism of pain through exercise therapy, namely: exercise therapy is one of the treatments in physiotherapy that in practice uses body movements both actively and passively so that it can accelerate the healing of injuries of osetoarthritis or other diseases that have changed normal lifestyle (Tashani & Mi, 2009).

OA treatment

In patients with OA in the knee joint, what is complained of is a deep pain in the knee and is getting worse when the patient is doing activities, especially when walking, going down the stairs, and getting up from his seat (Hernandez et al., 2019). For this reason, treatment of Osteoarthritis aims to reduce pain and improve physical function and quality of life of patients in their daily activities. Some treatments for patients with Osteoarthritis are:

Lifestyle modification

One risk factor for OA is obesity. Weight loss in patients with knee osteoarthritis can reduce the symptoms of pain caused by the disease. Of course, this can be achieved if the patient is able to exercise well and regularly. Also, exercise can help regulate muscle strength (Woolf, 2010). Conservative therapy that can be done includes education to patients, lifestyle settings; if the patient is obese, they must reduce weight, if possible, keep exercising (light exercise options such as cycling, swimming) (Bliddal, Leeds, & Christensen, 2014).

Pharmacotherapy

Paracetamol is a group of non-steroidal anti-infammatory drugs proven to reduce the symptoms of pain that arise and become the frst line in the treatment of osteoarthritis. Giving intra-articular glucocorticoids can eliminate joint efusion due to infammation, hyaluronic acid, and chondroitin sulfate is believed to signifcantly reduce pain around several weeks after injection (Aydogdu, Karakose, Celik, & Atesci, 2014).

Surgical approach

Surgical therapy can be performed on patients with severe pain and does not respond to conservative therapy or pain that causes substantial functional disability and afects lifestyle. Some joints, especially knee joints, can be replaced with artifcial joints. Surgery can improve joint function and movement and reduce pain. Among the surgeries that can be done if the treatments cannot respond appropriately or are inefective in osteoarthritis patients are Arthroscopy, Osteotomy, and Arthroplasty (Katz, Earp, & Gomoll, 2010).

Physical therapy

Physical therapy for OA patients includes traction, stretching, transverse friction (special massage techniques for patients with OA), muscle stimulation exercises, and the latest approach is through core stability exercise (Hoglund, Pontiggia, & Kelly, 2018).

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Anatomy of Core Stability Muscle

Core muscle generally is interpreted as a muscle where the center of gravity of the body (center of gravity) is located, and all movements in the body originate from the core muscles. Core muscles support the entire movement and balance of the human body (Sadeghia, Shariata, Asadmanesh, & Mosavat, 2016).

Specifically, the core muscle is the structure of the muscles that support the entire structure of the spine, abdomen, pelvis, and pelvis, or what is referred to as LPHC (Lumbo-Pelvic Hip Complex). Strong core muscles are useful for maintaining the balance of the proportion of the body's muscles in doing the whole kinetic chain of our body movements. In the dynamic motion of the human body, the core muscles control the efficiency of acceleration/ deceleration movements and stabilize the body to prevent injury (Shah & Varghese, 2014).

The core muscles cover the abdominal trunk to the bottom of the torso. Muscles in this area include the Gluteus Muscle Group (buttock muscles, middle hip, and hamstring or back muscles of the thigh), Hip Muscle Group (upper and pelvic hips), Abdominal Muscle Group (front and side abdominal muscles, oblique or waist area muscles), Spine Muscle Group (muscles in the backbone area) (Kibler, Press, & Sciascia, 2006).

Core stability exercises as a form of exercise that aims to form and strengthen the main muscles in the lower back and pelvis, where these muscles play a significant role in maintaining stability and balance in the body. Core stability exercise is a synergistic activation exercise that contracts the stabilizer of the core muscle muscles consisting of travel sum abdominus, rectus abdominus, multifidus, internal oblique, and external oblique muscles. Strong core muscle can improve balance and stability with good stability center of mass (COM), and center of gravity (COG) can be held above the base of support (BOS) the best balance is when the center of mass and center of gravity are maintained above the base of support resulting in an increase in postural and increased productivity (Kisner & Colby, 2011).

Core Stability Exercise (CSE)

"Core" terminology refers to a lumbopelvic-hip complex, muscular area consisting of the muscles of abdominal, paraspinal, gluteus, diaphragm, pelvic girdle, and pelvic floor. This muscular complex controls the position of the trunk and plays the leading role in pelvic movements. The "core" as a source of force production, and as the kinetic chain that transfers and control motion until the distal part of the body (Hernandez et al., 2019).

Core stability exercise is defined as an exercise to improve neuromuscular ability. This exercise is intended to increase control than lumbopelvic. This increase in lumbopelvic can be done in two ways, namely, first, increasing the coordination and control of the lumbopelvic muscles and second, increasing the strength of the lumbopelvic muscles (Pardis, Mahla, Ali, Maryam, & Ramin, 2018). The core stability exercise model is based on spinal stability, depending on the contribution of muscles. In other words, muscle activity is needed to maintain the position of the spine. Many muscles are in the lumbopelvic and contribute to spinal control and stability.

In the core stability, the focus is to re-train the function of deep muscle (transverse abdominus and multifidus) and integrate the activity of deep muscle and global muscle in their work (Chang, Lin, & Ping-Tung Lai, 2015). Coordinated deep muscle is very important in the movement of the intervertebral segments of the spine and pelvis, although these muscles do not contribute significantly to the spine but are very important to stabilize the spine. The

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e f ect of core stability training will develop the work of the dynamic muscular corset muscles. With the onset of a contraction coordinated and concurrent (co-contraction) of these muscles will provide colander rigidity to support the trunk, consequently intradiscal pressure is reduced and will reduce the workload of the lumbar muscles and lower extremity such: hip and knee joint, so that tissue is not easily injured, abnormal lumbar muscle tension is reduced (Javadian, Akbari, & Talebi, 2015). With the occurrence of muscle relaxation, it is expected that there will be an improvement in the muscle pump which results in increased blood circulation to the back muscle tissue. Thus the supply of nutrition and oxygen in the muscle tissue to be better, the pain caused by spasm will be reduced.

The Procedure of Core Stability Exercise

Core stability training is intended to train the muscles related to the balance of the core in our body. That way, to increase these muscles needed systematic and programmed training and must follow the existing training program. This exercise will also be more e f ective if done with our body position in accordance with the body's biomechanics (Bliven & Anderson, 2013).

Core stability exercise is an exercise program that emphasizes the existence of stretching and strengthening of the core between the pelvis and vertebra. This exercise is also an essential component in providing local strength and balance in maximizing activities to be more e f cient. The types of core stability exercises include 5 types: (1) seated abdominal contraction, (2) seated oblique twist, (3) legs lift, (4) bridge exercise, and (5) lying spinal rotation (Suadnyana, Nurmawan, & Muliarta, 2014). Core stability exercises that can increase muscle strength will ultimately improve the postural balance of the elderly. This exercise can be done 4-6 weeks with a frequency of 3 times a week (Hoglund, Pontiggia, & Iv, 2018; Chevidikunnan, Saif, Gaowgzeh, & Mamdouh, 2016).

Evidence of Core Stability Exercise in Knee Osteoarthritis Treatment

There is a vicious circle in osteoarthritis-related to pain, physical dysfunction, and muscle weakness. Where muscle weakness is related to pain, it leads to physical dysfunction, thereby a f ecting disease progression. Core muscle exercise plays a vital role in the management of knee osteoarthritis.

Electronic searches of published literature were conducted from 2015 to the latest literature. Search strategies used in the search term 'core stability exercise'; "osteoarthritis ';' knee '; We apply the following algorithm in Pubmed, Google Scholar, and free text words: "(core stability exercise) AND osteoarthritis ';' AND knee."

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Table 1. List of core stability exercises in knee OA evidence

Author; year	Type of Study	Result
Dabholkar (2016)	Correlation experimental design	A study of 19 patients with knee osteoarthritis, underwent core muscle strength was assessed using pressure biofeedback apparatus. There is a significant correlation of the core stability measures with the functional activity level in knee osteoarthritis.
(Chevidikunnan et al., 2016)	Quasi-experimental study	Study of 20 female patients (16 - 40 y.o) with patellofemoral pain syndrome, and given four weeks given an additional core muscle strengthening. There is a significantly higher improvement in the intensity of pain and dynamic balance
Hoglund et al. (2018)	Pre-post intervention design, pilot study	Study of 10 females with Patellofemoral Joint (PFJ OA). PFJ OA patients underwent ten twice-a-week hip strengthening and core stabilization exercise sessions. The participants reported the improvement of pain, symptoms, daily living function, sports activity, and quality of life all improved within six weeks.
Subramanian & Suganthi (2017)	Case study	Subject aged 87 years knee with osteoarthritis was treated with specific core exercises during the period of 6 months with weekly twice frequency. A reduction in BMI ($P<0.05$) and *Womac* osteoarthritis index ($P<0.05$) with significant statistical analysis
Zarei & Rahnama, (2017)	Quasi-experimental study	Twenty-five women with knee osteoarthritis performed core exercises for eight weeks, and each consisted of 3 sessions. A significant increase was observed in the static and dynamic balances, the score of fear of falling ($p<0.001$).
Khisty (2019)	Pre - post experimental study	Thirty patients with unilateral medial tibiofemoral osteoarthritis of the knee. The patients underwent core exercise training included three types of exercises: static abdominal contractions, pelvic bridging, abdominal crunches. There was a statistically significant difference in Knee Injury, and Osteoarthritis Outcome Score (KOOS) questionnaire Score and Visual Analogue Scale (VAS) post the intervention ($p<0.05$)

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Effect of Core Stability Exercise in Knee Osteoarthritis

Knee Osteoarthritis is known to be associated with a decrease in muscle strength and atrophy of the muscles that stabilize this joint. Core stability training can improve the coordination and stability of the trunk, pelvis, hips, and knees by stimulating the crucial muscles of the lumbopelvic-hip complex and the periarticular muscles of the knee. Appropriate training programs that aim to regain muscle strength have been shown to have the potential to protect joints against pathological stressors (Hernandez et al., 2019).

Core stability exercise will develop the work of dynamic muscular, with the occurrence of coordinated and concomitant contractions of these muscles will provide rigidity to support the trunk, resulting in reduced intradiscal pressure and will reduce the workload of the lumbar muscles and lower extremity, so that the surrounding tissue is not easily injured, abnormal lumbar muscle tension is reduced (Kisner & Colby, 2011). With the stretching of the muscles, it is hoped that there will be an improvement in the muscle pump which results in increased blood circulation to the back muscle tissue. Thus the supply of blood and oxygen in the muscle tissue to be better so that the pain caused by spasm will be reduced. Besides activating the core muscles that function as spinal stabilizer muscles will make the surrounding muscles that had been spasms relaxed, thus also obtained excellent spinal stability and the position of the spine in a neutral state (Kisner & Colby, 2011). Good spinal stability will be more comfortable for a person to do functional activities. Besides, reduced intradiscal pressure will make it easier for patients to perform functional activities. Among other patients will be easier to carry out activities of lifting, walking, sitting, standing, and when doing recreational activities.

Core Stability is the ability to control the position and motion of the trunk to the pelvis, which is used to make an optimal movement with the transfer of body weight and stepping during the process of walking. The activation of the core muscles is used for resulting in spine rotation. Increased core stability activation patterns also result in increased levels of activation of the extremities or limbs to develop capabilities to support or move the extremities. Which will help maintain good posture in motion and be the basis for all movements of the arms and legs (Kibler et al., 2006).

CONCLUSION

According to the literature review, it has been shown that core stability exercise is potential in the management of knee osteoarthritis. Several studies have proven that core stability exercise is effective in reducing pain and improving physical function in patients with osteoarthritis of the knee.

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Literature Review

Role of inhaled nitric oxides in pregnancy with Eisenmenger syndrome

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ABSTRACT

Eisenmenger Syndrome (ES) is congenital heart disease with pulmonary hypertension and shunting turning from right to left. The resistance of pulmonary vascular more than 7.5 mmHg/L/min. The right ventricle and pulmonary artery always enlarge. During pregnancy, there will be hemodynamic changes that will affect the ES. It can be understood the possible dangers that can occur, like right heart failure; an increase in pulmonary arteries or the aggravation of pulmonary hypertension because there is no decrease in pulmonary resistance; A sudden decrease in venous return in supine hypotension syndrome can cause a relative increase in pulmonary arterial pressure so as to aggravate pulmonary hypertension and reverse shunting. Physiological effects of inhaled nitric oxide (INO) therapy cause selective pulmonary vasodilation: Hypoxia alveoli causes reversible vasoconstriction, thereby increasing pulmonary wedge pressure. INO can lower it. Moderate cardiac output and systematic arterial pressure are not affected; Selective in pulmonary because it is activated by hemoglobin; Selective vasodilation in the ventilated area, local hypoxia alveoli constricts the surrounding vascular tissue and redistributes blood flow to the ventilated lungs better and higher intraalveolar oxygen pressure. INO enhances this mechanism by increasing blood flow through a well-ventilated lung; Bronchodilators; Pulmonary surfactant, The combination of high concentrations of inspired oxygen and high concentrations of INO reduces the minimum surfactant surface tension.

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INTRODUCTION

Research on Nitric Oxide (NO) continues to grow since the identification of this molecule in 1987 has the same effect as the endothelium-derived relaxing factor (EDRF) (Steudel, Hurford, & Zapol, 1999); (Anas & Marlina, 2018). Many views about the mechanism of action of NO were put forward, since the application of inhaled nitric oxide (INO) in the laboratory and patients with primary pulmonary hypertension in 1991. In children and adults who experience severe pain and hypoxemia, INO improves arterial oxygenation and decreases pulmonary arterial hypertension selectively. The combination of INO with a ventilator can reduce the need for extracorporeal membrane oxygenation (ECMO) (Anggard, 1994); (Atz & Wessel, 1997); (Chen, 1997); (Finer & Barrington, 1997); (Steudel et al., 1999); (Barrington, Finer, Pennaforte, & Altit, 2017).

Pregnancy in ES is indicated. However, if the pregnancy continues, it needs special attention. During childbirth and childbirth, it is recommended to be done in the intensive care room with swan Ganz catheter and arterial pathway for serial measurement of arterial blood gas. The preload condition must be maintained by administering fuids, and excessive vasodilation must be avoided. Regional anesthesia should be avoided because it causes enlarged R-L shunting (Gibbs, 1988); (Sullivan & Ramanathan, 1988); (Goodwin, Gherman, Hameed, & Elkayam, 1999); (Brennan & Hatch, 2018).

Inhalation nitric oxidation is a potent and selective pulmonary vasodilator. Relaxation of pulmonary blood vessels that is dependent on endothelium in the Eisenmenger syndrome is impaired. Inhaling NO directly can reduce pulmonary hypertension and increase oxygenation due to the optimization of the ventilation-perfusion relationship. INO also has antithrombotic effects. And it is also used for the preparation of pulmonary heart transplants (Atz & Wessel, 1997); (Chen, 1997); (Cheung, Salas, Schulz, & Radomski, 1997); (Finer & Barrington, 1997); (Goodwin et al., 1999); (Lust, Boots, Dooris, & Wilson, 1999); (Steudel et al., 1999); (Barrington et al., 2017); (Brennan & Hatch, 2018).

PREGNANCY WITH EISENMENGER SYNDROME

Effects of Pregnancy on Eisenmenger Syndrome

In pregnancy, cardiovascular changes and oxygen transport will occur. Oxygen consumption in a state of rest increases in pregnancy. Improvements were apparent from the second trimester and an average increase of 33% above the mean before pregnancy. Oxygen consumption increases during labor. The average increase to the end of the second stage is approximately twice that of oxygen consumption before delivery (Ueland & Ferguson, 1988); (Cheitlin, Sokolow, & Melroy, 1993b); (Biswas & Perlof, 1994); (McAnulty, Metcalfe, & Ueland, 1994); (Cunningham et al., 2014).

Blood volume and its components increase during pregnancy - an average increase of 40% above the average value of nonpregnant women. The increase occurred mainly due to an increase in plasma volume, clearly seen in pregnancies 6-24 weeks and peaks at 30 weeks (Ueland & Ferguson, 1988); (Cheitlin et al., 1993b); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014).

During pregnancy, cardiac output at rest increases by an average of 40% above the value of not getting pregnant. This increase starts from the frst trimester of pregnancy. During labor (frst stage of labor), cardiac output will

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increase with each uterine contraction, with an increase of approximately 24% above cardiac output before contraction. In vaginal delivery (second stage), the increase ranged from 59 to 80% while in labor with a cesarean section about 25-57% above the resting value. Hemodynamic changes due to uterine contractions depend on the position of the mother. In the supine position, there is an increase in cardiac output by 25%; the heart rate decreases by 15%, causing an increase in stroke volume by 33%, while the slanted position changes as follows 7.6% - 0.7% and + 7.7%. So the degree of hemodynamic stability is in the oblique position (Ueland & Ferguson, 1988); (Cheitlin et al., 1993b); (Biswas & Perlo f , 1994); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018); (Karelkina et al., 2019).

Anesthesia has a vital role in modifying cardiovascular responses during childbirth and delivery. Anesthesia does not modify signi f cant changes related to labor (Gibbs, 1988); (Ueland & Ferguson, 1988); (Biswas & Perlo f , 1994); (Brennan & Hatch, 2018); (Karelkina et al., 2019).

Estimated bleeding at 500 ccs vaginal delivery while cesarean section 1000 cc. Three days after delivery, the decrease in blood volume was the same in both types of labor (16.2%). The di f erence is only in vaginal hematocrit increased by 6% while cesarean section decreased by 6% Normal values such as the state before pregnancy, achieved less than two weeks after delivery. As a result of these changes will occur cardiovascular adaptation in the form (Gibbs, 1988); (Ueland & Ferguson, 1988); (Biswas & Perlo f , 1994); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018):

1. Ventricular enlargement as a result of hyperdynamic circulation during pregnancy.
2. Decreased systematic or pulmonary vascular resistance due to the in f uence of pregnancy hormones, and
3. Suppression of inferior vena cava by the gravid uterus (especially in the third trimester of pregnancy), resulting in a decrease in cardiac output.

From these changes, it can be understood the possible dangers that can occur in pregnancy with ES. During pregnancy can occur (Gibbs, 1988); (Biswas & Perlo f , 1994); (McAnulty et al., 1994); (Cunningham et al., 2014):

1. Right heart failure, even if there is no signi f cant increase in pulmonary artery pressure.
2. Increased pulmonary arteries or increased pulmonary hypertension because in patients with Eisenmenger Syndrome, there is no decrease in pulmonary resistance during pregnancy.
3. A sudden decrease in venous return in supine hypotension syndrome can cause a relative increase in pulmonary arterial pressure to aggravate pulmonary hypertension and reverse shunting.

This danger can occur at any time during pregnancy, especially in old pregnancy, childbirth, and postpartum (McAnulty et al., 1994). In ES with secondary pulmonary hypertension or in primary pulmonary hypertension, decreased peripheral resistance when associated with decreased preload induced by changes in position or bleeding during labor. Which causes hypotension so that the right ventricle is unable to maintain blood f ow through pulmonary arteriolar tissue with high resistance (Gibbs, 1988); (De Swiet, 1993); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018).

In the f rst stage of labor, there is an increase in pulmonary artery pressure because of his and pain. Aside from that, caution should be given when administering analgesics or anesthetics because the hypotensive e f ect can relatively

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increase pulmonary arterial pressure (Gibbs, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018).

In the second stage, it should be accelerated because of his pain, and straining can increase pulmonary artery pressure to aggravate pulmonary hypertension. Also, in the second and post-partum labor, the occurrence of bleeding or hypovolemia should be prevented because it can suddenly aggravate pulmonary hypertension or cause severe shortcuts. Circumstances that cause extensive thrombosis of small blood vessels in the pulmonary arterial system that occur in the postpartum period also cause increased pulmonary hypertension (Gibbs, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014).

Regional anesthesia should be avoided because a decrease in systemic pressure causes the R-L shunting to enlarge. Also avoid hypoxia because it will increase pulmonary vascular resistance and further increase RL shunting (Gibbs, 1988); (Ueland & Ferguson, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018).

Effects of Eisenmenger Syndrome on Pregnancy

In cyanotic congenital heart disease that persists into adulthood, decreased blood vessel resistance causes an increase in R-L shunting by increasing cyanosis. Pregnancy in ES is contraindicated, and usually, spontaneous abortion occurs. Decreased oxygenation causes impaired fetal growth (Sullivan & Ramanathan, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014).

In the case of pregnancy with cardiac abnormalities, aside from determining the functional effects, it is also essential to know the etiology. Mothers based on congenital heart abnormalities will increase the risk of cardiac malformations in their children, both due to genetic factors or due to impaired blood flow to the uterus. Whittemore et al. reported that 11% of infants with congenital heart abnormalities from 66 pregnancies of 36 mothers with ASD (Atrial Septal Defect) (McAnulty et al., 1994).

The occurrence of heart functional disorders in the form of heart rhythm disorders, heart failure that occurs pulmonary hypertension is something that needs to be treated more carefully because the prognosis for the mother or fetus is not good. Fetal growth and development are influenced by the severity of circulatory physiology and arterial oxygenation saturation. Reportedly, in pregnant women with pulmonary hypertension, the incidence of preterm birth is 55%, IUGR (intrauterine growth restriction) 30% and perinatal death 28% (Sullivan & Ramanathan, 1988); (De Swiet, 1993); (McAnulty et al., 1994). Maternal mortality with ES or pulmonary hypertension ranges from 30-70% (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014). Karelkina et al. reported outcomes of 13 pregnancy in women ES, 4 cases, a transfer to mechanical ventilation was required. Intensive therapy included a combined use of vasodilators, the use of inotropes, the prevention of thromboembolic complications. Three women died within six months of delivery (9, 14, and 15 days post-delivery). Eleven children were discharged from the hospital in a satisfactory condition (Karelkina et al., 2019).

The danger of maternal death can occur both during pregnancy, especially advanced pregnancy, childbirth, and early postpartum. Regarding the cause of death, it is not known with certainty, suspected (Pitts, Crosby, & Basta, 1977); (Midwall, Jaffn, Herman, & Kupersmith, 1978); (Sullivan & Ramanathan,

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1988); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018); (Katsurahgi et al., 2019):

1. Because of a sudden increase in pulmonary arterial pressure, it can cause a "thrombotic occlusion pulmonary artery channel," which is a blockage of the small pulmonary arteries by the thrombus, which had previously been chronically narrowed.
2. Blockage of small pulmonary arteries by embolism
3. Cardiac arrhythmias that can occur due to a sudden decrease in cardiac output resulting in impaired coronary perfusion, and
4. Right ventricular failure due to a sudden increase in pulmonary artery pressure.

Management of Pregnancy with Eisenmenger Syndrome

If found congenital heart abnormalities with Eisenmenger Syndrome, it is advisable to end the pregnancy. According to Gleicher et al., Termination of pregnancy is less dangerous than if the pregnancy is continued. However, during the procedure, strict monitoring of pulmonary artery pressure, cardiac output, rhythm, and heart rate should be monitored. Besides that, an active examination should be carried out to detect congenital abnormalities in the fetus before birth (Sullivan & Ramanathan, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (Cunningham et al., 2014).

For a pregnancy that remains desirable, the maternal hemodynamic status and fetal growth are closely monitored. The mother's hemodynamics are kept stable until postpartum. She has been given prophylactic antibiotics. Infectious diseases should be treated quickly and adequately because infections can increase the work of the heart and especially respiratory infections, which can increase pulmonary vascular resistance so that it worsens pulmonary hypertension and its backfow (Sullivan & Ramanathan, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014).

They should be hospitalized since the second trimester and remain treated for at least two weeks post-delivery. During childbirth and childbirth, it is recommended to do in an incentive care room with Swan Ganz catheter and arterial pathways for serial measurement of arterial blood gas (Sullivan & Ramanathan, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018).

At the time of labor, pain needs attention. Analgesics can be given, but still, need to be careful. Preferably with general anesthesia or intra-tidal morphine because analgesic efects are perfect, and there are no motor and autonomic efects (Heytens & Alexander, 1986); (Bistch, Johansen, Wennevold, & Osler, 1988); (Buckshee, Biswas, Mittal, & Agarwal, 1988); (Gibbs, 1988); (Sullivan & Ramanathan, 1988); (Roberts & Keast, 1990); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014); (Brennan & Hatch, 2018).

If labor induction is needed, intra-cervical prostaglandin administration (for priming and induction of labor) followed by oxytocin drip after 6-12 hours later (Heytens & Alexander, 1986); (Bistch et al., 1988); (Sullivan & Ramanathan, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Cunningham et al., 2014).

Labor is carried out by vaginal delivery, fred by cunam or vacuum extraction. However, some have suggested that cesarean section planning is better than vaginal delivery because of maternal stress on labor, and is a planned procedure so that it can be optimally prepared, hemodynamics and ventilation can be well controlled. Also, it was suggested

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that in vaginal delivery, the contents of the stroke, cardiac output, and left ventricular work increase during uterine contractions. There is also a sudden increase in preload and venous return during uterine contractions and placental release. So it is not surprising that the death of two-thirds of mothers occurred at that time. What is important to note in labor is to prevent excessive blood loss. Therefore, uterotonics are given immediately as soon as the placenta is born, and if there is bleeding it is immediately treated, and adequate correction is made (Sullivan & Ramanathan, 1988); (Roberts & Keast, 1990); (De Swiet, 1993); (McAnulty et al., 1994); (Cunningham et al., 2014).

Vasodilators such as tholazolin or others are not routine. Anticoagulant is also not routinely given. Oxygenation or phlebotomy (Pitts et al., 1977); (Jones et al., 1981); (Lieber, Dewilde, Huyghens, Traey, & Gepts, 1985); (Heytens & Alexander, 1986); (Bistch et al., 1988); (Buckshee et al., 1988); (Sullivan & Ramanathan, 1988); (Roberts & Keast, 1990); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Weiner & Thompson, 1997); (Weiss et al., 2000); (Brennan & Hatch, 2018).

Postpartum care can be done early mobilization but by using stockings (long socks). This activity is to prevent thromboembolism and a sudden decrease in venous return. Breastfeeding is not recommended for subsequent pregnancies, the best choice is sterile (Lieber et al., 1985); (Sullivan & Ramanathan, 1988); (Cheitlin et al., 1993b); (De Swiet, 1993); (McAnulty et al., 1994); (Cunningham et al., 2014).

USE OF INHALATION NITRIC OXIDES IN EISENMENGER SYNDROME IN LABOR AND POST-LABOR PREGNANCY

Inhalation of nitric oxide in pulmonary hypertension

Robinson et al. (1999) reported that pulmonary hypertension therapy in pregnancy includes diuretics, digoxin, and oxygenation with limited efficacy. INO has demonstrated effectiveness and safety in the acute management of patients with pulmonary hypertension. The continuous use of extended INO affects a selective pulmonary vasodilator and is useful in the management of pulmonary hypertension in pregnancy (Robinson, Banerjee, Landzberg, & Thiet, 1999). The effect of INO's work on pulmonary circulation can be seen in the image

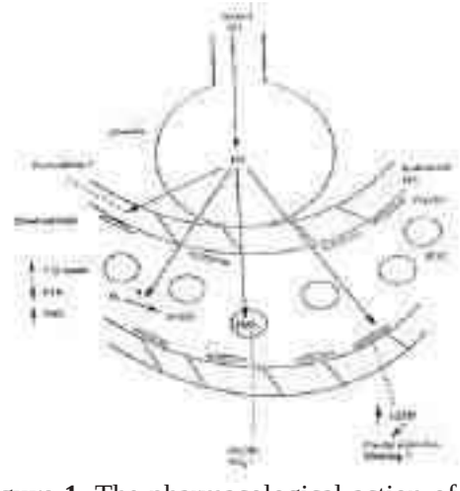

Figure 1. The pharmacological action of inhaled nitric oxide shows the effect on pulmonary veins by improving the accuracy of perfusion (V / Q) ventilation, decreasing PVR, and increasing PaO2. Nitric oxide also affects platelets, by inhibiting platelet function and increasing the tendency for bleeding. Red blood cells that contain oxyhemoglobin activate nitric oxide by converting it to methemoglobin and nitrate. Quoted from (Cheung et al., 1997).

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Experiments on goat-born babies born with ligation of the ductus arteriosus get conditions such as primary pulmonary hypertension. Furthermore, INO is given at various concentrations to see changes in the hemodynamic parameters of the pulmonary circulation. Decreased pulmonary artery wedge pressure and pulmonary vascular resistance so that pulmonary blood flow and systemic oxygen pressure increase. (Steinhorn, Morin, & Fineman, 1997).

Kinsella et al., (1997) reported experiments on rabbits who were very premature with IMV (intermittent mandatory ventilation) found conditions that worsen the progressive gas exchange and increased pulmonary arterial pressure. With immediate and continuous INO administration 20 ppm, a gradual improvement in the condition of gas exchange and hemodynamic circulation of the pulmonary circulation results (Kinsella & Abman, 1997).

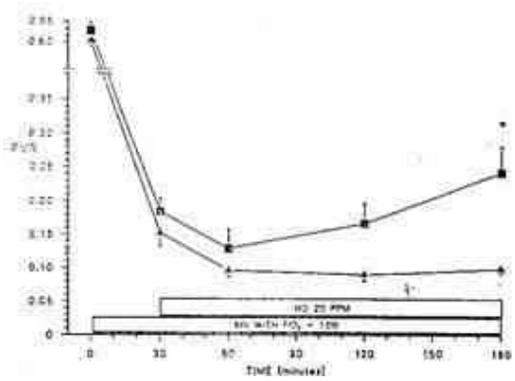

Figure 2. Early and ongoing management with low-dose inhalation nitric oxide prevent an increase in PVR associated with tidal volume ventilation in premature goats in 78% of the term ■ (control) ▲ (inhaled nitric oxide). Quoted from (Kinsella & Abman, 1997).

Fineman et al. (1997) in Chen (1997) found that the continuous release of nitric oxide is essential in the reasonable regulation of pulmonary vessels. Dysfunction of nitric oxide release is one of the causes of primary pulmonary hypertension in neonates. Neonates who get inhaled nitric oxide show a marked increase in oxygenation in the first 20 minutes and then (Chen, 1997). Weiss et al. (2000) found that treatment that immediate and continuous treatment with INO and Prostasklin IV or inhalation can improve pulmonary endothelial cell function, abnormal platelet aggregation, right hemodynamic heart, and life expectancy of patients with primary pulmonary hypertension (Weiss et al., 2000).

Finer et al. (2000) found that in neonates near term or near term with hypoxic respiratory failure given INO showed increased oxygenation, and there was a decrease in the incidence of death and the need for ECMO. Pedersen et al. (1997) say that nitric oxide is a pulmonary vasodilator and can correct inaccurate perfusion ventilation in cases that affect the lung parenchyma (Pederson, Hansen, & Henneberg, 1997).

Anggard (1994) says low concentrations of INO (50-80 ppm) are selective pulmonary vasodilators and increase arterial oxygenation. This effectiveness is demonstrated in changes in pulmonary vasoconstriction due to hypoxia in humans without causing systemic vasodilation (Anggard, 1994). Prostacyclin Analog, Iloprost inhalation is a prostacyclin analog that has a longer half-life of up to 25 minutes after inhalation so that it can be given 6-8 times per day and has minimal systemic side effects, but the efficacy in patients with adult Eisenmenger Syndrome has not been studied (D'Alto, Merola, & Dimopoulos, 2005); (Oechslin et al., 2010).

Inhalational Nitric Oxide in Pregnancy with Eisenmenger Syndrome

Kazue (1995) found that INO, even at low doses, is a potent and selective pulmonary vasodilator in congenital heart disease complicated by pulmonary hypertension. The results of his study found a positive correlation between initial pulmonary artery pressure and

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pulmonary artery vasodilation (Kazue, 1995). Goodwin et al. (1999) reported a case of a 27-year-old woman. Gravida 2 para 1 with 36 weeks of gestational age diagnosed with ASD with SE (Goodwin et al., 1999).

Furthermore, IUGR was obtained, so termination was carried out with drip oxytocin. Patients are given epidural narcotics, ampicillin, and gentamicin. Moreover, oxygen with 100% FiO2, but SaO2 keeps going down so that it adds INO 20 ppm for 5 minutes and baby boy 2640 gr AS 8-9 with low forceps. INO was continued for 45 minutes and obtained SaO2, and pulmonary arterial pressure returned to the baseline, and the hypoxemia was corrected (Goodwin et al., 1999).

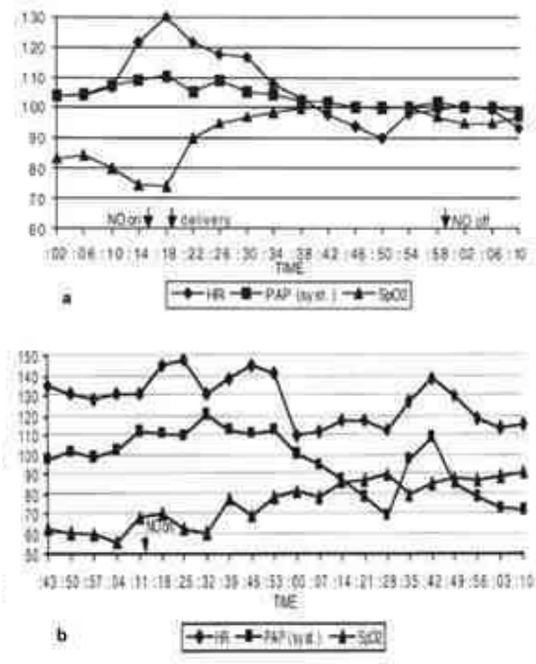

Figure 3. a) Effects of NO on oxygen saturation and hemodynamic parameters during labor and postpartum, b) Effect of nitric oxide on oxygen saturation and hemodynamic parameters postpartum; HR: Heart Rate; PAP: Pulmonary Artery Pressure; SpO2: O2 saturation. It modified from (Goodwin *et al*., 1999).

Until two days postpartum, the condition is stable, then an increase in pulmonary artery pressure. Trying to reduce it with nifedipine and hydralazine did not work because of a decrease in systematic pressure. Day 3 hypoxemia is heavy even with maximal O2. INO is given by titrating up to 80 ppm, and the hemodynamic and SaO2 parameters are improved. Several attempts have been made to reduce INO, but there has been a marked desaturation. Due to the limitations of INO, on the 5th day, INO was stopped after 48 hours of therapy, and a significant reduction in SaO2 was obtained. Prostacyclin is given peripherally. After improving briefly, his hypoxemia worsened and died on the 6th day postpartum. At autopsy, ES was obtained with ASD and a 1 cm diameter thrombus in the pulmonary artery. The goal of therapy is to try to go through a period of maximum stimulation to the deterioration of pulmonary hypertension that is characteristic of the peripartum period. Although death is reported no later than two weeks postpartum, most occur daily (Goodwin et al., 1999).

Differ with the case reported by Katsurahgi et al. (2019). They collect 15 patients with ES that the characteristics are shown in Table 1. These cases included 3 with ASD, 9 with VSD, and 3 with PDA. Ten patients (3 ASD, 5 VSD, 2 PDA) selected termination of pregnancy, while 5 (4 VSD, 1 PDA) chose to continue with the pregnancy after counseling regarding the maternal and fetal prognoses. Of the 5 ES cases, the 5th case, VSD case, was the hardest. Hospitalization has been carried out since the 9th week of SpO2 81%, and its condition worsened at the 26th week of NYHA III so that the termination is done at the 28th week and birth weight is 1027 grams. The description of the case can be seen in figure 4.

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Clinical characteristics of the five delivery cases.

Parameter	Case 5
Type of CHD	VSD
SpO_2 (before, late preg) (%)	86, 81
PaO_2 (before, late preg) (mmHg)	54, 48
Mean PABP (before, late preg) (mmHg)	76, nd
PVR (before, late preg) (dyne × s/cm^2)	1560, nd
NYHA (pre-preg → late preg → 1 year after delivery)	II→III→II
Hospitalization (gestational weeks)	9
Worsening of exertional fatigue (gestational weeks)	26
Oxygenation, drugs	18 w ~ O_2 2L, tadalafil, epo, NO, bosentan
NYHA class, drugs 2 year after delivery,	II, bosentan, tadalafil
Delivery (week-days)	28−2
Newborn weight (g) (SD)	1027 (−0.9)

CHD; congenital heart disease; PDA, patent ductus arteriosus; pulmonary vascular resistance; preg, pregnancy; NO, nitric oxide; epo, epoprostenol; HOT.

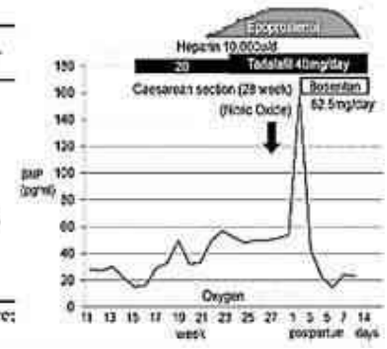

Figure 4. The clinical course of an ES-complicated pregnancy treated with drugs for PAH (case 5). Heparin, tadalafil, and epoprostenol were administered during pregnancy. Epoprostenol infusion therapy was started at 0.5 ng/kg/min and increased gradually in increments of 0.5 ng/kg/min twice weekly until a dose of 8 ng/kg/min was reached. Because the NYHA class worsened to Class III, the cesarean section was performed at 28 weeks. During the operation, inhaled nitric oxide 5 ppm was administered. In the postpartum course, bosentan was initiated, and epoprostenol was decreased gradually. After one month, there are no complications, and NYHA was class II, so the patient discharged. It is modified from (Katsurahgi et al., 2019).

Pregnancy and neonatal outcomes In the five delivery cases, the Cesarean section was performed at 30.6 [29.4-31.9] weeks because of heart failure in all cases. Patients had dyspnea, fatigue, persistent cough, bloody phlegm, and decreased LV function. Cesarean section was selected due to an immature cervix. The median birth weight was 1240 [1050-1376] g. In one case, epoprostenol and tadalafil were administered during pregnancy (Fig. 4). In this case, fetal growth was appropriate, whereas 3 of the remaining 4 cases delivered small-for-gestational-age babies (-1.9, -2.2, -3.0 SD). None of the neonates had congenital heart disease. Maternal and neonatal survival was 100%. At two years after delivery, all of the neonates showed healthy growth and proper neurological development. During pregnancy and postpartum, none of the cases exhibited excessive bleeding, thromboembolism, or an arrhythmia that required medical therapy (Katsurahgi et al., 2019).

Chronic pulmonary hypertension has two components, fixed and reactive. The remodeling of pulmonary arteries causes the fixed component due to a chronic response to increased pulmonary pressure or pulmonary flow. Pulmonary artery vasoconstriction usually caused by hypoxia, which contributes to the reactive component. Although the fixed component is less responsive to pharmacological manipulation, especially in ES, INO provides a real response in this case with decreased pulmonary arterial pressure and improved arterial oxygenation. What is unfortunate is the creation of INO only at urgent needs, so it is not possible to supply it permanently for definitive purposes (Fishman, 1994); (Kazue, 1995); (Atz & Wessel, 1997); (Pederson et al., 1997); (Robinson et al., 1999); (Steudel et al., 1999).

The effects of NO on chronic constricted pulmonary blood vessels are greatly affected, especially if the smooth muscle of the blood vessels is far from the alveoli, which allows diffusion of sufficient constraints because of the decrease in venous smooth muscle pressure by NO is always inhibited by intra-

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vascular hemoglobin. Changes in endothelial morphology contribute to the limited response to NO. Signifcant clinical responses appear without any efect on systemic blood vessels (Finer & Barrington, 1997); (Goodwin et al., 1999); (Steudel et al., 1999); (Omer, Rohilla, Rohilla, & Kushnoor, 2012).

At an inhalation dose of less than 100 ppm, methemoglobin formation is reported to be very small. Even so, these patients received episodes of methemoglobin that required a reduction in the INO dose and required the administration of methyl blue. There were no reports of NO tolerance or loss of selectivity in the pulmonary artery during exposure to INO. Back reactions such as vasoconstriction and hypoxemia after INO's sudden release have been explained and precipitated cardiopulmonary collapse (Atz & Wessel, 1997); (Goodwin et al., 1999); (Steudel et al., 1999).

The safety of long-term use of INO has not been established. Continuous use of INO is reported no later than 68 days in primary pulmonary hypertension patients awaiting pulmonary heart transplantation. Side efects of INO use are not signifcant if the concentration is 50,4±23 ppm (Atz & Wessel, 1997); (Goodwin et al., 1999); (Robinson et al., 1999); (Steudel et al., 1999).

Among ES patients, most deaths occur in the aftermath of early labor and are preceded by refractory hypoxemia. The cause of oxygen desaturation is unclear. Hemodynamic changes immediately before and after labor exacerbated by hypoxemia that initiates death often show a slight but slight association. Small and large pulmonary artery emboli are believed to be contributing factors. In fact, in this patient, there was a hemodynamic disorder, although adequate anticoagulation was given. This shows that there are other mechanisms involved. Signifcant changes in estrogen levels in the frst 2 weeks postpartum contribute to changes in blood vessel reactivity, especially in the pulmonary circulation (Lieber et al., 1985); (Heytens & Alexander, 1986); (Buckshee et al., 1988); (Roberts & Keast, 1990); (Weiner & Thompson, 1997); (Goodwin et al., 1999).

Sudden death due to thromboembolism and systematic hypotension with backfow causes hypoxemia and induces arrhythmias, or causes right ventricular failure. Transient hypotension is seen in normal labor but also general anesthesia or infltration. Unfavorably, sudden death in ES is not always consistent after hypotensive episodes. Furthermore, thromboembolism is enough to cause sudden death. The typical scenario of the gradual disorder is multiple small pulmonary artery emboli or recurrent hypoxemia that triggers pulmonary vasoconstriction (Lieber et al., 1985); (Heytens & Alexander, 1986); (Gibbs, 1988); (Roberts & Keast, 1990); (Finer & Barrington, 1997); (Goodwin et al., 1999).

Kopp et al., (1997) in Weiner and Thompson (1997) found that nitric oxide synthesis increases starting in early pregnancy before prostacyclin synthesis increases, this increase is in line with the increase in plasma estradiol. This increase can be blocked with estrogen receptor antagonists such as tamoxifen (Weiner & Thompson, 1997).

Lust et al. (1999) reported a 29-year primigravida case with a 26-week pregnancy diagnosed with ASD with ES. Patients were MRS-treated, bed rest, O2, and heparin. It has bee planned elective vaginal delivery at 34 weeks' gestation. Betamethasone, ampicillin, and gentamicin are given. When induction with PGE2, heparin is stopped. Epidural morphine anesthesia was given and transferred to an intensive care room (Lust et al., 1999).

Inhalation nitric oxidation is given by titrating in 80% FiO2 until a maximum

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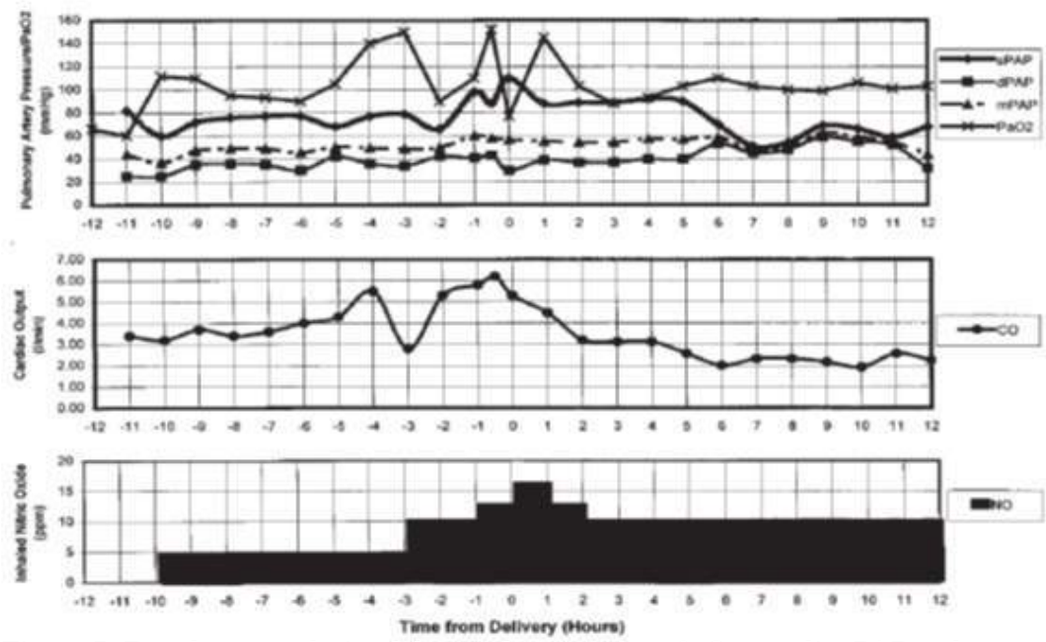

Figure 5. Development during labor. Labor occurs at 0. S, systolic; PAP, pulmonary artery pressure; d, diastolic; m, average value. It quoted from (Lust et al., 1999).

reduction in pulmonary arterial pressure and an increase in gas exchange is achieved. During labor, pulmonary pressure is increased given prostacyclin nebulizer and systematic hypotension and type II deceleration without changes in pulmonary arterial pressure. When maximal dilatation is performed, an amniotomy and birth of a female baby 1823 gr AS 10-10 by vacuum extraction during neonates is not problematic (Lust et al., 1999).

Ten ppm inhalation nitric oxidation is continued with 80% FiO2, and pulmonary arterial pressure decreases gradually. Cardiac output increases within 24 hours after delivery. The second day after childbirth, there is a lot of vaginal bleeding and persistent and supraventricular tachycardia without clinical changes in oxygenation or the incidence of heart failure. Pulmonary arterial pressure increases, and cardiac output increases during supraventricular tachycardia. Bleeding is stopped with steady cardiac output and increased pulmonary diastolic pressure which shows a shift in fuid after delivery (Kazue, 1995); (Finer & Barrington, 1997); (Kinsella & Abman, 1997); (Pederson et al., 1997); (Lust et al., 1999); (Robinson et al., 1999).

Many factors are involved in the progression of pulmonary hypertension during the 14 days postpartum, which causes heart failure and death. Including postpartum bleeding causes a decrease in pulmonary blood fow. The patient had never experienced clinical hypotension, and pulmonary diastolic pressure remained high during the postpartum period. He gets an arrhythmia, but it is not related to an increase in cardiac output. Both events are related to the development of in situ pulmonary thrombus and the deterioration of pulmonary hypertension (Buckshee et al., 1988); (Roberts & Keast, 1990); (Lust et al., 1999).

Pregnancy and childbirth add to the burden on patients with fxed pulmonary circulation resistance. Blood volume increases by 50%, stroke volume, and cardiac output increased in the frst trimester, second trimester, and during labor. Increased pulmonary artery pressure

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causes enlargement of the right ventricle, arrhythmias, and heart failure. R-L shunting by hypoxemia is worsened by the regular decrease in systemic vascular resistance. During labor, uterine contractions cause autotransfusion and increase cardiac output by 25%. This increase in pulmonary arterial pressure precipitates heart failure or arrhythmias. A decrease in cardiac output may occur during stage II as a result of increased intrathoracic pressure when striking. In stage III, autotransfusion of 500 ccs occurred. Stroke volume and cardiac output return to normal gradually in the two weeks postpartum. These factors contribute to maternal death during childbirth and childbirth (Gibbs, 1988); (Ueland & Ferguson, 1988); (De Swiet, 1993); (Biswas & Perlof, 1994); (McAnulty et al., 1994); (Lust et al., 1999); (Cunningham et al., 2014).

Giving NO through nasal cannula and catheter through the trachea is useful in this patient because it allows him to communicate with family and food and drink needs. The use of catheters through the trachea can prevent sudden hypoxic crises and increased pulmonary arterial pressure associated with terminating the mask release system (Atz & Wessel, 1997); (Lust et al., 1999); (Steudel et al., 1999).

This patient was monitored at the intensive care unit during labor day and 21 days postpartum until he died. During this period, the management of pulmonary heart transplantation remains the potential to be continued. NO is continued with the catheter versus the trachea to maintain oxygenation and additional benefts in decreasing pulmonary artery pressure and the risk of pulmonary arterial thrombosis (Cheung et al., 1997); (Finer & Barrington, 1997); (Kinsella & Abman, 1997); (Lust et al., 1999).

Immediate management of factors known to cause adverse shunting dynamics such as hypoxemia, arrhythmias, fuid balance, and acidosis, should be carried out, as well as prophylactic antibiotics for bacterial endocarditis and careful anticoagulant therapy. The postpartum monitoring period is related to the severity of the underlying cardiovascular disease. This patient is dependent on NO to improve oxygenation and requires intensive care. The contribution of the difculty of anticoagulant therapy in increasing pulmonary artery pressure is unclear. Cardiopulmonary transplantation in ES due to ASD is essential because these patients will be able to get pregnant with good results (Pitts et al., 1977); (Jones et al., 1981); (Lieber et al., 1985); (Heytens & Alexander, 1986); (Fremes et al., 1990); (McCarthy et al., 1991); (De Swiet, 1993); (Biswas & Perlof, 1994); (Weiner & Thompson, 1997); (Lust et al., 1999).

Inhalation nitric oxidation is useful for improving oxygenation and decreasing pulmonary arterial pressure. Maintaining improved oxygenation during childbirth and the postpartum period and vasodilation and anti-thrombotic efects of NO limit the increase in pulmonary arterial pressure, so expect an increase in cardiac output during childbirth among patients with fxed pulmonary artery disease. Despite prompt treatment by improving oxygenation and anti-coagulants, the prognosis of this patient remains poor. Death is caused by progressive arrhythmia and pulmonary hypertension before a pulmonary heart transplant is carried out. ES remains a life-threatening condition when it comes to pregnancy. Patients with ES abnormalities must explain the risks of pregnancy, contraception, and early termination if contraception fails. Fruitful of labor can be enhanced by improved oxygenation using INO in patients with pulmonary hypertension and hypoxemia (Lieber et al., 1985); (Roberts & Keast, 1990); (Cheitlin, Sokolow, & Melroy, 1993a); (McAnulty et al., 1994); (Kazue, 1995); (Pederson et al., 1997); (Lust et al., 1999); (Robinson et al., 1999); (Steudel et al., 1999); (Weiss et al., 2000).

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CONCLUSION

Pregnancy in ES is a contraindication, but if the pregnancy continues, during the process of giving birth and delivery, it is recommended to be carried out in an intensive care room with a strict monitor. The preload condition must be maintained by administering fuids, and excessive vasodilation must be avoided. Regional anesthesia should be avoided because of the enlarged R-L shunting.

Inhalation nitric oxide is a potent and selective pulmonary vasodilator. In ES, relaxation of the endothelium-dependent pulmonary blood vessels is disturbed. Patients with ES who inhale NO can directly reduce pulmonary hypertension and increase oxygenation due to the optimization of the ventilation-perfusion relationship. Inhalation nitric oxide also has an antithrombotic efect and is also used in preparation for a pulmonary heart transplant.

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Literature Review

Fiber consumption effect on non-communicable disease: How big is the impact?

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ABSTRACT

Non-communicable diseases have effects on the quality of human resources because, in addition to causes of death and morbidity, they also reduce productivity. Fiber intake was allegedly affecting the incidence of non-communicable diseases. The purpose of this literature review is to look at the link between fber intake and the incidence of non-communicable diseases and the effect of fber supplements to treat non-communicable diseases. Several literature indicate that fber intake is associated with cardiovascular disease, diabetes mellitus, cancer, and obesity. Research also shows fber supplementation can improve metabolic profles, blood sugar, insulin resistance in cardiovascular and diabetes mellitus patients. Fiber supplementation also reduces the risk of breast cancer. Fiber intake is related to the incidence of non-communicable diseases and can overcome some non-communicable diseases

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INTRODUCTION

Indonesia's national development goals are inseparable from the development of human resources, therefore, improving the quality of human resources is part of the development process. While the impact of non-communicable diseases on the resilience of human resource is tremendous because it causes death, morbidity, and decrease in productivity. In the 2015-2019 National Medium Term Development Plan (Rencana Pembangunan Jangka Menengah Nasional or RPJMN) it was stated that the reduction target of the prevalence of high blood pressure was 25.8% in the initial year (2015) to 23.4% (2019). The prevalence of overweight and obesity in 18-year-old residents is also sought to remain stable as the initial incidence is 28.9% (Bappenas, 2015).

Non-communicable diseases are currently the government's primary concern because besides being the leading cause of death, the prevalence tends to increase. Based on the results of the 2018 Riskesdas, the incidence of hypertension as much as 34.1% increased from the 2013 Riskesdas, which was 25.8%, while the prevalence of Diabetes Mellitus was 8.5%, higher than the previous 6.9% (Kemenkes, 2018).

The existence of the epidemiological transition from infectious diseases to non-communicable diseases is estimated due to socio-economic, environment, and population structure changes. People have adopted unhealthy lifestyles, such as smoking, lack of physical activity, harmful eating patterns, and alcohol consumption, which are the risk of non-communicable diseases (Bonita, 2013).

In terms of diet, it is estimated that there are risk factors for non-communicable diseases, especially fber intake. Based on the results of the 2013 Riskesdas, 93.5% of Indonesian fruit and vegetable consumption is still lacking. Therefore, it is assumed that fber diets are also lower than WHO recommendations, 25-35 grams per day.

LITERATURE REVIEW

Fiber Definition and Composition

Dietary fber is a part of plants including carbohydrates, which cannot be digested and absorbed in the small intestine, either entirely or partially fermented in the large intestine of humans. They include polysaccharides, oligosaccharides, lignin, and related plant substances (Prosky, 2001). Intake of dietary fber has been reported to be benefcial in reducing serum cholesterol and blood pressure. Therefore, it is believed that a lack of dietary fber can contribute to the epidemic of cardiovascular disease.

Diferent compositions of various fbers explain the diversity of functions, including water retention capacity, absorption properties (bile salt binding capacity, glucose, and fat absorption), tendency to form gels, viscosity, fermentability and the ability to modify the composition of intestinal microbiota. These components can reduce metabolism and change certain CHD risk factors, improve CHD prognosis, and reduce the probability of cardiovascular events (Bocanegra, 2009). Generally, Dietary Fiber (DF) is grouped based on solubility in water, water-soluble dietary fber (pectin, pectins, gums, and mucilages and storage polysaccharides) and dietary fber insoluble in water (cellulose, hemicellulose and lignin) (Papathanasopoulos, 2010) . One source of potentially rich dietary fber is whole grain products. Intake of whole grains is positively related to health.

This article is a review of the results of research studies and meta-analyzes that assessed the relationship between fber and non-communicable diseases that are widely published. It also discusses about cardiovascular

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disease, diabetes mellitus, and cancer, or biomarkers that are considered to contribute to the disease such as lipid profles (TG, TC, LDL-C, HDL-C), insulin resistance, and blood pressure.

Fiber and Cardiovascular Disease

Most of the studies showed that fber intake afected the occurrence of cardiovascular disease. Research from four meta-analyses of the efect of fber diet and the risk of cardiovascular disease has been found by Rae (2017), Wei et al. (2017), Kim and Je (2015) and Wu et al. (2014). Mc. Rae (2017) found a signifcant reduction in cardiovascular disease mortality, as well as the incidence of cardiovascular disease, coronary heart disease, and strokes on a high-fber diet. Wei et al. (2017) showed there was a curvilinear relationship found between fber consumption and the prevalence of Metabolic Syndrome (MetS). Compared with non-fber intake, OR Metabolic Syndrome at all levels of fber intake were 0.85 for the intake of 10 g/d and 0.73 for the intake of 40 g/d.

Wu et al. (2015) proved that fber diets based on fber subtypes (cereals, fruit, and vegetable fber) were also shown to reduce the risk of coronary events, where the RR of all coronary events was 0.93 (p = 0.001) and 0.83 (p = 0.001) for mortality. According to Kim and Je (2015), the RR (Relative Risk) of CVD and CHD were 0.77 and 0.76, respectively, for the highest versus lowest dietary fber category.

Other studies that show similar results to those of the meta-analysis were researched by Park et al. (2011), Tayyem et al. (2017) and Xu et al. (2016). Threapleton et al. (2013) have diferent fndings, which is fber intake is not associated with fatal CHD, stroke, or cardiovascular disease risk (CVD). However, it shows the possibility of protection of cereal fber at risk of fatal stroke in women with excess weight. Xu et al. (2016) said that the ratio of protein and fber intake signifcantly afected the incidence of CVD, where the protein-fber ratio was 1.15 times higher than the average, would increase Hazard Ratio. Dietary fber is not signifcantly associated with CVD events.

Fiber and Diabetes Mellitus

Efect of fber intake on the risk of diabetes mellitus is estimated through intermediate outcomes/biomarkers (e.g., blood sugar). Research by Fuji et al. (2013) found a high-fber diet reduced cardiovascular risk in patients with diabetes mellitus. A high-fber diet also has a negative relation with blood sugar and metabolic syndrome (Cholesterol levels, Glucose, HOMA-IR, blood pressure). Gof et al. (2017) also found a high-fber diet associated with a decrease in blood sugar, thus decreasing the risk of Diabetes Mellitus Type 2 (DMT2).

Fiber and Cancer

The efect of fber intake on cancer has been shown in several meta-analysis studies including a meta-analysis by Dong et al. (2011), where the RR of breast cancer between the highest dietary fber intake compared with the lowest was p = 0.444. A signifcant result is shown by Aune et al. (2011) in a meta-analysis study where RR for the highest versus lowest intake at risk of breast cancer was 0.93 (p = 0.00). Based on a meta-analysis by Kim and Je (2015), the highest dietary fber intake shown the risk of death of all types of cancer was 0.86 times lower than the lowest intake.

Another result of this study is the efect of fber on esophagus cancer, where Coleman et al. (2013) proved that there was a signifcant relationship between the highest fber intake with esophagus cancer. Similar results showed that regular fber intake reduced the risk of esophagus cancer (Tang et al. (2013). Zhang

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Table 1. 1 Research Summary on The Effects of Fiber on Non-Communicable Diseases

NO	SOURCE	DESIGN	SAMPLE	VARIABLE	OUTCOME	CONCLUSION
1.	McRae (2017)	Meta-Analysis	Adults	Fiber diet	Cardiovascular diseases	There is a statistically significant decrease in (RR) cardiovascular disease mortality, as well as the incidence of cardiovascular disease, coronary heart disease and stroke in those with a high-fiber diet
2.	Wei *et al*. (2017)	Meta-Analysis	Adults (n=28241)	Fiber diet Coronary artery disease risk and Stroke	Metabolic syndrome	There was a curvilinear relationship found between fiber consumption and the prevalence of Metabolic Syndrome.
3.	Wu *et al*. (2014)	Meta-Analysis	Adults (n=672408)	Fiber diet by type Coronary artery disease risk and Stroke	Risk of coronary events and CHD mortality	There is a significant relationship between fiber intake and CHD incidence and mortality (p <0.001)
4.	Kim and Je (2015) Meta-Analysis Study - Diet	Meta-Analysis	-	Fiber diet	CVD and the risk of death due to all types of cancer	Dietary fiber reduces the RR of CVD, CHD, and the risk of death from all types
5.	Park, *et al.* (2011)	Cohort Prospective	CHD patient (n = 219.123 males and 168.999 females)	Food fiber	Risk of death due to CHD	Dietary fiber intake reduce the risk of death from CHD
6.	Tayyem *et al.* (2017)	Case-Control	CHD patient	Fiber dietary pattern	CHD Risk	Fiber high diets significantly reduce the odds of CHD (OR = 0.55, 95% CI = 0.27 - 0.92)
7.	Xu *et al*. (2016)	Prospective Cohort	Male adults with CKD (Chronic Kidney Disease) (n=390)	Protein diet, fiber diet, and the ratio of protein and fiber diets	CVD Event	Protein intake ratio - fiber associated with CVD incidence. Food fiber only is not significantly associated with CVD events

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8.	Threapleton *et al.* (2013)	Cohort Prospective	CVD patient (n =31,036 women)	Fiber diet	CHD dan Stroke risk	Total dietary fiber and fiber from different food sources not related to fatal CHD, stroke or CVD risk
9.	Fuji *et al.* (2013)	Cross Sectional	Diabetes patient (n=4399)	Fiber diet	Cholesterol levels, Glucose, HOMA-IR, blood pressure (metabolic syndrome) and cardiovascular risk factors	High-fiber diets reduce cardiovascular risk in people with diabetes mellitus, are negatively related to blood sugar levels and metabolic syndrome.
10.	Goff *et al*. (2017)	Cross-Sectional	Adults	Fiber diet	Glucose levels	A high-fiber intake is associated with a decrease in blood sugar so that reducing the risk of DMT2
10.	Dong *et al.* (2011)	Prospective Cohort	Woman (n= 712,195)	Fiber diet	Breast cancer	There was a decrease in RR breast cancer between the highest compared to the lowest dietary fiber intake
11.	Aune *et al.* (2011)	Meta-Analysis	-	Fiber intake	Breast cancer	RR for the highest versus the lowest consumption was 0.93 (95% CI 0.89–0.98, Ɍ= 0%) for dietary fiber
12.	Coleman *et al.* (2013)	Meta-Analysis	-	Fiber diet Gastric cancer	Esophagus cancer	There was a significant relationship between fiber intake and the incidence of esophagus cancer
13.	Tang *et al.* (2013)	Case-Control	Oesophageal cancer patients (n = 359)	Fiber diet	Oesophageal cancer risk	Higher fiber intake decreases the risk of oesophageal cancer (p = 0.004)
14.	Zhang *et al.* (2013)	Case-Control	-	Fiber diet	Gastric cancer	The odds ratio of gastric cancer is lower on a high fiber intake diet compared to low fiber intake

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High Fiber Supplements And Diets To Overcome Non-communicable Diseases

The following studies have shown the influence of supplementation and fber intake to treat these diseases. Alba et al. (2016) reported increase soluble fber from Partially Hydrolysed Guar Gum (PHGG) on a normal diet towards type 2 diabetes patients and MetS improved cardiovascular and metabolic profles by reducing WC, HbA1c, UAE and trans-FA. Routine increase and consumption of Dietary Fiber (DF) soluble causes a signifcant improvement in blood glucose levels, insulin resistance and metabolic profle, without improving the secretory function of Islets of Langerhans, during the short-term intervention period in DMT2 patients (Chen et al., 2016)

According to Post et al. (2012), interventions involving fber supplementation for patients with type 2 diabetes mellitus can reduce fasting blood glucose and HbA1c. Meta-analysis studies proved increasing fber intake also increased glycemic control, suggesting this should be considered to be a treatment of patients with type 2 diabetes (Silva et al., 2013).

For cancer, a dose-response analysis showed that each 10-g/d increase in dietary fber intake was associated with a signifcant 7% reduction in breast cancer risk (Dong et al. (2015). A meta-analysis study by Kim and Je (2015) showed that RR for a 10 g/day increase in dietary fber was 0.91 for CVD, 0,89 for CHD, and 0.94 for all types of cancer.

CONCLUSION

Fiber intake is related to the incidence of non-communicable and can overcome some non-communicable diseases, especially cardiovascular diseases, diabetes mellitus, and cancer.

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Research Article

The relationship of smoking with the quality of life on chronic obstructive pulmonary disease patients at Dr. Reksodiwiryo Hospital, Padang

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a lung disease with the limitation of the airway, which is not completely reversible and is progressive. One of the risk factors of this disease is exposure to cigarette smoke for a long time. The purpose of this research is to know the relationship of smoking with the quality of life of chronic obstructive pulmonary disease patients at Dr. Reksodiwiryo Padang Hospital. This cross-sectional research has been implemented in February-May 2019 and involving 35 research subjects that meet inclusion and exclusion criteria. In this study, data was obtained that 97.1% of male gender research subjects, aged 60-69 years, 37.1%, 45.7% had moderate smoking status, poor quality of life 54.3% and there was a relationship with quality of life in Dr. Reksodiwiryo Padang Hospital (P-value < 0.05). In this research can be concluded that there is a smoking relationship with the quality of life patients of chronic abortive pulmonary disease patients in Dr. Reksodiwiryo Hospital, Padang.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a lung disease that has the limitation of the airway that is not completely reversible and is progressively caused by chronic inf ammation due to exposure to particles or toxic gases for a long time. This disease has a characteristic of the limited f ow of incoming air and can generally be prevented and hospitalized. (Perhimpunan Dokter Paru Indonesia et al., 2015). The World Health Organization (WHO) predicts 64 million people su f ering from COPD and predicting COPD will be the third-largest cause of death in 2030(WHO, 2014) In 2006, the number of moderate to severe COPD su f erers in the Asia Paci f c had a 6.3% prevalence rate. In Indonesia, the prevalence of PPOK amounted to 3.7% of the population with the most regions in East Nusa Tenggara (10.0%)(Badan Penelitian dan Pengembangan Kesehatan, 2013) This f gure can increase with the number of smokers because 90% of COPD patients are smokers or former smokers (Oemiati, 2013).

West Sumatera Province was ranked 23rd by the number of PPOK su f erers in Indonesia, with a prevalence of 3.0% (Badan Penelitian dan Pengembangan Kesehatan, 2013). Based on the number of visits in the hospital Dr. Reksodiwiryo Padang has a number of su f erers PPOK quite a lot, based on the initial survey of research obtained the number of patients who visited the hospital in the Lung clinic Dr. Reksodiwiryo Padang on June to November 2018 as much as 1642 people with average monthly visits is 274 people.

The main problem and the most frequent reason that causes the COPD su f erer to seek treatment is the shortness of breath su f ered that is persistent and progressive (Jones, Watz, Wouters, & Cazzola, 2016). The typical overview of COPD is the presence of very various airway obstruction, ranging from asymptomatic, mild to severe symptoms. This phenomenon leads to limitations in the daily activity of the su f erer, depending on the severity of the breathless (Arne et al., 2009). As a result of shortness of breath, patients with COPD tend to avoid physical activity and daily activities, thereby causing immobilization, patient relationships with decreased social activity and will eventually a f ect the quality of Life su f erer (Zamzam, Azab, El Wahsh, Ragab, & Allam, 2012).

The severity of airway obstruction in f uences the process of deterioration in the quality of life in COPD patients. Factors contributing to the enhancement of COPD include low socioeconomic status, genetics, age, asthma, chronic bronchitis, infections, and sex. Gender is very in f uential in patients with COPD. In the case of the incidence of the death of COPD, more males than females. The most in f uential main factors are the increasing symptoms and exposure to cigarette particles. People who smoke have a high chance of emerging respiratory symptoms, pulmonary function abnormalities, decreased FEV1, and increased mortality rates than in people who do not smoke (Salawati, 2016).

The relationship between the cigarettes with COPD shows the dose-response relationship, which means smoking many cigarets every day and longer; the risk of disease caused will be greater. The dose-response link can be assessed in the Brigman index, i.e., the amount of cigarette consumption per day multiplied smoking pages in years (Hasni & Warlem, 2019; Nathan & Scobell, 2012). Measurement of quality of life is important in COPD patients because this disease causes progressive damage to the lung function (assessed in VEP1) whose manifestations are congested, and ultimately causes a worsening of conditions in the quality Health that impacts social life and psychic su f erer that overall a f ects the quality of life. Another reason is the importance of such

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measurements because the quality of life also determines the measure of the success of therapy in COPD patients (Zamzam et al., 2012).

One of the measuring instruments used to view the quality of life of COPD patients using Saint George's Respiratory Questionnaire for COPD (SGRQ-C). It contains questions about symptoms, activities, and effects of COPD disease (Weatherall et al., 2009). Based on the explanation above, researchers are interested in researching to know the relationship of smoking with the quality of life of chronic obstructive pulmonary disease patients at Dr. Reksodiwiryo Hospital, Padang.

METHODS

This research was conducted after obtaining permission from the committee of Ethics of Medical Faculty, Universitas Baiturrahmah, with letter number 036/etik-fkunbrah/03/04/2019. Cross-sectional research aims to analyze the smoking relationship with the quality of life of COPD patients at Dr. Reksodiwiryo Padang Hospital using the SGRQ-C questionnaire. This research has been conducted in February – May 2019 by involving 35 people of research subjects recruited by consecutive sampling methods after fulfilling the criteria of inclusion and exclusion. The inclusion criteria of this research were patients who diagnosed with COPD by a lung specialist, were undergoing treatment on an outpatient basis, has a history of smoking, and willing to pursue consent. Research exclusion criteria were patients in acute exacerbation within one month. Categoric Data will be presented in the form of frequencies and percentages. Numeric Data will be presented on average and standard deviation. Analysis of the smoking status relationship and the quality of life of COPD patients conducted with the chi-square test (X2). Statistic significance is specified if P is < 0.05.

Table 1. Demographic and clinical characteristics Data for research subjects

Characteristics	*n(%)*
Sex:	
Male	34(97.1)
Female	1(2.9)
Age:	
40-49 y.o	3 (8.6)
50-59 y.o	8 (22.9)
60-69 y.o	13 (37.1)
>69 y.o	11 (31.4)
Smoking Status:	
Mild	12(34.3)
Medium	16(45.7)
Heavy	7 (20,0)
Quality of Life:	
Good	16(45.7)
Poor	19(54.3)
Total	**35(100)**

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Table 2. Relationship Status of smoking with the quality of life of COPD patients who have outpatient in the lung clinic Dr. Reksodiwiryo Hospital, Padang

Smoking	Quality of Life		Total	P-value
Status	Good	Poor		
	n (%)	n (%)	n (%)	
Mild	10 (83.3)	2 (16.67)	12 (34.3)	
Medium	4 (25.0)	12 (75,0)	16 (45.7)	0.005
Heavy	2 (28.57)	5 (71.43)	7 (20.0)	
Total	16 (45.71)	19 (54.29)	35 (100)	

In table 2 obtained respondents' data that have a poor quality of life in respondents who have a moderate and severe smoking status of 75% and 71.43%. Test result statistic (Chi-square) obtained value P = 0.005 (P < 0.05), It can be concluded that there is a smoking relationship with the quality of life of COPD patients who undergo outpatient in the lung clinic of Dr. Reksodiwiryo Hospital, Padang.

DISCUSSION

The research was obtained from 35 respondents, as many as (97.1%) Male gender in COPD patients who undergo outpatient in the lung clinic of Dr. Reksodiwiryo Hospital, Padang. The results of this research in line with previous research conducted by Muthmainnah in 2015 in patients COPD stable in poly lung Rsud Arifn Achmad Riau Province acquired results (80.28%) Patients with male gender and also the research of Lisa in 2013 was also obtained as many results (87.5%) Respondents were men (Lisa, Saad, & Suyanto, 2013; Muthmainnah, 2015).

Smoking is the most signifcant risk factor of COPD. Men are more smoking than women, so the number of COPD events is more common in men than women. Data from SUSENAS (*Survei Sosial Ekonomi Nasional*) In Indonesia shows that 64% of the population of Indonesians whose male sex is a smoker and only 4.5% of female smokers in 2014 (Statistics Indonesia, 2015). Not all smokers will develop into COPD, but as much as 20-25% of smokers will risk suffering COPD (Tanni, Pelegrino, Angeleli, Correa, & Godoy, 2010).

Males have a higher smoking prevalence compared to women. This phenomenon is considered to trigger high cases of severe COPD weight in males because smoking can cause the magnifcation of the mucosa and hyperplasia of goblet cells in the respiratory tract. (Salvi, 2014). This result is also following the results of research conducted by Sidabutar DKK in RSUP H. Adam Malik Medan in 2012 that the majority of COPD patients were males of 86.4%. The research done by Nugraha in 2014 in RSUP Dr. Ario Wirawan Selatiga from a total of 40 PPOK patients gets the full number of 40 people (100%) Male sex (Nugraha, 2013; Sidabutar, Rasmaliah, & Hiswani, 2012).

The research was obtained from 35 respondents, as many as (37.1%) Aged 60-69 years in COPD patients who undergo outpatient in the lung clinic, Dr. Reksodiwiryo Hospital, Padang. The results of this study supported the previous research conducted by Octaria in 2010 at Dr. Moewardi Surakarta HOSPITAL The majority of COPD patients were > years 60 years by 62.9% and also research conducted by Lisa in 2013 at RS. Ahmad Muchtar Riau also obtained the result that 36.3% of respondents are at the age of 61-70 years (Lisa et al., 2013;

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Prabaningtyas, 2010).

The risk factors for COPD are increased at the age of 50 years and above. Where the cardiorespiratory system at the age of 50 years will suffer from decreased endurance. This decline occurs because the lungs, heart, and blood vessels begin to decline its function. Lung function has decreased due to the elasticity of the lung tissue, and the chest wall is increasingly reduced to breathing. As a result of the damage to the lung tissue, there is a small bronchial obstruction that has undergone closure or obstruction of the early expiratory phase, the air is easy to enter into the alveoli, and there is air buildup (Incalzi, Scarlata, Pennazza, Santonico, & Pedone, 2014).

This study obtained results from 35 respondents, as many as 45.7% have moderate smoking status in COPD patients who have outpatient in the lung clinic, Dr. Reksodiwiryo Hospital, Padang. The results of this study supported the previous research conducted by the 2013 Nugraha also obtained the results as many as 50% of the respondents were moderate smokers and the research of Octaria P in the year 2010 stating that the tendency of patients with COPD has History of smoking weight of 73.10% (Nugraha, 2013; Prabaningtyas, 2010).

The behavior of smoking in some respondents had already begun when they were small, and the number of cigarettes they consumed was there that up to two to three packs per day, it increased when they entered the workforce. Environmental factors can induce Increasing consumption of cigarettes (Maritz & Mutemwa, 2012).

The World Health Organization (WHO) mentioned that 215 billion cigarettes in consumption in Indonesia annually. Indonesia ranks fifth among countries with the highest levels of tobacco consumption in the world. The more cigarettes the cigarette is sucked in, and the longer the time of becoming a smoker, and the greater the risk can be COPD (WHO, 2015). The risk for COPD is dependent on its smoking dose, such as the age of the person starting to smoke, the number of cigarettes smoked per day and how long the person is smoking. Components in cigarette smoke can cause damage to the respiratory tract. The Komonen does damage the cilia so that the longer it can tighten the infection. Meanwhile, mucus production is increasing, and this condition is very conducive to germs growth. If the condition persists, inflammation and respiratory tract narrowing, and the decrease in elasticity will occur. These smoking habits can increase the risk of fatigue in the Salura breath, such as narrowing in the case associated with COPD (de Oliveira, 2016; Tanni et al., 2010)

In research obtained results from 35 respondents, as much as (54.3%) Have a poor quality of life in COPD patients who undergo outpatient in the lung clinic of Dr. Reksodiwiryo Hospital Padang. The results of this research in line with the previous research conducted by Mutmainnah in 2015 in patients COPD stable in poly lung RSUD Arifin Achmad Riau Province acquired results (61.97%) Respondents with a good quality of life (Muthmainnah, 2015). This research shows that more than 50% of respondents have a good quality of life. This result may be due to the progressiveness of COPD disease. COPD is also chronic and irreversible. COPD patients must obtain continuous and frequent involvement of COPD patients with acute exacerbation of the disease so that all of these conditions can reduce the quality of patient life (Zamzam et al., 2012).

One of the things that affect a person's quality of life is characteristic. One's characteristics can affect the pattern and quality of one's life. The characteristic can be seen from several points of view; for example, the first gender in the study shows that patients with COPD are more in men. This can result from a greater

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smoking prevalence in males than females. Other factors can also be because of the male task as the head of the family that causes it to work inside and outside of the home that often contacts with COPD risk factors, such as farmers, mine workers, and others. In research conducted by Mutmainnah year 2015 that there are gender differences in men and women in the relationship of quality of life. Where men show a poorer quality of life than women (Muthmainnah, 2015). Quality of life can also be influenced by the age factor. Aged years have decreased from their body function and often have disabilities in conducting activities based on their body condition. This is due to many patients who are elderly COPD suffering from other degenerative chronic diseases, to reduce the function of his body that affects the quality of his life (Incalzi et al., 2014).

This study obtained data that subjects having a moderate and heavy smoking status had a poor quality of life of 75% and 71.43%. Statistic test results (CHI-square) obtained the value P = 0.005 (P < 0.05), then it can be concluded that there is a smoking relationship with the quality of life of COPD patients who undergo outpatient in the lung clinic of Dr. Reksodiwiryo Hospital, Padang. The relationship is due to the distribution of respondents to this study because most of them are smokers. Generally seen, cigarettes can cause respiratory damage where cigarette smoke has thousands of free radicals and irritant substances that interfere with health. The irritant material goes into the respiratory tract next, sticking to the cilia that are always slimy. The irritant material is also able to burn cilia, so that gradually occurs buildup of irritant material that can cause infection. Meanwhile, mucus production is increasing, and this condition is very conducive to germs growth. If the condition persists, inflammation and respiratory tract narrowing and decrease in elasticity. The small intensity and timing of exposure to irritant materials in cigarette smoke will affect the condition of the respiratory tract. The greater the intensity, dose, and time of exposure, it will accelerate the occurrence of damage or abnormalities in the respiratory tract. In other words, the habit of smoking can increase the risk of respiratory tract abnormalities, such as narrowing, which in this case is associated with the incidence of COPD (de Oliveira, 2016; Maritz & Mutemwa, 2012).

CONCLUSION

Based on the gender the most men were 34 people (97.1%) And by the most age group at the age of 60-69, which is as much as 13 people (37,1%). Based on the smoking status, the most were in the moderate smoking status of 16 people (45.7%). Based on the most quality of life, it has a poor quality of life of 19 people (54.3%). There is a smoking relationship with the quality of life of COPD patients who undergo outpatient in the lung clinic, Dr. Reksodiwiryo Padang (p-value = 0.005).

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Research Article

Relationships between body mass index with cholelithiasis

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ABSTRACT

Gallstones formed due to imbalance of bile components, excessive/ high level of cholesterol, nor bilirubin. Obesity was a condition where body mass index (BMI) was excess, which can cause health problems such as an increase of cholesterol, triglycerides, insulin levels, and blood pressure. There's growing attention to cholelithiasis in Indonesia, but there wasn't any data on the prevalence due to the limited amount of study related to cholelithiasis and BMI. This study aimed to analyze the relationship between BMI and cholelithiasis in Dr. Soetomo General Hospital. An analytical descriptive study with the case-control design was conducted, and the data were collected from medical records. The sample was 124 patients from the internal outpatient clinic Dr. Soetomo General Hospital. The data were analyzed using a t-test 2 independent sample. The ratio between female and male patients was 3:1, mean of age was 36-45 years, 45.2% had weight range from 61-70 kg, 51.2% had height range 150-159 cm, the BMI from patient with cholelithiasis speci f cally 45.3% on at-risk scale and 40% on obese I, the result showed p-value 0.089 (p>0.05), which means that there was no signi f cant di f erences with the BMI from patients with cholelithiasis and without cholelithiasis. In conclusion, BMI could not be used as a parameter to determine the occurrence of cholelithiasis on an individual.

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INTRODUCTION

Obesity is a condition where body mass index (BMI) is excess, which can cause health problems such as an increase of cholesterol, triglycerides, insulin levels, blood pressure, apnea, orthopedic complications, and mental health problems (Nihiser, 2007). Initially, this problem only considered in countries with high income, but now overweight and obesity were currently dramatically emerging in countries with low and middle income, especially in urban areas (Bonfrate, 2014). The prevalence of overweight in Indonesia compared to Malaysia was 21% to 44.2% (WHO, 2015).

Overweight and obesity were defined as an abnormal or excessive accumulation of fat that can cause health risks. Measurement of obesity population can be done directly by BMI, a person's body weight (kg) divided by the square of a person's height (meters). A person with a BMI of 30 or more was generally considered obese. Whereas someone with a BMI equal to or more than 25 were considered as overweight (WHO, 2015).

Cholelithiasis is the presence of stones in the gallbladder. The imbalance of bile-forming ingredients formed gallstones. Gallstones were formed when the bile contains an excess of cholesterol, excess of bilirubin, or insufficient bile salts. Gallstones were divided into two types; there were cholesterol stones and pigment stones. Cholesterol stones were formed from hardened cholesterol. In the United States, more than eighty percent of gallstones were cholesterol stones.

In Indonesia, the attention about cholelithiasis has begun, however there was still no national data due to the limited research related to cholelithiasis. In Dr. Soetomo General Hospital, the prevalence of people with cholelithiasis in 2016 is 8% of all the disease where the average annual rate of cholelithiasis patients is 860 people.

A recent study from Shamai (2010) found that there was a positive correlation between body mass indexes with cholesterol in the general population. It means that when the body mass index was increased, cholesterol serum will increase too. Meanwhile, cholesterol has a high effect on cholelithiasis occurrence. But there was no research about the relationship between body mass indexes with cholelithiasis yet. This study aimed to analyze the relationship between body mass index (BMI) and cholelithiasis in Dr. Soetomo General Hospital.

METHODS

This was an observational retrospective study using case-control design, where patients with cholelithiasis were the case group, and non-cholelithiasis patients were the control group. This study had approval by the ethical committee (No: 674/Panke.KKE/XI/2016). The population was patient on the Internal Medicine outpatient clinic. The sample was obtained from the patient's medical record, which was taken using non-random purposive sampling. There were 124 samples, divided into two groups with 62 cholelithiasis patients as case group and 62 non-cholelithiasis patients as control group.

The instrument in this study used the BMI formula, BMI in the Asian population, and medical records of patients with cholelithiasis and non-cholelithiasis in the internal outpatient clinic of Dr. Soetomo General Hospital. The variables of this study were the characteristics of cholelithiasis and non-cholelithiasis patients (consisting of gender, age, weight, and height) and patient's BMI. Data were analyzed using descriptive statistics and parametric statistical comparison test between two groups of independent samples using t-test 2 independent samples in SPSS software.

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Table 1. The proportion of sample groups according to gender

Type	Cholelithiasis		Non-Cholelithiasis		Total	
Gender	**n**	**%**	**n**	**%**	**n**	**%**
Male	24	19.36	15	12.09	39	31.45
Female	38	30.65	47	37.9	85	68.55
Total	62	50.01	62	49.9	124	100.0

Table 2. Frequency distribution of patients' age

Age (year)	Cholelithiasis		Non-Cholelithiasis		Total	
	n	**%**	**n**	**%**	**n**	**%**
16-25	1	0.80	2	1.61	3	2.41
26-35	6	4.84	9	7.26	15	12.1
36-45	17	13.71	10	8.07	27	21.78
46-55	16	12.90	9	7.26	25	20.16
56-65	16	12.90	21	16.94	37	29.84
66-75	6	4.84	9	7.26	15	12.1
76-85	0	0	2	1.61	2	1.61
Total	62	49.99	62	50.01	124	100.0

RESULTS

The subject of this study were 124 patients consisting of 62 with cholelithiasis and 62 with non-cholelithiasis. The proportion of each group (cholelithiasis and non-cholelithiasis) according to gender, were shown in Tabel 1.

Based on Table 1, from 62 patients with cholelithiasis, there were 19.36% (24) male and 30.65% (38) female, whereas, from 62 non-cholelithiasis patients, 12.09% (15) male and 37.9% (47) female were found. The number of female patients was higher than male patients.

The demography characteristics of age were shown in Table 2. Mostly cholelithiasis patients' age (17%) was 36-45 years, and non-cholelithiasis patient was 56-65 years group (21%).

The distribution of the patient's height is shown in Table 3, while the distribution of the patient's weight is shown in Table 4. Most of the cholelithiasis (13.71%) patients' height range of 155-159 cm and 165-169 cm. As same as with non-cholelithiasis patients' height (20.16%) range 155-159 cm. Most of cholelithiasis (22.58%) patients' weight range 61-70 kg (excess). Meanwhile, non-cholelithiasis patients' weight range is 51-60 kg. In conclusion, cholelithiasis patients' were fatter than non-cholelithiasis patients.

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Table 3. Distribution of patient's height (cm)

Height (cm)	Cholelithiasis		Non-Cholelithiasis		Total	
	n	%	N	%	n	%
150-154	15	12.1	14	11.29	29	23.39
155-159	17	13.71	25	20.16	42	33.87
160-164	8	6.45	9	7.23	17	13.68
165-169	17	13.71	11	8.87	28	22.58
>170	5	4.03	3	2.42	8	6.45
Total	62	50	62	50	124	100.0

Table 4. Distribution of patient's weight (kg)

Weight (kg)	Cholelithiasis		Non-Cholelithiasis		Total	
	n	%	n	%	n	%
<50	1	0.81	4	3.23	5	4.04
51-60	24	19.35	31	25	55	44.35
61-70	28	22.58	22	17.74	50	40.32
71-80	8	6.45	5	4.03	13	10.48
>81	1	0.81	0	0	1	0.81
Total	62	50	62	50	124	100.0

Table 5. Distribution of patient's BMI

BMI	Cholelithiasis		Non Cholelithiasis		Total	
	n	%	n	%	n	%
Under-weight	1	0.81	0	0	1	0.81
Normal	13	10.48	27	21.77	40	32.2
At-risk	27	21.77	20	16.13	47	37.9
Over-weight	21	16.93	14	11.29	35	28.22
Obese	0	0	1	0.81	1	0.81
Total	62	49.99	62	50.01	124	100.0

The distribution of the patient's BMI is shown in Table 5. The highest number of patients (21.77%) with non cholelithiasis had normal weight (n=27). Whereas, most of the cholelithiasis patients were at risk as many as 27 people. From this data, it can be seen that there was an increase number of Obese I in cholelithiasis patients, while in patients with non cholelithiasis the distribution on each scale

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Table 6. BMI's distribution by groups

Variable	Groups	n	Mean	SD	*P*
BMI	Cholelithiasis	62	23.7702	2.52181	**0.089**
	Non-Cholelithiasis	62	24.5119	2.29300	

Based on Table 6, the average BMI of non-cholelithiasis patients was 23.7702, and patients with cholelithiasis were 24.5119. The data distribution was very close to the mean value. The normality of the data distribution was tested using the One-Sample Kolmogorov-Smirnov Test in the SPSS application. The p-value for non-cholelithiasis patients was 0.200 (p> 0.05) and p-value for cholelithiasis patients was 0.086 (p> 0.05), which mean that data from each group was normally distributed.

Independent samples t-test comparative test were used to see differences between the BMI of patients with cholelithiasis and non-cholelithiasis. The results showed that the p value was 0.089 (p> 0.05), which means that there were no significant differences in BMI from patients with cholelithiasis and non-cholelithiasis in the Dr. Soetomo General Hospital.

DISCUSSION

In this observational study, we found that there were less significant differences in the BMI of both the cholelithiasis and non-cholelithiasis patients. Our results are consistent with the previous study. Study conducted by Shrestha (2012) found that cholelithiasis patients with normal BMI were 60% (n = 72) and overweight were 27.5% (n = 33). It means that not all cholelithiasis patients were obese patients, but there was an impact of gender (female). The incidence of cholelithiasis was higher in females than males, increasing with age and BMI.

Cholelithiasis or gallstones are common in women due to high estrogen levels (Omana, 2013). This result found that the prevalence of female cholelithiasis patients was 61.29% (38 from 62 people). This is consistent with a study by Sharma et al. (2013). Estrogen is the primary reproductive hormone in women, this hormone binds to several receptors. It regulates both healthy and sick mechanisms by regulating cholesterol synthesis and transport of HDL and cholesterol through receptors such as ESR1, SR-BI, and ERα (Maruyama, 2013). ESR1 activates SREBP-2 and Cholesterol7α-hydrolylase sterol27-hydroxylase, which will affect the synthesis of cholesterol and bile salts resulting in supersaturation of bile salts with cholesterol (Sharma, 2013).

From Table 2, this study found an increase in prevalence at the age of 36-45 years by 27.4%, 46-55 years at 25.8%, and 56-65 years at 25.8%. These facts are related to the speed of gallstone formation by age. Gallstones can occur at any age but are very rarely found at less than 30 years of age (Panpimanmas & Manmee, 2009). A study using population screening with ultrasound explained that the prevalence of cholelithiasis in Mexican-American, Cuban-American, and Puerto Rico mainland populations increased related to age.

Height and weight are physiological measurements carried out in medical practice and used to measure growth, nutritional status, and influential health risk factors (Engstrom, 2003). In this study, measurements of height and weight were taken from medical records. From 124 samples, most patients' height, either

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cholelithiasis or non-cholelithiasis, was spread evenly (155-159 cm). Height and weight are used routinely to measure BMI, to assess the nutritional status of patients, and to screen malnourished patients.

Bodyweight is not a direct measurement of body fat, but there is a correlation between body weight and body fat (CDC, 2015). Excessive weight gain or rapid weight loss that is unnatural can cause cholelithiasis because people with above-normal weight have more cholesterol levels in the gallbladder (Acalovschi, 2001).

From 124 samples, an increase in the occurrence of cholelithiasis was seen in the range of 61-70 kg (22.58%). This is influenced by the consumption of high-fat foods which will increase the risk for cholelithiasis (Panpimanmas & Manmee, 2009). The saturated fats and processed sugars were associated with the occurrence of cholelithiasis (Nunes & Beckingham, 2005). Therefore, weight can indirectly describe the condition of fat in a person's body.

Height and weight are used routinely to measure BMI, to assess the nutritional status of patients, and to screen malnourished patients (DiMaria, 2006). BMI was categorized according to BMI classification in Asians, underweight (<18.5), normal weight (18.5-22.9), at-risk (23.0-24.9), obese I (25-29.9), and obese II (> 30) (Who.int, 2015). This is not a direct measurement of body fat but is correlated with body fat. The BMI more than the normal range will increase risk of health problems such as Coronary Heart Disease (CHD), Hypertension, stroke, Diabetes Mellitus Type 2, hypercholesterolemia, metabolic syndrome, cancer, osteoarthritis, sleep disorders, hypoventilation syndrome in patients with obesity, reproductive health problems and gallstones (Shrestha, 2012).

Based on the result, 21.77% of cholelithiasis patients' BMI were on a risk scale. Meanwhile, most of non-cholelithiasis patients (21.77%) have normal BMI. So that BMI cannot be used as a parameter for the occurrence of cholelithiasis in a person but increases the risk of the occurrence of health problems.

This study cannot be generalized because the number of research subjects was limited and only taken in one location. The other limitation is the measurement of body fat was not done, so no more specific results were obtained to explain the relationship between body mass index and cholelithiasis.=

CONCLUSION

BMI is not a direct measurement of body fat but has a relationship with body fat. In conclusion, BMI cannot be used as a parameter for cholelithiasis, but it can increase the risk factor for health problems.

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Research Article

Contamination of water and soil of rice fields with soil transmitted helminths as source of transmission to farmers in Grogol sub-district, Kediri district

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ABSTRACT

Soil-transmitted helminths (STH) are the worms which transmitted through the soil. The people of Dusun Semen, Grogol, Kediri have a habit of defecating in the river. Farmers who work in direct contact with water and soil are possible to be infected with STH. The purpose of this study was to investigate the contamination of water and soil of the rice feld with STH by identifying the species of STH in water, soils, and farmers' fecal samples to fnd out the transmission to the farmers. Water samples were collected from three spots of river A and B, soil samples from 43 rice felds, and fecal samples from 50 farmers. Water samples were examined by sedimentation, soil samples by foatation, and fecal samples by Kato-Katz method. The data were then analyzed by Chi square test. Out of 18 water samples, 12 samples (66.7%) were positive, consisted of 4 samples (22.2%) contained *Ascaris lumbricoides*, and 8 samples (44.4%) contained *Trichuris trichiura*. Total soil samples were 129, where 8 samples (6.2%) were positive for *A. lumbricoides*, and 10 samples (7.7%) for *T. trichiura*. Out of 50 farmers, only 39 gave the fecal samples, where 12 samples (31.0%) were positive consisted of 5 samples (12.8%) for *A. lumbricoides*, 8 samples (20.5%) for *T.trichiura*. Two species of STH found in the media of water, soil, and feces of farmers were *A. lumbricoides* and *T. trichiura.* Positive farmers' samples prove STH transmission from STH contaminated water and soil of rice felds.

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INTRODUCTION

Soil-transmitted helminths (STH) are the worm those transmitted through the soil. The cases of worms' infections become a signifcant problem for world health, where more than 1.5 billion people or 24% of the total population worldwide infected with STH (WHO, 2012). The STH infections affect the poorest and most deprived communities. These worms are transmitted by the eggs present in human feces, which in turn contaminate the soil in areas where sanitation is poor. The main species that infect people are roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and hookworm (*Ancylostoma duodenale* and *Necator americanus*). Infections are widely distributed in tropical and subtropical areas, with the greatest numbers occuring in Sub-saharan Africa, the America, China, and East Asia (WHO, 2019). The current comprehensive prevalence rate of STH in Indonesia is difficult to be ascertained. The prevalence rate in children is higher than in adults due to poor personal hygiene (Lee & Ryu, 2019). Indonesia has more than 60 million cases of ascariasis and trichuriasis, and 60 million cases of hookworm infection (Hotez & Ehrenberg, 2010).

The people of Dusun Semen, Grogol Sub-district, Kediri District in East Java Province, Indonesia, have a habit of defecating in the river that may contaminate the water with STH. When the contaminated water is used to irrigate the rice fields, it may contaminate the soil of rice fields. Farmers are one group that has a high risk infected by helminths. In the daily activities, they do not use any personal protective equipment or PPE (Prayitno, Hanaf, & Sholihah, 2017) such as glove and boots, in direct contact with contaminated water and soil are possible to be infected by STH (Winita, Mulyati, & Astuti, 2012). The biggest risk of wastewater irrigation in agriculture is to helminth infections due to their long survival in the environment (Amoah, Adegoke, & Stenstrom, 2018).

The purpose of this study was to investigate the contamination of water and soil of rice field with STH by identifying the species of STH in water and soils microscopically, and followed by examination of fecal samples of the farmers to find out the STH transmission through those media.

METHOD

The study was an observational analytic study with a cross-sectional approach. The water samples were collected by quota sampling method from two different rivers, river A and B from there sample were collected from 3 spots of each river (Singarimbun, 1989). The sampling method for soil sample was total sampling, where the samples were collected from a total 43 rice fields. Soil samples were then collected from 3 spots of each rice field (Yeshaneh, 2015). The fecal samples were collected by total sampling method from 50 farmers who were residing in the village and working in those rice fields. This research has passed the ethical test with ethics certificate number: 208/EC/KEPK/FKUA /2019 issued by the Faculty of Medicine, Universitas Airlangga.

Table 1. Location of water sampling

Name of river	Name of spot	Location on the river
A and B	A1 and B1	At the base of the entry of water to the village
	A2 and B2	Between A1 and before entering the rice field
	A3 and B3	At the point of the entry of water to the rice field

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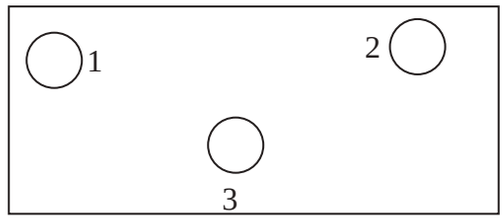

Figure 1. Soil sampling point

Soil sampling procedure

The types of soil based on the texture of the rice feld soil in the study area are sandy and clay. Each rice feld was divided into three spots, as shown in Figure 1. Spot one and two were at the corners of feld, and spot 3 was at about the middle of the feld.

The spots of sample collection were cleaned from the grass. Soil samples were collected from the surface of the rice feld by scraping using a plastic spoon because eggs or larvae spread on the surface of the soil. Surface soil was scraped of at the spot ± 40 x 40 cm2 depth and ± 30 cm width as much as ± 100 grams. The samples were stored in sample-pots of 5 cm in diameter, closed tightly, and protected from the sunlight by carrying in an icebox, then sent to the Laboratory of Parasitology, Bhakti Wiyata Institute of Healthy Science in the district of Kediri.

Fecal sampling procedure

An explanation of the current research was delivered to the farmers and provided the sign of informed consent prior to fecal sample collection. About 2-5 grams of solid feces or 10-15 ml of diarrhea stool or half the volume of the pot were collected in the morning before working in the rice felds (WHO, 1991). The farmers were also asked to fll the questionnaire. Samples were examined immediately on the same day; otherwise, the hookworm eggs will be damaged or hatch into larvae. If this is not possible, then the feces were pored with 5-10% formalin until the time of examination.

Sedimentation method for water samples examination

The water sample was transferred into a 15 ml centrifuge tube and was centrifuged at 1500 rpm for 2 minutes. The supernatant was removed. One drop of sediment was then placed on a glass object; eosin was added, and covered with a cover glass. Slides were then observed under a light microscope with the magnifcation of 100x and 400x.

Floatation method for soil samples examination

A fve grams sample was transferred into a 100 ml of beaker glass containing saturated NaCl solution and stirred well. The sample was then transferred into a glass tube until convex then covered with a cover glass and allowed to stand for 30-40 minutes. The cover glass was then placed on an object-glass prior to light microscopy examination.

Kato Katz Method for fecal samples examination

A gram of fecal sample was taken with a stick and placed on flter paper and then put wire mesh on the feces. Cardboard that has been perforated was placed on the glass object. The wire mesh was placed on top of the feces; then, the cardboard holes were flled with feces, and cardboard was removed. Feces on object glass was then covered with cellophane that has been soaked in the Kato solution. Cellophane tape was pressed with other glass objects to fatten the stool, and it was left for 20 - 30 minutes at room temperature. Objects glass was then examined under a light microscope using a 10x objective lens, and the number of worm eggs was counted.

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RESULTS

The Characteristic of Participants

The total number of farmers who gave the fecal samples was 39, where 19(49%) were male farmers, and 20(51.85%). The ages of participants were group into 25-35 years old were 15(38%), and 46-45 were 24(62%). Out of 39 samples, 12(30.77%) were found infected with STH, consisted of 7(36.84%) male and 5(25%) female.

Microscopy examination of water, soil and fecal samples

The results of light microscopy examination of water, soil, and feces were presented in Table 2. The number of positive water samples was 6 (66.7) from either river A or river B. More positive samples were found in sandy soils (19.0%) than in clay (9.1%). Positive fecal samples were 12 (31.0%) less than negative samples which were 27 (69.0%).

Table 2. Number of positive and negative samples in each sampling area

Area	Number (%)		Total (%)
	Positive	Negative	
Water samples			
River A	6 (66.7)	3 (33.3)	9 (50.0)
River B	6 (66.7)	3 (33.3)	9 (50.0)
Total	**12** (66.7)	**6** (33.3)	**18 (100)**
Soil samples			
Sandy	12 (19.0)	51 (81.0)	63(50.0)
Clay	6 (9.1)	60 (90.9)	66(50.0)
Total	**18 (14.0)**	**111 (86.0)**	**129 (100)**
Fecal samples			
Fecal samples	12 (31.0)	27 (69.0)	39 (100)
Total	**42**	**144**	**186**

Table 3. Distribution of STH species in water, soil, and fecal samples

Kind of sample	Number (%)		Total
	A. lumbricoides	*T. trichiura*	
Water samples			
River A	2 (33.3)	4 (66.67)	6
River B	2 (33.3)	4 (66.67)	6
Total	**4(33.3)**	**8 (66.7)**	**12**
Soil samples			
Sandy	7(58.3)	5(43.7)	12
Clay	1(16.7)	5(53.3)	6
Total	**8(4.4)**	**10(59.6)**	**18**
Fecal sample	4 (33.4)	8(66.6)	12
Total	**4 (33.4)**	**8(66.6)**	**12**

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Table 4. Prevalence of STH species in water, soil, and fecal samples

Type of sample	Number (%)		*Negative*	*Total*
	A. lumbricoides	***T. trichiura***		
Water samples				
River A	2 (22.3)	4 (444)	3 (33.4)	9
River B	2 (11.1)	4 (222)	3 (33.4)	9
Soil samples				
Sandy	7(11.1)	5 (7.9)	51 (81.0)	63
Clay	1(1.5)	5 (7.5)	60 (91.0)	66
Fecal samples				
Fecal samples	4(10.3)	8(20.5)	27 (69.2)	**39**
Total	**17**	**26**	**143**	**186**

Twelve (66.7%) out of 18 water samples were positive, consisted of 4 samples (22.2%) as *A.lumbricoides* which 2 (33.3) out of them distributed either in river A or river B. Eight samples (44.4%) were found containing *T.trichiura*, which 4 (66.7) was distributed either in river A or river B. Seven positive samples (58.3%) of *A. lumbricoides* were found in sandy soil and 1 (16.7%) in the clay of paddy fields. The eggs of *T.trichiura* were found in five samples (43.7%) in sandy soil and five samples (53.3%) in clay. Of the 39 faecal samples, 12 samples (31.0%) were positive, consisted of 4 samples (33.4 %) for *A.lumbricoides*, 8 samples (66.6%) for *T.trichiura*. The results of the Chi Square analysis showed that there was a relationship between STH species found microscopically in water, soil, and feces. The distribution of STH species was shown in Table 4.

DISCUSSION

The STH infection in children has received more attention than in farmers as shown by the implementation of deworming and providing albendazole treatment to school children in Indonesia (Sungkar, Ridwan, & Kusumowidagdo, 2017), even though STH can infect people in all age groups (Novianty, Dimyati, Pasaribu, & Pasaribu, 2018) including the farmers (Amoah & Stenstrom, 2018; Apsari, Arwati, & Dachlan, 2019).

The investigation of water, the soil of rice fields, and fecal samples of the farmers in Grogol Sub-district, Kediri District, which was previously suspected as transmission media of STH among the farmers, has been proved by the finding of STH species in all those samples sources. Based on examination of 18 water samples using the sedimentation method found four samples (22.2%) containing *A.lumbricoides* eggs and eight samples (44.4%) containing eggs *T.trichiura* and negative results are six samples (33.33%). These results showed that the water in the rice fields has been contaminated with STH because the water to irrigate the rice fields came from the river used for defecation by the villagers. This behavior is resulting in the biological hazard like STH that contaminated the water and soil of rice fields. The positive fecal samples collected from the farmers who work without any PPE, such as boot, gloves, and shoes, indicated the STH transmission has occurred through the water and soils where they work every day. The use of PPE was indeed important to protect the transmission of STH among the farmers and other workers who work in direct contact with soil. A study in Barito Kuala District, South Kalimantan Province, Indonesia, showed that the farmers who did not use complete PPE were more at risk of infection by helminth eggs than the farmers use complete PP (Prayitno *et al., 2017)*.

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Usually, during lunchbreak, the farmers washed their hands before and after lunch using the same water that uses to irrigating the rice fields without soap, then continue working again after lunc break. Handwashing using contaminated water without soap during a lunch break is one way of STH transmission from hand to mouth.

The different source of STH transmission has been found in Hanam Province of northern Vietnam where the infection of *A. lumbricoides* (24%) and *T. trichiura* (40%) related to the use of wastewater and excreta in agriculture (Pham-Duc *et al*., 2013). The STH transmission among vegetable farmers in Ghana related to the wastewater irrigation used to water the crops, which proved by the finding of STH positive samples collected from wastewater, soils, and stools of farmers and their family members (Amoah *et al*., 2018).

Human behavior that often pays little attention to the importance of using clean water for life contributes to the occurrence of STH infection. This can lead to a reduced balance between the population and the environment. As a result, the condition of environmental sanitation is bad, and disease transmission can occur quickly. Environmental health is closely related to the problem of lack of clean water facilities that risk to the transmission of STH. River water contaminated with worm eggs is often used for various purposes and activities such as defecation, watering vegetable plantations, bathing, and washing. Soil is the primary medium of STH transmission because their transmission cannot occur without passing the soil. The STH distribution depends on fecally contaminated environment containing STH eggs. Soil contamination, especially by *A.lumbricoides* eggs, occurs mostly in rural areas, suburban areas, and urban areas that are densely populated (Suriptiastuti, 2006).

Temperature is critical to track the STH to continue its life cycle. Each species has a different optimum temperature. For the development of *A.lumbricoides* eggs in the soil can develop into infective eggs require a temperature of 20°C-25°C, *T.trichiura* approximately 30°C and *N.americanus* require optimal temperatures between 28 ° C-32 ° C. Humidity also an essential factor for maintaining worm life. If humidity is low, *A.lumbricoides* and *T.trichiura* worm eggs will not develop properly, and worm larvae will die quickly (Bethony *et al*., 2006).

Another factor that plays a role as supporting the development and distribution of STH worms is the type and nature of soil particles. The development of *A. lumbricoides* and *T. trichiura* eggs require clay, moist, and protected from sunlight. Contrary, the larvae of hookworms require oxygen for their growth. The most suitable and beneficial type of soil for hookworm is sand, loose, humus, and protected from direct sunlight (Mabaso, Appleton, Hughes, & Gouws, 2004; Brand, 1973) Therefore, no hookworms were found in this research area, because hookworms prefer sand soil (Bethony *et al*., 2006), while the soil in this study was clay and sand mixed soil.

There were only two species of *A.lumbricoides* and *T.trichiura* found in either water, soil and feces of farmers. Chi-square test which showed a relationship between samples of water, soil, and feces of farmers with a significance value of $p = 0.000$, indicated that there was a relationship among those sources of samples. This result proves that water and soil are a medium of transmission for STH infections in farmers. The farmers who defecate in the river, feces containing STH eggs pollute the river's water then contaminate the soil. Healthy farmers can also acquire STH infection if they work in this contaminated paddy field. This chain of STH transmission will continue if there are no changes in their habit in defecating manner and must be involving the government's

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participation. The enlightenment about STH infections includes the way of infection, transmission and treatment, not defecating in the river, the importance of PPE when working in the fields, and washing hands and feet using soap and running water that is not contaminated with STH before eating. The procurement of family toilets or public toilets is also important. All that can be done if researchers or residents work together with the relevant government.

CONCLUSION

The presence of STH eggs, especially *A. lumbricoides* and *T. trichiura* in the water, soil, and fecal samples of the farmers, proved the chain of transmission among those three media. By enlightenment about STH infection, transmission and administration, and the importance of using PEE during working in the field, followed by the treatment of STH-infected villagers, will reduce or break the transmission.

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Research Article

Zero maternal death with KECUBUNG featured in SATE Krembung application (integrated queue system) in Krembung Community Health Center in 2017 until 2018

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ABSTRACT

There are some special programs in Maternal and Child Health that have not yet been reached and have a bad trend like the number of Low Birth Weight (LBW), cases of stillbirth, and babies died. There was a congenital defect in babies, increased obstetric complications, and there is one case of maternal death. There were neo-complications in infants and babies. The problem that often results in the death of pregnant women is the lack of early detection at first-level facilities in the Krembung Health center. Early detection and treatment or planning in cases of high-risk pregnant women is lacking, and then we created a SATE Krembung application in 2017. Making SATE Krembung application, socializing to the community, socializing the features of KECUBUNG to report mothers at high risk, and bringing services closer to the community and to evaluate reports from residents. Activities are collected, analyzed, and processed into mature data. The number of people activities collected during the collection of data during this research from 500 users of application from 2017 until 2018. There was a decrease in maternal mortality rates to zero patients in 2017 and 2018. The use of SATE Krembung is quite effective in reducing maternal mortality to zero patients in the Krembung health center work area, but this must be improved with the development of applications. The application of SATE Krembung with KECUBUNG feature can reduce maternal mortality by empowering health cadres and the community to be aware of the environmental conditions surrounding them.

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INTRODUCTION

The background of this innovation is because there are some special programs in Mother-Child Health (Kesehatan Ibu dan Anak or KIA and nutrition that have not yet been reached and have a bad trend, namely the number of LBW in 2015 as many as six babies, 2016 LBW as many as 13 babies. Cases of stillbirth in 2015 as many as two babies and babies died in 2016 as many as one baby. 2015 congenital defects of 5 babies and birth defects in 2016 were four babies. Obstetric complications in 2015 were 91 mothers (35.71%), while 2016 increased to 168 mothers (65.73%). In 2015 maternal deaths of 1 person and 2016 2 people. Neo-complications in 2015 were 27 infants (2.41%), and in 2016 64 infants (5.71%), these incidents of total births in 2015 were 1158, and in 2016 was 1186 (Puskesmas Krembung, 2018). Based on the above data, the Krembung community health center must make an innovation program to save the mother and the baby she is carrying.

The existing solutions have been emphasized more on educating pregnant women and health workers only while husbands and communities still have not received enough education regarding the handling of danger signs for pregnant women. Community factors and husbands also influence the number of maternal deaths due to environmental factors that are less careful and care about the condition of the mother. The health culture of the Indonesian people themselves is still very minimal, as evidenced by data from the Indonesian Health Office that only 1 out of 5 husbands in Indonesia is categorized as SIAGA (Siap Antar Jaga or Ready-Deliver-Take care). Also, public attention to the health of pregnant women is still low in Indonesia, especially in the Krembung health center area (Kementerian Kesehatan RI, 2014)

According to UNICEF, there are five ways to reduce maternal mortality, which means : 1. Educate, means to educate pregnant women husbands and the community. 2. Respect means increasing awareness of the surrounding community to pregnant women. 3. Empower means empowering the community, family, and husband, in particular, to pay more attention to pregnant women. 4. Invest, means preparing health services for pregnant women including preparation for childbirth. 5. Protect is to protect pregnant women from violence and abuse. (Kementerian Kesehatan RI, 2018)

Therefore, a new breakthrough is needed to provide education about the health of pregnant women to the community more communicatively and innovatively. The community and family can receive information well, and facilitate the provision of assistance in emergencies. The application can be used by residents to report high-risk pregnant women. One of them is using the SATE Krembung application that was triggered by one of the best health workers in Sidoarjo Regency (Jawapos, 2018)

The advancement of information technology as part of inseparable globalization from modern society brings a huge demand for society to the government as a service provider to be more open, more effective and efficient in carrying out their government duties and provide access to information, especially information about government. The government must be encouraged to implement a good governance concept. The government must adapt to technological developments so as not to be left behind. Hage and Powers mentioned that one feature that stands out in this era of advancement in communication and information technology is the use of computer technology. E-government, to create communication between the government, the community, the business world, and other interested parties to provide services quickly and precisely. In 2003, the government issued Presidential

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Instruction Number 3 of 2003 as a further e f ort to support the implementation of e-government to improve the quality of services to the community, especially information services, and create good governance. Because of this basis, the formation of the SATE Krembung application is very much needed as an e f ort to help the government in reducing mortality by involving the wider community. (Watulingas and Tangkuman, 2018) (Atthahara, 2018) (Reformasi and Republik, 2014) (Hardiansyah, 2018)

Methods:

Making applications with BLUD (Badan Layanan Umum Daerah / regional public service agency) funds and submitting permits to the Occupation and Civil Registry Service (Dinas Kependudukan dan Catatan Sipil), as well as managing NIK (Nomor Induk Kependudukan / Citizen number) usage permits to the Ministry of Home A f airs (Kementrian Dalam Negeri / Kemendagri) to be able to use the NIK on the application. The next step is to launch the application to the Google Play Store.

Figure 1. Display of the application on the google apps store

Patients who are in the Krembung community health center, smartphone users, are given information about the SATE Krembung application along with its features and the application usage process or how to operate it. The process of dissemination is carried out through many media, including promotional videos and promotional videos via television for promotions in the waiting room, website of the public health center Youtube, Instagram, Facebook, and WA groups in each village and

Figure 2. Display of Krembung SATE application

After the patient downloads, the display will appear as above. After that, the o f cers routinely socialized at the mother's meeting and the activities of the P4K activists in the village regarding the KECUBUNG program and the features found in the SATEKrembung application.

Figure 3. Display of KECUBUNG Features

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Figure 4. Display menu report pregnant women with high risk

After the patient downloads the SATE Krembung application in Google Play Store, the patient can use or click the KECUBUNG feature. After clicking on the KECUBUNG feature, there will be an explanation of the dangers of pregnancy. In the KECUBUNG feature, there will be a LAPOR BUMIL RISTI (High-risk pregnancy report) facility that can be clicked on, and the display will appear as shown below.

After that, the patient can report the name of the pregnant woman with high risk, complete address, and cellphone number of the patient or family that can be contacted. There will be a notification to the officers at the Krembung community health center, and the next day, a home visit and examination of the patient will be carried out as a follow-up to the residents' report. Patients who have this risk will be monitored for disease and educate their families and their environment and pay more attention to giving birth.

All of the data according to SATE Krembung (KECUBUNG feature) is collected, such as low birth weight, Maternal death, infant death, obstetric complication, and neonatal complication. All data will be compared during the implementation of the application.

RESULTS

The following is a graph obtained after the launch and implementation of the SATE Krembung application with the KECUBUNG program. With the use of this application,500 users, there has been a decrease in maternal mortality in the Krembung community health center in Sidoarjo Regency since 2017 and 2018. However, the number of cases such as low birth weight, obstetric complications, infant mortality, and neonatal complication increased from the year before the SATE Krembung application; the KECUBUNG feature was formed.

Table 1. The success of the SATE KrembungProgram through the KECUBUNG program

	2015	2016	2017	2018
Low Birth Weight	6	13	20	17
Maternal Death	1	2	0	0
Infant Death	2	1	7	4
Obstetric Complication	91	168	210	207
Neonatal Complication	27	64	77	85

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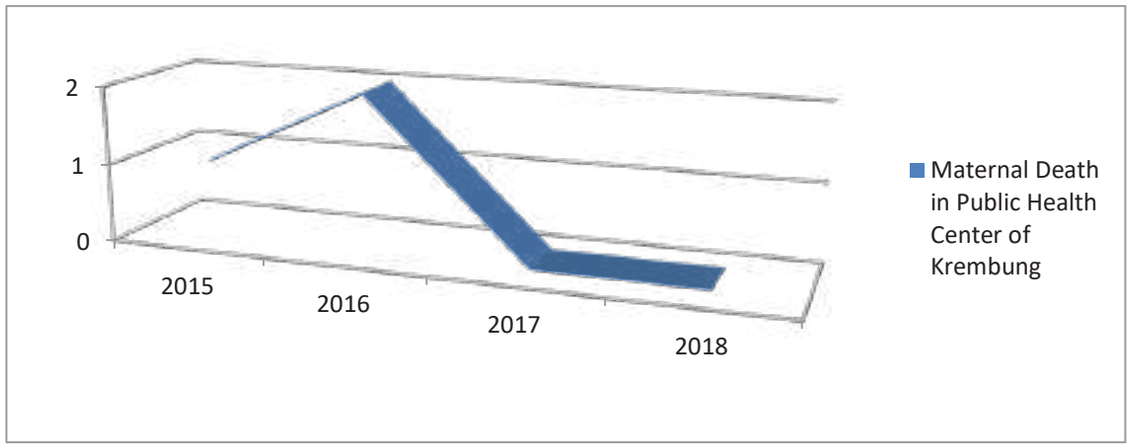

Figure 5. The decrease in Maternal Death in Krembung community health center

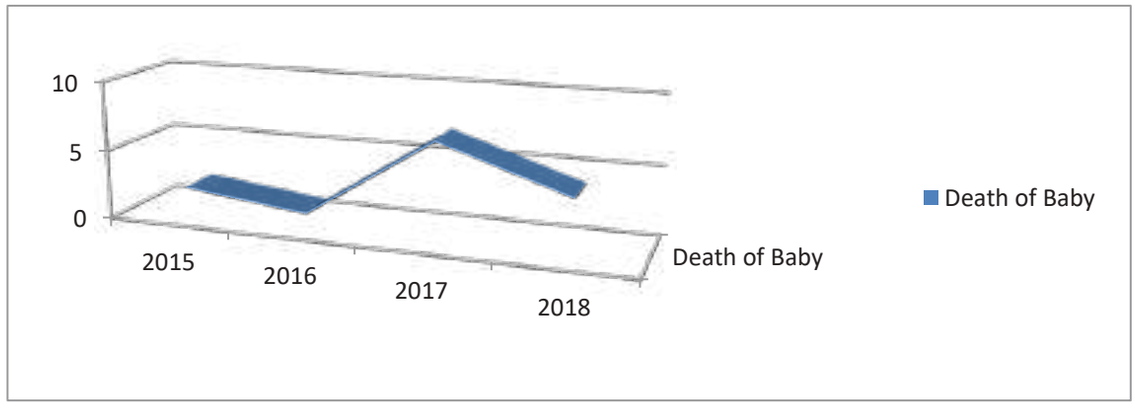

Figure 6. Death of Baby in Krembung

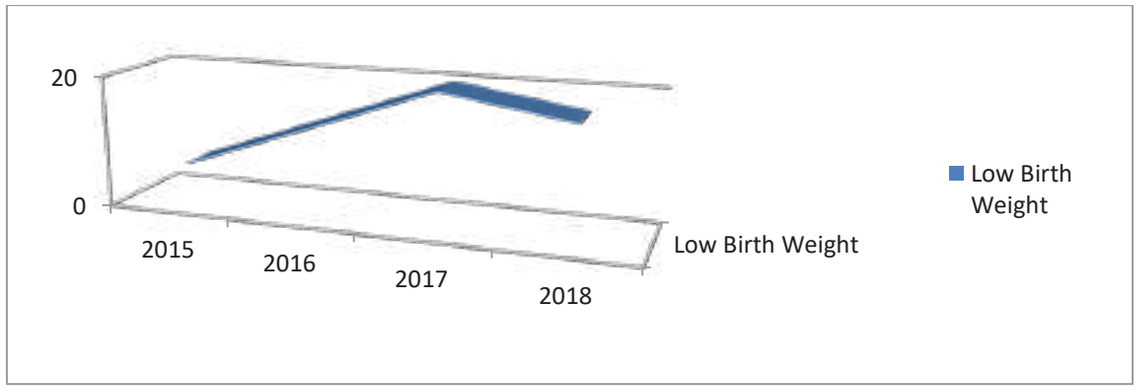

Figure 7. Low Birth Weight in Krembung

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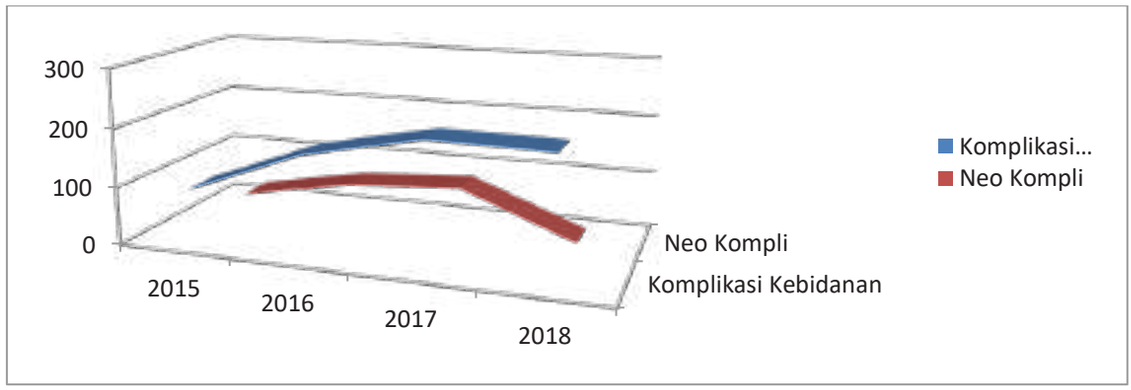

Figure 8. Obstetric and Gynecology Complication and Neonatal complication

From the table above, there are 20 low birth weight babies because there are 4 Gemelli births, and in 2018 there are 6 Gemelli births and the other low birth weight due to preeclampsia. From the graph above, it was found that the maternal mortality rate decreased compared to 2015 and 2016, where cases of death were high in Sidoarjo. With this case being zero, the Krembung community health center does not contribute to the maternal mortality rate in the Sidoarjo Regency. The infant mortality rate in the Krembung community health center area in 2017 had risen during the implementation of the SATE Krembung application, but after evaluating the implementation of the SATE Krembung application, in 2018, the infant mortality rate decreased compared to 2017.

There is an increase in the low birth weight case in the Krembung community health center area since the implementation of the SATE Krembung application with the KECUBUNG feature. However, this increase has several justifable causes.

From the graph above, it was found that the incidence of obstetric complications was found with increasing numbers each year, while the cases of neo complications were found to decrease with the implementation of the application and socialization to the community.

DISCUSSION

The mobile health apps industry growth had greatly changed the care services model. (Lu et al., 2018) (Ernsting et al., 2017) Health mobile applications have a function to offer people to access medical service easily (Lamprinos et al., 2014)

The purpose of making the SATE Krembung application is to help reduce the mortality rate of pregnant women in the work area of Krembung community health center, Sidoarjo. By using smartphone applications that can provide education about pregnancy, and how to recognize danger signs for pregnant women. SATE Krembung is also can use to report high-risk pregnancy cases; the community cares more and can help pregnant women in an emergency in their surroundings.

Based on the data above, the use of SATE Krembung with the KECUBUNG feature can be used to increase the number of case finding from high-risk cases in pregnancy. This can be done by socializing and increasing understanding of the problem of any complications and symptoms that can arise in pregnant women in their families, husbands, neighbors, cadres, and all residents in the Krembung community health center area.

After that, all residents in the Krembung community health center area were asked to download and can use the application in a

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responsible manner, such as reporting cases of high-risk pregnant women. All residents can report someone who is suspected of having a high risk of pregnancy by disseminating a Program Perencanaan Persalinan dan Pencegahan Komplikasi (P4K) card or Childbirth Planning Program and Complication Prevention that is attached to the home of a pregnant woman (Permenkes No 97 Tahun 2014). With this, it is expected that reports of patients with high-risk pregnant women will be obtained early and quickly intervened. After receiving a report, the village midwife will visit, and the next day the patient will be advised to go to the health center to get further medical treatment and be given education to the husband and family about the dangers that can occur along with symptoms or signs.

With the use of this application, there has been a decrease in maternal mortality in the Krembung community health center in Sidoarjo Regency since 2017 and 2018. However, the number of cases such as low birth weight, obstetric complications, infant mortality, and neonatal complication increased from the year before the SATE krembung application was formed (KECUBUNG feature).

This application can help reduce the number of maternal mortality in Sidoarjo regency. In 2017 the number of deaths in the Sidoarjo Regency was 30 pregnant women, while in 2018, it fell to 23 pregnant women. Even so, Sidoarjo Regency is still included in the top 10 city districts in East Java, with the highest number of maternal deaths. In 2017, 90% of deaths occurred in hospitals and 40% of mothers who have passed twice the referral relay (Dinas Kesehatan Kabupaten Sidoarjo, 2018). Therefore, it is expected that the sustainability of this application will be able to reduce the incidence.

Maternal mortality in Sidoarjo 2017 is caused by bleeding (40%), severe preeclampsia/eclampsia (33%), infection (7%) and other causes (20%). The coverage of ANC K1 in 2017 reached 100% and K4 at 99.63%, and postpartum visits had reached 97.66 percent, but the number of maternal deaths was still in the high range (Dinas Kesehatan Kabupaten Sidoarjo, 2018). Therefore, researchers feel the importance of applications with a reporting model like this can be developed and carried out a merger with several other applications owned by Sidoarjo regency so that the handling of critical cases above will be faster and more comprehensive with obey to patients satisfaction. (Anderson, Barbara, and Feldman, 2007) (Yu, Xiaohui, 2014).

With the use of this application, there is an increase in the number of obstetric complication cases in 2017 as much as 210, and in 2018 by 207, the increase is not only through reports from the SATE Krembung application, but some patients can also report by Whats Apps, Short Message Services (SMS). This increase in numbers through application reporting can be considered a good achievement because it can reveal the phenomenon of the iceberg that has been hidden and appears only when there is a maternal death. (Iribarren et al., 2016)

The neonatal complication in 2017 is 77, and in 2018 is 85. Low birth weight in 2017 increased by 20 and 2018 by 17 patients. From the explanation above, there are 20 low birth weight babies because there are 4 Gemelli births and in 2018, there are 6 Gemelli births and the other low birth weight due to preeclampsia. This shows that using the application can reduce infant mortality due to cases of Preeclampsia/ eclampsia by 30%. With this result, we can use this application to reduce maternal mortality (Hasan et al., 2017)

With the use of this application, the reduction in maternal mortality in 2017 and 2018 to zero death, this could indicate that involving all residents to detect high-risk pregnancies would reduce maternal mortality from 2015 and 2016 by 6 and 13 maternal deaths.

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Also, it is expected that the community will better understand preventive measures (prevention) so that pregnancy complications do not occur, but when pregnancy complications occur, the community and husband can provide help as soon as possible. Therefore the support from the government is expected for the development of applications and the sustainability of this application to help the government in reducing maternal and infant mortality.

CONCLUSION

The reduction in maternal mortality in the Krembung Subdistrict area can be reduced by early detection of emergency cases in pregnancy by using the KECUBUNG feature on the SATE Krembung Application.SATE Krembung application can be used as a tool to improve community empowerment in reducing maternal mortality by media reporting of emergency cases by address. The number of downloaders must be increased to all residents in the Krembung community health center area so that the application can run effectively and more reports so that early treatment can be given to high-risk pregnant women.

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Research Article

Sensitivity and specificity comparison between *Apfel, Koivuranta,* and Sinclair score as *PONV* predictor in post general anesthesia patient

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ABSTRACT

Post Operative Nausea Vomiting (PONV) are the two most common and unpleasant side effects after anesthesia and surgery. Without proper prophylactic administration, the PONV incidence is currently around 20% -30% in normal patients and 70% in high-risk patients (Butterworth et al., 2013). Recently, many PONV predictor scores have been used to determine the PONV severity and prophylactic administration. Objective: To compare the scores of Apfel, Koivuranta, and Sinclair as predictors of PONV in adult patients after general anesthesia at RSUD Dr. Soetomo. A cross-sectional study design conducted in 100 patients who underwent elective surgery under general anesthesia at RSUD Dr. Soetomo Surabaya. Patients who meet the criteria will be recorded in the clinical research form and being followed to evaluate the assessment using Apfel, Koivuranta, and Sinclair scores when the patient is in the recovery room and the ward. A diagnostic test is performed to assess the accuracy between these scores. In this study, the prevalence of PONV after general anesthesia in elective surgery at GBPT RSUD Dr Soetomo Surabaya is 26%. The Apfel score obtained has a sensitivity value of 79.5%, a specificity of 45.9% with an AUC value of 0.701. The Koivuranta score has a sensitivity value of 96.2%, a specificity of 27% with an AUC value of 0.628. The Sinclair score has a sensitivity value of 73.1%, a specificity of 48.6% with an AUC value of 0.619. Apfel's score is more accurate PONV prediction score and has a simpler score determination variable.

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INTRODUCTION

Post-Operative Nausea Vomiting (PONV) are the two most common and unpleasant side effects after anesthesia and surgery. Without prophylactic administration, the overall incidence of PONV is currently around 20%-30% and in patients at high-risk PONV conditions, this incidence is as high as 70% (Butterworth, J.F., Mackey, D.C., Wasnick, J.D., Morgan, G.E., Mikhail, M.S., Morgan, G.E, 2018).

PONV condition is a simple problem yet often complained by the patient rather than post-operative pain (Tramèr & Fuchs-Buder, 1999). PONV would affect to worse operation's outcome and increase the risk of aspiration (Butterworth, J.F., Mackey, D.C., Wasnick, J.D., Morgan, G.E., Mikhail, M.S., Morgan, G.E, 2018). These effects may increase the morbidity; prolong the hospitalized period, and increase the hospitalized cost. On the other hand, these effects may cause a patient's stress and discomfort (Habib, Chen, Taguchi, Henry Hu, & Gan, 2006).

Recently, PONV predictor score has been used to classify patients based on their PONV risk. This classification would be useful for the clinician to give PONV prophylactic to the patient. Some of these PONV predictor scores are Apfel score, Koivuranta score, Sinclair score, Palazzo score, Gan score, and Scholz score. Unfortunately, there was no literature that compares these scores to know which predictive score can be used as a gold standard in predicting PONV based on its' accuracy. Because of that, the researcher was interested in experimenting with comparing the sensitivity and specificity of Apfel, Koivuranta, and Sinclair score as PONV predictor in post general anesthesia patient in RSUD Dr Soetomo Surabaya, Indonesia. The researcher hoped that the outcome of this study could find the most perfect PONV predictor score to be used in the daily assessment of post general anesthesia patients, especially in RSUD Dr Soetomo Surabaya, Indonesia.

METHODS

This study was observational descriptive with a cross-sectional design study. This study has been ethically approved by Komite Etik Penelitian Kesehatan RSUD Dr. Soetomo Surabaya under the ethical clearance certificate number of 0622/KEPK/Ix/2018. The sample of this study was 100 patients who have undergone an elective operation with general anesthesia in RSUD Dr. Soetomo Surabaya, Indonesia during September – October 2018 that met the inclusion and exclusion criteria. The inclusion criteria of this study were: (1) patient with age of 17 – 65 years old; (2) ASA (American Society of Anesthesiologists) Physical Status Score of 1 – 2; (3) patient with elective surgery in GBPT RSUD Dr. Soetomo Surabaya, Indonesia; (4) the general anesthesia was done with isofurane inhalation anesthesia. Meanwhile, the exclusion criteria of this study were: (1) patient with antiemetic drugs during the operation (perioperative); (2) patient with high intracranial pressure; (3) patient with pregnancy; (4) patient with TIVA (Total Intra-Venous Anesthesia) general anesthesia procedure; and (5) patient who refused to be included in this study.

The patient that met the criteria were collected as a study's subject with random sampling. These subjects were interviewed to assess the PONV predictor score. The PONV predictor score used were Apfel score, Kovuiranta score, and Sinclair score that were recorded in the clinical research form. All of the study's subjects were fasted for 8 hours before the operation and received isofurane inhalation and O2 as a general anesthesia procedure during the operation. After the operation, the subjects were observed in the recovery room until the subject gained an Aldrete score of ≥9. When the

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subjects had an Aldrete score of ≥9, the subjects were moved to the inpatient room.

The PONV predictor score was assessed by anesthesiology residents who were in charged of pain and recovery room rotation in 24 hours post-operative. The subjects were classified into PONV if there were vomiting, nausea, and retching in 24 hours. If the subjects experienced the PONV symptoms above, the management given were maintained the airway, tilt the patient's head, give ondansetron 4mg or metoclopramide 10mg as pharmacotherapy, and maintain the hydration state.

The data collected then being analyzed with SPSS software. The descriptive data valued with their frequency, average, and standard deviation. The significance limit was 5% and a confidence interval was 95%. The analytic data were analyzed to find the sensitivity, specificity, and AUC of every score.

RESULTS

100 patients that became the subject of this study consisted of 53 males and 47 females. The characteristic of the subject was described in table 1.

The type of operation undergone by the subjects were ophthalmology operation 15 patients (15%), urology operation 15 patients (15%), ENT (ear, nose, and throat) operation 14 patients (14%), orthopedic operation 11 patients (11%), oncology operation 8 patients (8%), digestive operation 8 patients (8%), head and neck surgery operation 8 patients (8%), plastic surgery operation 8 patients (8%), oral surgery operation 7 patients (7%), and gynecology operation 6 orang (6%).

From this study, 26 patients experienced PONV. 7 (7%) patients among them had nausea, and 19 (19%) patients among them had vomiting. The highest PONV incidence was happened to head and neck surgery patients as many as 4 patients (15%) and digestive patients as many as 4 patients (15%). The incidence of PONV based on gender was 12 patients male and 14 patients female.

Table 1. the characteristic of subjects

	Amount(%)	Mean±SD
Gender		
Male	53 (53)	-
Female	47 (47)	-
Smoking status		-
Not smoking	77 (77)	-
Smoking	23 (23)	
ASA score		
I	25 (25)	-
II	75 (75)	-
Age		
(17-65 years old)	-	43.30±14.046
Body mass		
(40-90 kg)	-	59.38±10.766
History		
Motion Sickness	5 (5)	-
PONV	3 (3)	-

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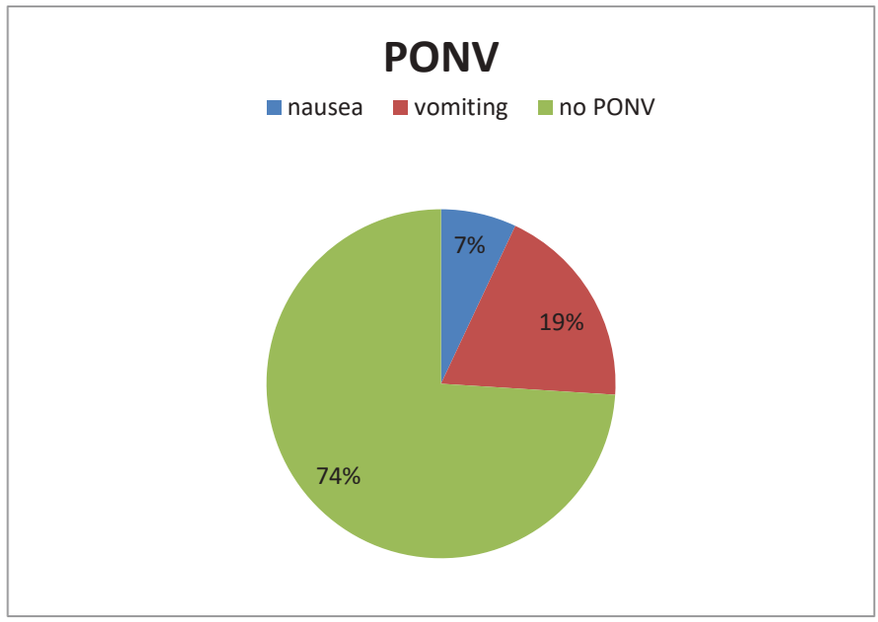

Graphic 1. The frequency of PONV in subjects

Table 2. the frequency of PONV based on the type of operation

Type of operation	Amount	PONV	No PONV
Ophthalmology	15	1 (6.7%)	14 (93.3)
Urology	15	3 (20%)	12 (80%)
ENT	14	2 (14.3%)	12 (85.7%)
Orthopaedic	11	3 (27.3%)	8 (72.7%)
Digestive	8	4 (50%)	4 (50%)
Plastic surgery	8	3 (37.5%)	5 (62.5%)
Oncology	8	3 (37.5%)	5 (62.5%)
Head and neck surgery	8	4 (50%)	4 (50%)
Oral surgery	7	2 (28.6%)	5 (71.4%)
Gynecology	6	1 (16.7%)	5 (83.3%)

The analysis result of sensitivity and specifcity of Apfel score were described by fgure 1.

Figure 1 shows that the sensitivity of the Apfel score was 79.5%, the specifcity was 45.9%, and the AUC score was 0.701 with the cutof point of >1.

From the ROC curve (Figure 2), the Koivuranta score has a sensitivity of 96.2%, the specifcity of 27%, and AUC 0.6 with the cutof point of >1.

From the ROC curve (Figure 3), the Sinclair score has a sensitivity of 73.1%, the specifcity of 48.6%, and AUC 0.619 with a cutof point of >4.

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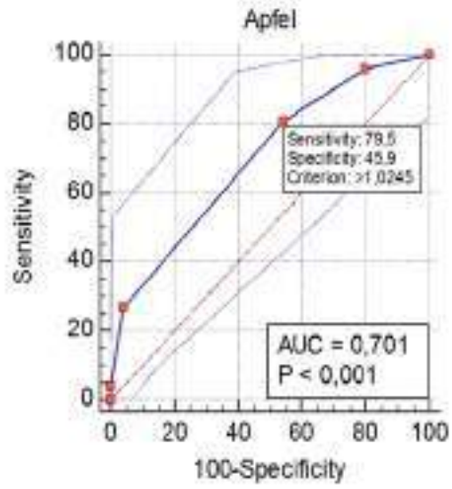

Figure 1. the ROC curve of Apfel score

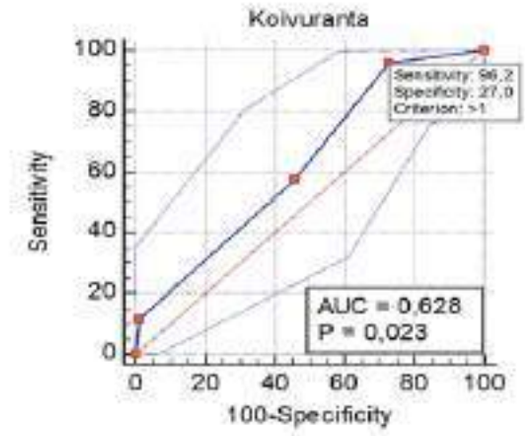

Figure 2. ROC curve of Koivuranta score

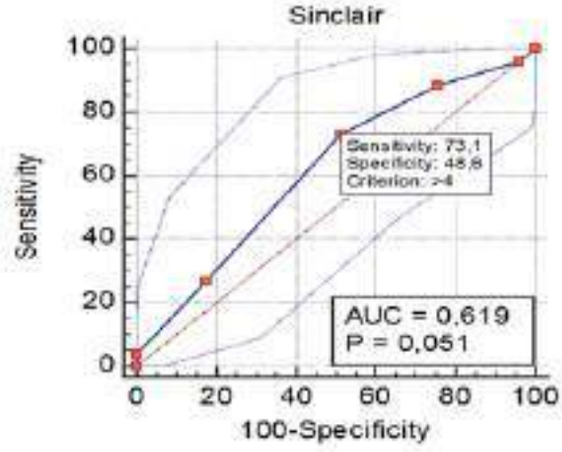

Figure 3. ROC curve of Sinclair score

Table 3. the diagnostic result based on the ROC curve of Apfel, Koivuranta, and Sinclair score

	Sensitivity	Specificity	AUC	p-value
Apfel	79.5%	45.9%	0.701	< 0,001
Koivuranta	95.2%	27%	0.628	= 0,023
Sinclair	73.1%	48.6%	0.619	= 0,051

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DISCUSSION

Recently, PONV predictive score has been used to lower the risk or to prevent the incidence of PONV. With this predictive score, the clinicians could classify the patients based on the PONV risk and quickly decide which patient, the PONV prophylactic should be given. The prophylactic of PONV is only given to those with the high-risk result of the predictive score because the PONV prophylactic given to a patient with low risk of PONV does not have a therapeutic effect (Apfel, Läärä, Koivuranta, Greim, & Roewer, 1999).

Apfel score identified the PONV risk with 4 indicators; women (1), PONV or motion sickness history (1), no smoking (1), and the usage of postoperative opioids inpatient (1). Every point increased on the Apfel score will increase the PONV possibility to 18% – 22%. The patient with Apfel score of 0 – 1 identified as low PONV risk, score 2 as moderate PONV risk, and score 3 – 4 as high PONV risk (Christian C. Apfel et al., 1999).

On the other hand, the Koivuranta score predicted the risk of PONV incidence using 5 criteria; women (1), no smoking (1), PONV history (1), motion sickness history (1), and the operation duration > 60 minutes (1). The patient who gets a score of 0 – 1 identified as low PONV risk, score 2 – 3 as medium PONV risk, and score of 4 – 5 as high PONV risk (Koivuranta, Läärä, Snåre, & Alahuhta, 1997).

Last but not least, Sinclair scores use 7 indicators to predict PONV risk on the patient. These indicators are age < 50 years old (1), women (1), no smoking (1), PONV history (1), motion sickness history (1), the type of operation (ENT, ophthalmology, plastic, abdomen, gynecology, and orthopedic especially the shoulder and knee operation) (1), general anesthesia (1), and the anesthesia duration > 30 minutes. The patient who gets Sinclair score of 0 – 2 identified as low PONV risk, score of 3 – 5 as medium PONV risk, and score of 6 – 7 as high PONV risk (Sinclair, Chung, & Mezei, 1999).

From this study, the incidence of PONV was 26% compared to the late study, where the incidences of PONV were around 20%-30% (Christian C. Apfel et al., 1999). Based on the comparison above, the incidence of PONV in RSUD Dr. Soetomo was still on a normal average.

This study consisted of 53 male patients and 47 female patients with PONV incidences based on gender were 11 PONV incidences on male and 15 PONV incidences of the female. This result showed that female have a 1.8 times higher risk of PONV than male does. The same result also was written by Apfel et al. (2012) that female (gender) is one of the strong predictors of PONV. The study before found that the risk of PONV increases 2.6 times higher in females than in the male (C.C. Apfel, Kranke, Eberhart, Roos, & Roewer, 2002). Even though the mechanism of higher PONV incidences in the female has not able to be explained.

The highest number of operation type that found in this study was ophthalmology operation and urology operation. Nevertheless, the highest incidences of PONV in this study were digestive operation and head and neck surgery operation, with the same amount of 4 PONV incidences each. The treatment done during the digestive operation stimulated the release of substance P and serotonin that led to vomiting response (C.C. Apfel et al., 2012). On the other hand, during the head and neck surgery operation, the passive blood flow from the oral cavity and nasal cavity to the stomach triggered PONV (Erkalp et al., 2014). Based on Sinclair's study (about Sinclair score), the type of operation is included in one of the predictor scores of PONV incidence. Meanwhile, based

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on Apfel's study, the type of operation is not included as the predictor score of PONV as many of the types of operation led to bias score.

The accuracy of PONV score was tested using the Area Under the Curve (AUC) calculation and Receiver Operating Characteristic (ROC) curve method. This curve is the incision between the true positive rate (sensitivity) and the false-positive rate (specifcity) from the score tested. The area with a score of 1.0 or 100% identifed as the perfect sensitivity and specifcity (Dahlan, 2014).

The diagnostic test of this study found that the sensitivity of Apfel, Koivuranta, and Sinclair score consecutively was 79.5%, 96.2%, and 73.1%. The specifcity of Apfel, Koivuranta, and Sinclair score consecutively was 45.9%, 27% and 48.6%. While, based on the ROC curve, the AUC of Apfel, Koivuranta, and Sinclair score consecutively were 0.701, 0.628, and 0.619.

From the results above, the most sensitive PONV predictive score was the Koivuranta score with 96.2% and the most specifc PONV predictive score was Sinclair score with 48.6%. However, based on the AUC, score Apfel (AUC 0.701) was the best PONV predictive score compared with the Koivuranta dan Sinclair score. From the ROC curve, it concluded that the Apfel score was better than Koivuranta and Sinclair score. Even though, from this study, the best AUC score was less than 0.8 which interpreted that Apfel, Kaoivuranta, and Sinclair score have a moderate level of trust to be used as PONV predictive score.

From another study, Apfel et al. (2002) found that the ROC of the Apfel score is higher than the Koivuranta score (0,68 dan 0,66). Another study was done by Pierre et al. (2002) (Pierre, Benais, & Pouymayou, 2002) also showed the signifcant difference between Apfel and Sinclair score, where Apfel has better accuracy than Sinclair (0,71 dan 0,64). These two studies support this study result where Apfel has better specifcity and sensitivity to be used as PONV predictive score.

Another result from this study was the cutof point for each PONV predictor score from the ROC curve. This cutof point is useful as a guide to classify whether a patient needs an antiemetic as PONV prophylactic or not. The cutof point of Apfel, Koivuranta, and Sinclair score consecutively were 1 point, 1 point, and 4 points. So that, for patients who get a score higher than the cutof point, the clinicians should consider giving PONV prophylactic agents as the risk of PONV incidence is higher on this patient.

CONCLUSION

The PONV incidence of post elective operation patients with general anesthesia aged 17 – 65 years old in GBPT RSUD Dr Soetomo without prophylactic was 26%. The highest PONV incidence was found in a patient with the digestive operation and head and neck surgery operation. From this study, it is recommended to use the Apfel score, as PONV predictor score, because the Apfel score was more accurate and had a simpler determination variable than Koivuranta and Sinclair score. This study also found that the cutof point of Apfel score was 1 point, where it is suggested that the PONV prophylactic agent is given to a patient who gets more than 1 point of Apfel score. This study might not perfect, the researcher suggested a larger number of samples in the next study in order to produce more valid results of PONV's best predictor score.

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Research Article

Wild Tembelek plant (*Lantana camara*) as a potential bioactive natural product againts *Streptococcus pyogenes* in Indonesia

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Abstract

Infectious diseases are common problems in most countries. Streptococcus pyogenes is the infectious agent that causes diseases such as pharyngitis, impetigo, toxic shock syndrome, and necrotizing fasciitis. Tembelek (Lantana camara) is a wild plant that can easily be found in every ecosystem in Indonesia whether in nature or settlements and known as a plant that has an antibacterial effect but the knowledge about its potential against Streptococcus pyogenes in this past five years remain scant. The aim of this study was to determine the potentiality of Lantana camara leaves and flowers extract against Streptococcus pyogenes. In this experimental study, in vitro using Post-test Only Control Group Designed, has been done and confirmed by the Indonesian Institute of Sciences. Lantana camara leaves and flowers extracts were obtained by maceration using ethanol. The extracts were diluted into eight concentrations and their antibacterial activity against Streptococcus pyogenes was tested using the Kirby-Bauer disc then proceeded Minimum Inhibitory Concentration (MIC) test and phytochemical assay. The data processed using SPSS software version 22. The results showed that flowers extract had the most significant inhibition zone (11.85 ± 0.119 mm) compared with the leaves extract (9.54 ± 0.07 mm) at the highest tested concentration was 640 mg/ml. The MIC of both extracts was 250 mg/ml. Flavonoids, phenolic, steroids, and saponins were found in both extracts whereas, alkaloid was found only in flowers extract. In conclusion, the Tembelek plant has an antibacterial effect against Streptococcus pyogenes. Future study is needed related to its mechanism of antibacterial effect.

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INTRODUCTION

Infectious diseases are common problems in most countries. According to 2016 data from Global Burden of Disease, they caused more than 10 million deaths in the world (Hay 2016); Basic Health Research data from 2018 showed that infections were still one of illness with high morbidity and mortality rate in Indonesia (Kemenkes 2018). The aforementioned data shows that infection is still a prevalent national pandemic and needs to be managed both in preventive and curative aspects.

Various types of microbes, including normal flora, either pathogens or opportunistic pathogens, cause infections. Streptococcus pyogenes, also known as Group A Streptococcus (GAS), is part of skin microbiota that responsible for lots of illnesses found daily in the clinical world, such as pharyngitis and impetigo. It can also cause fatal illnesses such as Toxic Shock Syndrome, which has a mortality rate of 12,1% (Strom, 2017). The drug of choice (DOC) to treat GAS infections is penicillin group (Peters, 2017). The problem is, the resistance rate towards this bacteria is increasing caused by its own beta-lactamase synthesis defense system, which disables penicillin-type medications such as amoxicillin (Katzung, 2012). Resistance to macrolide (Erythromycin), Clindamycin, and Lincosamide have also been reported (Berwal, 2019; Kumar, 2017). There needs to be an alternative medication to eradicate Streptococcus pyogenes. Herbal medicine, which has bioactive products and antimicrobial effects, is a potential alternative medication that can also reduce antibiotic resistance. It is also thought that herbal medicine has a cheaper price and fewer side effects than synthetic drugs used in allopathic medicine (Hay 2016).

Tembelek (Lantana camara) is a plant that, for generations, has been used by Indonesian ancestors to treat many diseases such as itchiness, lepra, hypertension, measles, ulcer, asthma, tetanus, and rheumatic. This plant has also been known to have antibacterial potency, especially its flower and leaf (Kumar, 2012). For example, ethanol extract of its leaf can effectively halt the growth of some pathogenic bacteria, such as Staphylococcus aureus, Escherichia coli, Salmonella typhi, and Pseudomonas aeruginosa (Agrawal, 2012; Obinna, 2013); it is also proven that it has a bactericidal effect to three strains of Mycobacterium tuberculosis (Kirimuhuzya, 2009). Overall, the extracts of Lantana camara exerts a broader inhibitory activity on Gram-positive bacteria than Gram-negative bacteria (Shakya, 2016). Unfortunately, until now, there is no international publication of its bioactive product's and antibacterial qualities' effects on Streptococcus pyogenes in Indonesia. Considering the prevalence of some diseases caused by Streptococcus pyogenes infection remain high in Indonesia, there needs to be research to analyse the effects of this plant's bioactive products as an antimicrobial agent against Streptococcus pyogenes.

METHODS

This is experimental in vitro study using a Post-test Only Control Group Design. The study was conducted in two places, mainly laboratory of Madang Campus Medical College Sriwijaya University and Microbiology Unit of Palembang Health Laboratory Center. The study was conducted from September 2015 until October 2015. This study was approved by Mohamad Hoesin General Hospital ethical committee, Palembang and Medical College Sriwijaya University ethical committee, Palembang.

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Plant Extract Preparation

The test sample was wild Lantana camara leaf extract, which was determined in the Biological Botany Research Centre of Indonesian Institute of Sciences in Cibinong, Bogor. It was extracted using the maceration method. Maceration is an extractive technique that is conducted at room temperature. It consists of immersing a plant in a liquid (water, oil, alcohol, etc.) inside an airtight container, for a variable time based on the plant material and liquid used. There were 32 grams of dry leaf powder and 51 grams of fower powder which was macerated using ethanol solution with a ratio of 1:1 for 3x24 hours in the macerator; it was then fltered to let only the liquids out. The macerate was then left to develop deposits, which was then separated carefully. The deposit was then macerated once again by means of the second fltration and then separated just like before. The resulting fltrate was then evaporated using rotavapor until the remaining solvent disappeared, and a thick extract was obtained. This method was chosen because it requires only simple equipment, which made it easily replicable and applicable in a majority of Indonesian laboratories. After the ethanol extract was acquired, it was preserved in a beaker. The extract was then dried using a hairdryer to obtain the dry extract, which is going to be used in tests against Streptococcus pyogenes.

Bacterial Specimen Preparation

The standard strain of bacteria which is still sensitive to standard therapies: Streptococcus pyogenes NCIMB 13285, which were obtained from the Palembang's Centre for Health Laboratory (CHL). The bacteria were incubated in a nutrient medium, which was placed inside a 37o C incubator for 24 hours.

Antibacterial Test Preparation

This test was done using disk di fusion by the Kirby-Bauer method. Flower and leaf extract were diluted serially: 640 mg/ml, 320 mg/ml, 160 mg/ml, 80 mg/ml, 40 mg/ml, 20 mg/ml, 10 mg/ml, dan 5 mg/ml. Then, a petri dish fled with blood agar, bacteria, and the extract was incubated in a 37o C incubator for 24 hours. This test was repeated fve times.

Minimum Inhibitory Concentration (MIC) test was done using the broth dilution method. MIC test demonstrates the lowest level of antimicrobial agent that greatly inhibits growth. The bacteria were prepared by making a suspension with a turbidity of 0,5 Mc Farland. Flower and leaf extract were diluted serially: 1000 mg/ml, 500 mg/ml, 250 mg/ml, 125 mg/ml, dan 62,5 mg/ml. The positive control was 20 µg/ml amoxicillin; the negative control was Dimethyl sulfoxide (DMSO). Then, both the extract and the control were given another bacterial suspension and incubated in a 37o C incubator for 24 hours. The lowest, clearest concentration was the MIC. The experiment on each tested specimen was repeated fve times, according to Federer formula.

Phytochemical Test Preparation

Phenol

In the phytochemical screening, the fltrate was tapped to a G60 F254 silica gel plate and was rubbed with ethyl acetate: formic acid: toluene: water = 6:1,5:3:0,5. Then, it was dried and examined under visible light, UV 366 nm. It was then sprayed using FeCl3, dried, and examined under visible light, UV 366 nm. Phenolic (+) will show as blackish dark green.

Alkaloid

The sample was given 2 N sulfuric acid drops and tested using Wagner reactors. Any changes were examined after 30 minutes. Test results were deemed positive if it showed as yellowish, and there was a brown deposit post-Wagner reactor.

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Flavonoid

In the phytochemical screening, the fltrate was tapped to a G60 F254 silica gel plate and was rubbed with hexane: ethyl acetate: formic acid = 6:4:0,2. Then, it was dried and examined under visible light, UV 366 nm. It was then sprayed using sitroborat, dried, and examined under visible light, UV 366 nm. Flavonoid (+) will show as yellow.

Saponin

A small sample was separated into a test tube and was given hot water. Changes in how bubbles formed were examined; the reaction was deemed positive if the bubbles were stable for 10 minutes and didn't go away after given a drop of HCl 2 N.

Steroid and Triterpene

The results were deemed positive if there is a green ring on the steroid and purple ring on the triterpene using the Liebermann-Bucchard test.

Data Analysis

The statistical data were analyzed using SPSS Software 22nd version. Normally distributed data were analyzed using t-test study to compare the mean inhibitory zone diameters of leaf extract with fower extract. Furthermore, one-way ANOVA study was conducted to observe whether there is a signi fcant di f erence between mean inhibitory zone diameters of leaf and fower extract with a signi fcance threshold of 0.05.

RESULTS

We performed in vitro culture of a standard strain of Streptococcus pyogenes to examine the e f ect of Lantana camara extracts with the results as following:

Table 1. Inhibitory zone diameters of the Tembelek leaf (*Lantana camara*) extract against *Streptococcus pyogenes*

Concentration (mg/ml)	Inhibitory zone diameters (mm)					Mean ± SEM
	I	II	III	IV	V	
5	6	6	6	6	6	6
10	6,1	6,3	6,52	6,4	6,2	6,3 ± 0,0736
20	6,8	7	7,27	7,21	7,1	7,076 ± 0,083
40	7,4	7,6	7,63	7,74	7,5	7,574 ± 0,058
80	7,9	8	7,95	8,05	8,01	7,98 ± 0,026
160	8,3	8,2	8,22	8,32	8,2	8,25 ± 0,026
320	9,3	8,8	9	8,92	9,1	9,024 ± 0,085
640	9,8	9,5	9,44	9,4	9,55	9,54 ± 0,07
Amoxicillin	40	41,1	39,4	32,5	36,46	37,89 ± 1,55
DMSO	6	6	6	6	6	6

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Table 2. Inhibitory zone diameters of the Tembelek flower (*Lantana camara*) extract against *Streptococcus pyogenes*

Concentration (mg/ml)	Inhibitory zone diameters (mm)					Mean ± SEM
	I	II	III	IV	V	
5	6	6	6	6	6	6
10	6	6	6	6	6	6
20	6	6	6	6	6	6
40	6	6	6	6	6	6
80	6	6	6	6	6	6
160	6	6	6	6	6	6
320	6,6	7,92	7,8	7,55	7,7	7,514±0,236
640	12,2	11,18	11,5	12	11,74	11,85±0,119
Amoxicillin	34	35,1	35	33,01	35,5	34,52±0,45
DMSO	6	6	6	6	6	6

Table 3. Minimum Inhibitory Concentration (MIC) of Tembelek leaf extracts (Lantana camara)

Concentration (mg/ml)	Turbidity level
1000	-
500	+
250	+
125	++
62,5	++
Amoxicillin	-
DMSO	++

Two hundred and fifty mg/ml was the lowest concentration which inhibited bacterial growth; this concentration also had a small growth in suspension. The 125 mg/ml concentration still showed a lot of bacterial growth in suspension, which was shown on the turbidity of the tube. DMSO, which was used as a negative control, shows a lot of bacterial growth; amoxicillin had no bacterial growth in suspension.

A similar result happened to the flower extract: 250 mg/ml was the lowest concentration which inhibited bacterial growth; this concentration also had a small growth in suspension. The 125 mg/ml concentration still showed a lot of bacterial growth in suspension, which was shown on the turbidity of the tube. DMSO, which was used as a negative control, shows a lot of bacterial growth; amoxicillin, as the positive control, had no bacterial growth in suspension.

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Table 4. Minimum Inhibitory Concentration (MIC) of Tembelek flower extracts (Lantana camara)

Concentration (mg/ml)	Turbidity level
1000	-
500	-
250	+
125	++
62,5	++
Amoxicillin	-
DMSO	++

Table 5. Phytochemical Screening of Tembelek Leaf Extract (Lantana Camara)

Alk	Flv	Fn	Trp	St	Sp
-	+++	+++	-	+++	+

Table 6. Phytochemical Screening of Tembelek Flower Extract (Lantana Camara)

Alk	Flv	Fn	Trp	St	Sp
+++	++	++	-	++	+

Alk = Alkaloid, Flv = Flavonoid, Fn = Fenol, Trp = Triterpen, St = Steroid, Sp= Saponin; + weak, ++ medium, +++ strong

Phytochemical Screening

The biochemical contents of the flower and leaf extract of wild *Lantana camara* is shown in Table 5 and Table 6. In the extracts, secondary metabolites such as flavonoid, phenol, steroid, and saponin, was found. Alkaloid was found in the flower extract.

DISCUSSION

Antibacterial Activities on the Extracts

This research proved that the extracts showed antibacterial activities against Streptococcus pyogenes. This is in line with a research which found that The Lantana camara showed good activity against dermatophyte bacterial strains Streptococcus pyogenes and Staphylococcus aureus (Agrawal, 2016). The flower extract, in particular, had a more potent inhibitory effect. Even though there still less publication about its antimicrobial effect against Streptococcus pyogenes, but it is proofed that every part of the plant has different capabilities in inhibiting the bacteria's growth as shown in a study done by Mahdi P.B. et al.: the leaf extract was proven to have more potent antibacterial effect than other parts of the plant towards Salmonella typhi (Badakhshan 2009). The extract also showed its antibacterial effects towards E.coli, P.aurigenosa, and B.subtilis; it is, however, ineffective against S.aureus (Ganiewala, 2009).

In this study, the inhibitory zone diameters of both extracts are significantly different from those of amoxicillin as a positive control group. This result may be affected by the extraction technique used in this study and thus implying a limitation of this study. The maceration technique used in this research is the simplest technique and, thus, was used by the researchers. The limitation of the maceration technique used is a low absorption capability of secondary plant metabolites, resulting in a low quantity of metabolite obtained.

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The leaf extract's antibacterial activity was passively caused by the presence of secondary metabolites in the plant (Agrawal, 2012). A phytochemical test was needed to know what kinds of secondary metabolite compounds were present in the plant. The test results, using Wagner method, showed that the contents were favonoid, phenol, steroid, and saponin; other tests, using Mayer method, found that there was alkaloid in the leaf extract (Naz, 2013): this means that, in the fower extract, there were alkaloid, phenol, favonoid, steroid, and saponin.

Alkaloid is a kind of organic compound which inspired the development of antibiotics such as the quinolone-type medications. Researches to develop new antibiotics were mostly centered on it, too (Cushine, 2014; Pervaiz, 2016). Alkaloids such as Berberine and Harmane are able to insert themselves to the DNA, which aids in inhibiting bacterial growth and disturb peptidoglycan components build in the bacterial membrane (Cushine, 2014). Phenol is a secondary metabolite from the plant, which has lots of benefts for humans. Phenol's ability to eradicate bacteria cannot be understated—bacteria are even unable to build resistance towards phenol (Keman, 2018). It has an antibacterial efect because phenol is able to cause protein coagulation, which in result, causes instability in the bacteria's membrane, causing lysis (Rempe, 2017). The favonoid, in some plant types, is known to have antibacterial efects by inhibiting nucleic acids synthesis, which disrupts cytoplasm membrane's function, inhibits energy metabolism, prevents sticking, and biofm creation, inhibits porin on the cell membrane, and disrupts the changing of membrane permeability (Xie, 2015). Saponin's mechanism as an antibacterial agent is by reducing surface tension, making the cell membrane more fragile. Saponin also creates a complex compound with the cell membrane by means of a hydrogen bond to disrupt the permeability of the cell wall, causing its death (Muharrami, 2019).

CONCLUSION

Wild Tembelek (Lantana camara) has a potential antibacterial efect against Streptococcus pyogenes. The fower extract is more potent in inhibiting the bacteria's growth compared to the leaf extract. In both extracts, bioactive natural products as secondary metabolites of plants such as favonoid, phenol, steroid, and saponin can be found; alkaloid is only found in the fower extract. Considering its potential antibacterial efect and bioactive natural products, this plant, especially the fower parts, could be used to synthesize a novel alternative treatment against Streptococcus pyogenes infection in Indonesia. Future study, especially in vivo study, is needed to further examine the mechanism of the antibacterial efect and the toxicity of Wild Tembelek plant.

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Case Report

Ankle arthrodesis with cannulated screw: Case series

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ABSTRACT

Ankle osteoarthritis patients are young and lack of available long last treatment. Ankle arthrodesis remains the gold standard and is the procedure of choice for younger patients who are heavy laborers. These case series evaluate and report fve patients undergone ankle arthrodesis at RSUD Dr. Soetomo Surabaya on 2012-2016. The data were collected from patient fles, radiographs, and a recent physical examination. The outcome has been assessed with SF-36 score and clinical scoring system Ankle-Hind foot American Foot and Ankle Society. Three male patients and two female patients underwent ankle arthrodesis with cannulated screw, caused by neglected severe ankle dislocation. One patient had open dislocation. Based on SF-36 scoring, the fve patients had average score 76,7 with highest and lowest score were 95,9 and 56,7. Based on clinical score ankle-hind foot American Ankle and Foot Society, the average score was 68(51 – 88). The scoring result includes general health, physic, emotional, and social. And clinical scoring ankle-hind foot American Foot and Ankle Society evaluation includes pain, function, and alignment. It shows that there was patient that gains an almost perfect result. Patient with the lowest score also had knee osteoarthritis contralateral from the operated ankle. Early weight bearing on ankle arthrodesis with cannulated screw was the major factor caused unsatisfactory result of this patient. Ankle arthrodesis with cannulated screw has satisfactory result eventhough remain complain on one patient. Nevertheless, ankle arthrodesis with cannulated screw still has an important role in the treatment of choice on ankle reconstruction.

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INTRODUCTION

Ankle osteoarthritis is a severe problem with an increasing prevalence that handicapped patients life. About 50,000 new cases are reported annually in the United States (Saltzman *et al*., 2009). From the cadaveric study, the prevalence of grade 3 and 4 ankle arthritis was found by 18% (Weatherall et al, 2013). Trauma is the most common cause of ankle osteoarthritis, up to 70% of cases. The most common causes are ankle rotational fractures (37%), recurrent ankle instability (14.6%), and history of sprains with persistent pain (13.7%). Primary osteoarthritis is only found in 7.2% of cases (Saltzman *et al.*, 2009).

Ankle osteoarthritis is unique compared to the hip and knee joints. Patients have a younger average age and therapy that can last for a long time has not been established yet. In the late stages, ankle osteoarthritis can cause joint deformity, disability, and reduced income. This can have an impact on the patient's quality of life.

In the case of post-traumatic ankle osteoarthritis, the choice of non-operative treatment includes NSAIDs, stick use, orthotics, orthosis, and injections including corticosteroids, hyaluronic acid, and platelet-rich plasma. While the choice of operative treatment includes joint surface reconstruction with allografts, arthroscopic debridement and osteophytic resection, joint distraction arthroplasty, supramaleolar osteotomy, total joint replacement, and fusion of ankle joints. Ankle joint fusion is still the gold standard for the management of ankle osteoarthritis, especially at a young age who are still working. Joint replacement is better used in older patients with not too many activities (Weatherall *et al.*, 2013).

In the current era, where the new interest is more towards total ankle joint replacement, joint fusion still has an important role and is widely used as an alternative reconstruction (Tenenbaum *et al.*, 2014). A fusion of the ankle joint, which was initially used as surgical therapy in cases of ankle joint tuberculosis, continues to play a role in patients with functional disorders of the ankle joint by various reasons (*Abidi et al.*, 2000).

Despite concerns about loss of movement from the ankle and subtalar joint, this combination of fusion of the two joints is still indicated in cases of severe bone loss, severe deformity, and advanced arthritis. Tibiotalocalcaneal joint fusion is still considered clinically successful in the treatment of advanced arthritis and/or severe deformity in the tibiotalar and subtalar joints. Although there are several surgical techniques for the fusion of tibiotalocalcaneal joints, the aim of all of these is to relieve pain and stabilize biomechanical plantigrade positions of the ankle and soles of the feet (Alfahd *et al.*, 2005).

The fusion of cannulated screw joints has high union numbers, minimal complications, better comfort for patients, and more simple surgical techniques. This can also reduce the need for additional surgery and extensive post-operative rehabilitation (Tenenbaum et *al*., 2014). These thoughts encourage us to evaluate patients undergoing cannulated screw fusion surgery at Dr. Soetomo Hospital Surabaya.

CASE REPORT

This case series evaluated 5 patients who had undergone ankle arthrodesis procedure at Dr. Seotomo Hospital Surabaya in 2012-2016. Data was collected through medical records, physical examinations, and radiography. The results were measured by the SF-36 scoring and the Ankle-Hind Foot American Foot and Ankle Society clinical scoring system. This study included three male and two female patients who had undergone cannulated screw ankle arthrodesis due to severe ankle dislocation. One patient with an open dislocation.

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Patient 1

A 61-year-old male patient with pain and bleeding in the right ankle after an accident. The patient was riding a motorbike and hit by a motorcycle from the opposite direction, 5 hours before arriving at the emergency unit. The patient is treated as fracture and dislocation of the right ankle joint with open fractures of the medial malleolus, lateral malleolus, and calcaneus. The patient also suffered a total rupture of the right extensor halucis longus and the right extensor digitorum longus.

Patients underwent emergency surgery for the debridement and application of external fixation at the emergency department of RSUD Dr. Soetomo on May 18, 2014. Patients underwent a post-operative follow-up examination on 1-day postoperative (Figure 2.A-C). Two weeks after, the patient underwent a follow-up examination dated June 3, 2014. (Figure 2.D) On three months postoperative, the patient underwent a follow-up examination dated August 8, 2014. (Figure 2.E) On examination, a plain photo of the ankle was found a union in the malleolus and fbula. External removal of trans ankle fxation was carried out on November 18, 2014. At six months post-externally fxation of trans-ankle, a plain photo of the ankle had been found with union of the malleolus and fbula. (Figure 2.F) On December 4th 2014, right ankle arthrodesis was performed. On 7 months postoperative examination, a patient's plain ankle photo had not shown any union in the ankle joint. (Figure 2.G) At present patients still complain of pain in the ankle, especially when walking and decreasing with rest. The patient cannot return to work as before the incident.

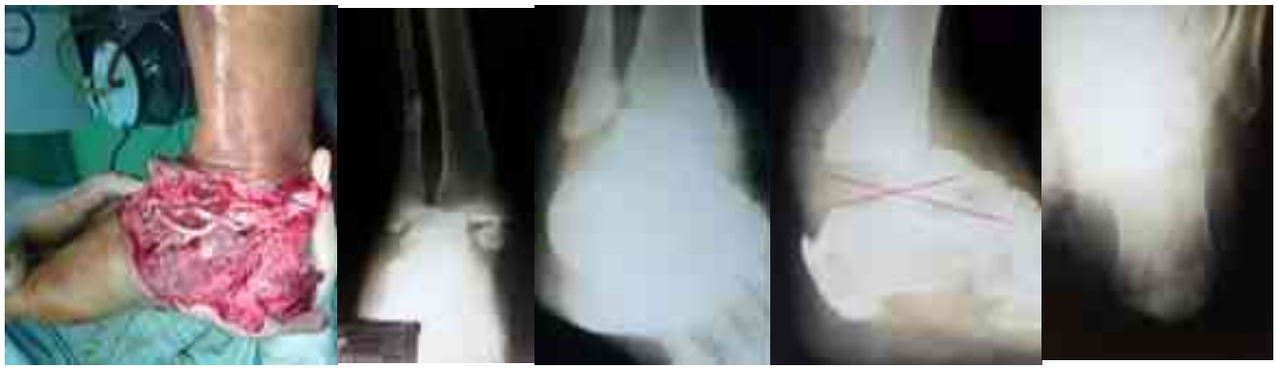

Figure 1. Pre-operative clinical and radiological

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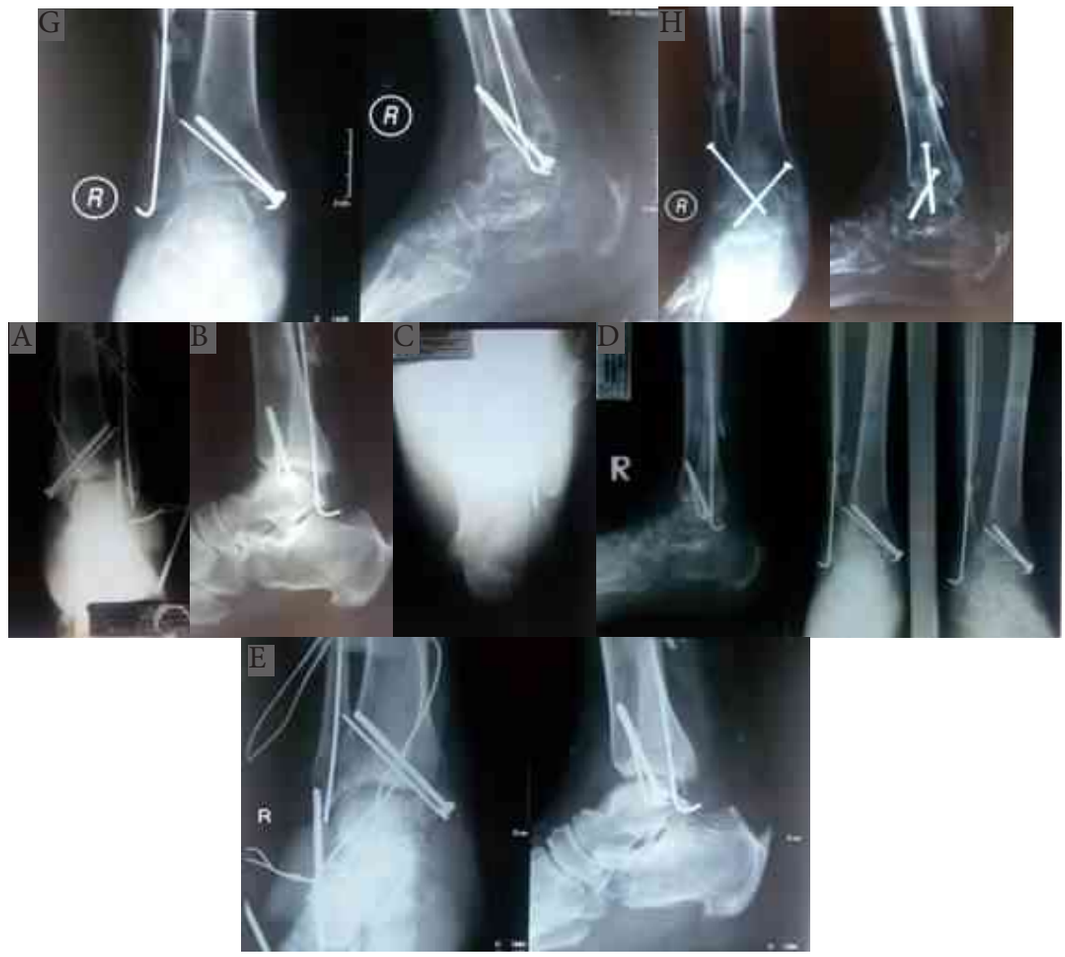

Figure 2. (A-C) post-emergency operative radiological (D) 2 weeks post-external fxation trans-ankle dextra radiological evaluation (E) 3 months post-external fxation trans-ankle dextra radiological evaluation (F) 6 months post-external fxation trans-ankle dextra radiological evaluation (G) radiological evaluation of post-operative of ankle joint fusion with cannulated screw

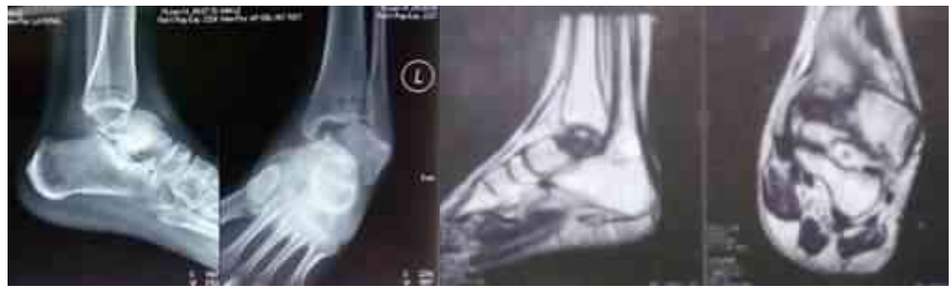

Figure 3. X Ray and MRI of left ankle before operation

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Patient 2

A 26-year-old female patient complained of limping and pain in the left ankle since falling from a height of 3 meters at two months before visiting the Orthopedic Clinic of RSUD Dr. Soetomo Surabaya. The patient went to alternative medicine immediately after falling. The patient's frst visit to the polyclinic was on January 15, 2014 and diagnosed with a neglected dislocation of the left ankle joint.

The patient underwent surgery of the talotibial and subtalar joints fusion by two cannulated screws and a bone graft on February 20, 2014 (Figure 4.A-C). The follow-up examination of 6 weeks postoperative on April 1, 2014 showed the union at ankle joint. (Figure 4. D-E). At ten weeks postoperative on 28 April 2014, the removal of the left-hand lateral ankle screw was carried out. The union of ankle joint was continuously found at three months (Figure 4.F-G), seven months (Figure 4.H-I), and 9 months (Figure 4.J-K) follow-up after removal of lateral ankle screw. A month after latest follow-up, the residual implant was removed on December 23, 2014. The ankle union was found from plain photo examination (Figure 4.L-N). During the last evaluation of 2 years postoperatively the patient did not feel any complaints of pain and obstacles in daily activities.

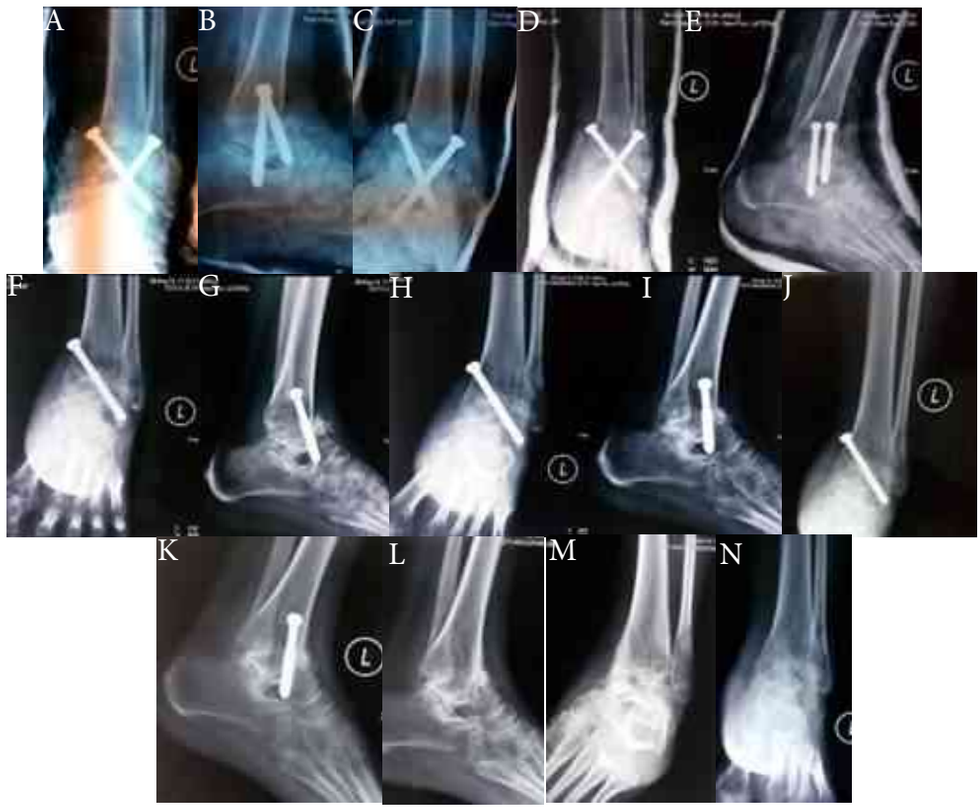

Figure 4. (A-C) Radiological evaluation after talotibial and subtalar surgery with 2 cannulated screws and bone graft. (DE) Radiological evaluation of left ankle 6 weeks after left ankle arthrodesis (FG) Radiological evaluation of left ankle 3 months after left ankle arthrodesis (HI) Radiological evaluation of left ankle 7 months after left ankle arthrodesis (JK) Radiological evaluation of left ankle 9 months after ankle Cystic arthrodesis (LN) Post implant release evaluation by evaluation of talotibial and subtalar joint fusion

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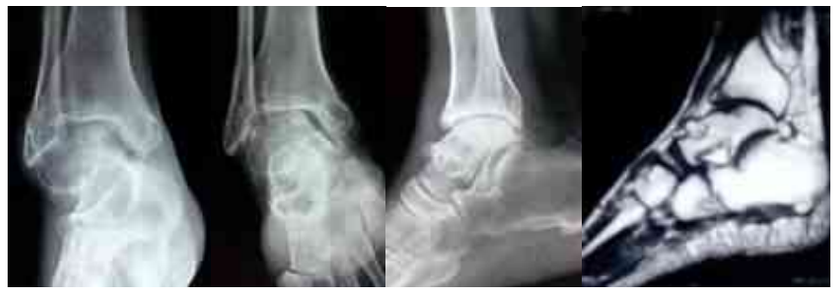

Figure 5. Overview of Plain Photographs and MRI of the right ankle shows subluxation and posttraumatic osteorthritis in patient 3

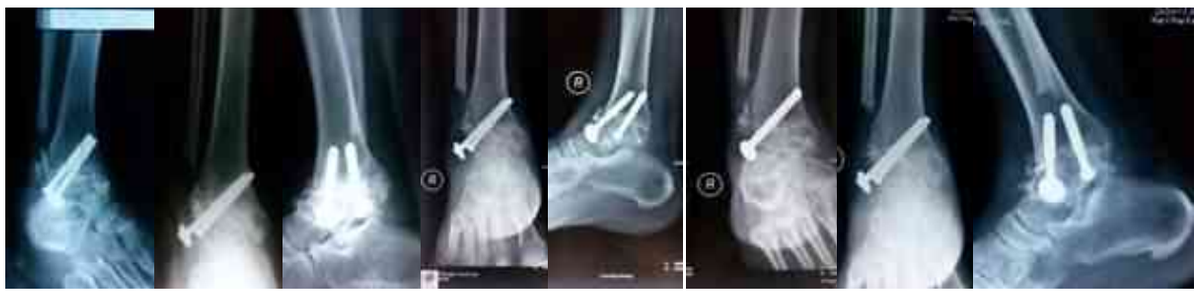

Figure 6. (A-C) Immediate radiological evaluation after fusion surgery (D-F) Radiological evaluation of extra ankle 2 months after extra ankle arthrodesis (G-H) Radiological evaluation of extra ankle four months after ankle arthrodesis dextra (A-C)

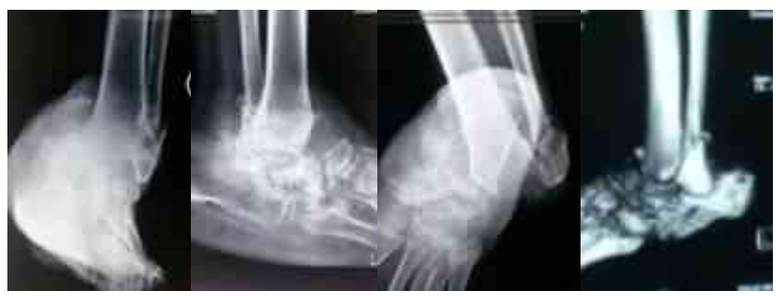

Figure 7. Plain X-Rays and CT-Scan of left ankle of patient 4 (pre-operation)

Patient 3

The 52-year-old male patient complained of right ankle pain since sprained while playing soccer two months before visiting the Orthopedic Clinic of Dr. Soetomo Hospital Surabaya. The pain was aggravated while walking and supporting body weight and decreased with rest. The patient also complained of swelling that diminished after 6 weeks after injury. The patient was diagnosed with neglected subluxation of the right ankle joint with post-traumatic osteoarthritis.

The patient underwent a talo-tibial joint fusion surgery by 2 parallel cannulated screws with distal fbular excision and the addition of bone graft on June 10, 2013 (Figure 6.A-C). Union was started seen on ankle radiological plain examination two months after surgery (Figure 6.D-F). Union was also obtained in ankle radiological plain examination of 4 months evaluation, on 23 October 2013 (Figure 6.G-H). During 3 years postoperative, patients do not complain of pain or obstacles in carrying out work activities.

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Patient 4

A 50-year-old male patient had left ankle pain since falling while pushing a cart eight years before going to the Orthopedic Clinic of Dr. Soetomo Hospital Surabaya. The patient had a history of going to alternative medicine and have only been able to walk with a stick since then. Patients were diagnosed with left ankle neglected dislocation with osteoarthritis of the joint.

The patient had been treated at the Clinic since February 2014 and underwent plantar fusion surgery with two crossing cannulated screws and the bone graft on June 23, 2014 (Figure 8.A-C). On one month after surgery on July 22 2014, the left ankle radiological examination showed no union yet (Figure 8.D-E). The union started to occur from ankle radiological follow-up at two months (Figure 8.F-H), three months (Figure 8.I-K), and eight months (Figure 8.L-M) post-operative. The union continued found on 14-months evaluation of the ankle joint (Figure 8.O-P). On the evaluation three years after surgery, the patient complained of left ankle pain with high impact activity while decreased by rest. The patient has not been returned to work as before the accident.

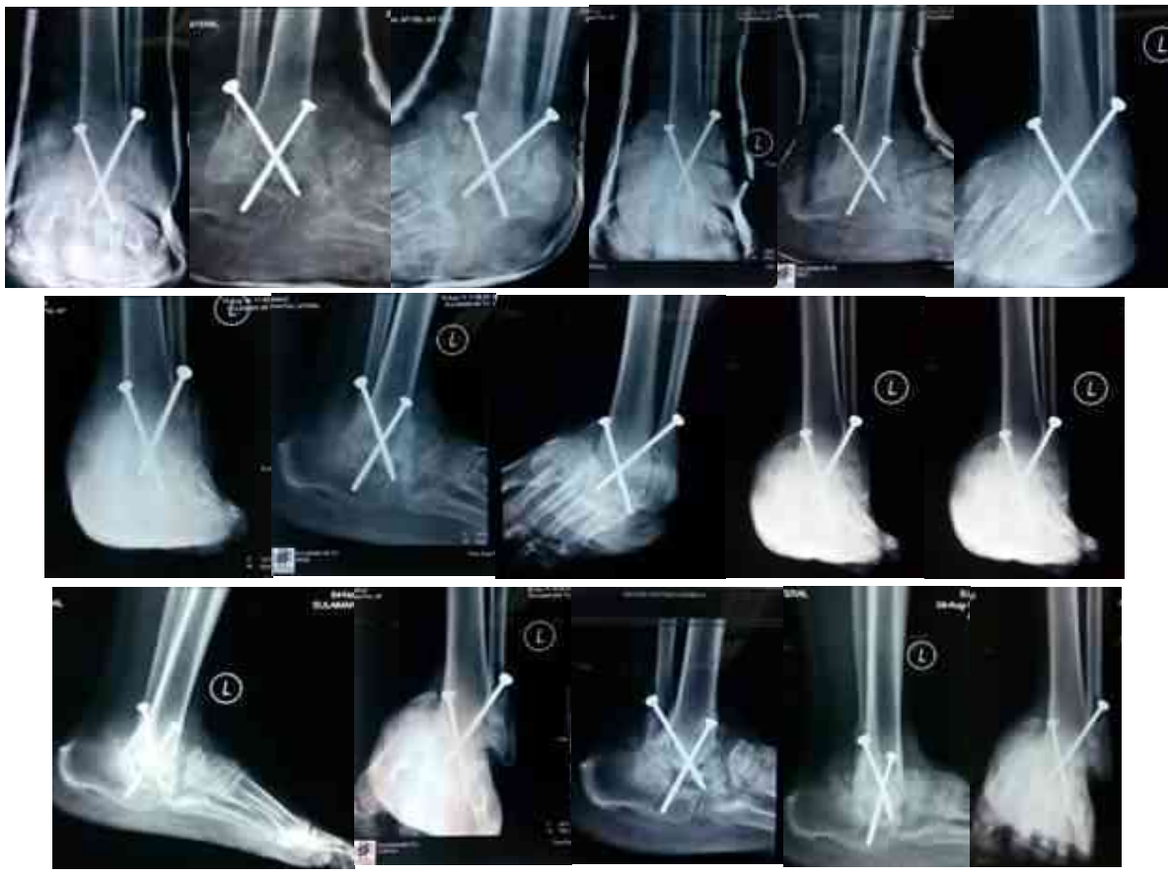

Figure 8. (A,B,C) Immediate radiological evaluation after fusion surgery (D,E) Radiological evaluation of left ankle 1 month after left ankle arthrodesis (F,G,H) Radiological evaluation of left ankle 2 months after left ankle arthrodesis (I,J,K) Radiological evaluation of left ankle 3 months after left ankle arthrodesis (L,M) Radiological evaluation of left ankle 8 months after left ankle arthrodesis and (O,P) 14 months postoperatively

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Patient 5

A 44-year-old female patient complained of pain and swelling of the left ankle after a motorcycle accident that crashed to the left side, four months before visiting the Orthopedic Clinic of Dr. Soetomo Surabaya. The patient went to alternative medicine right after the event. The patient complained that the pain was aggravated by walking and followed by swelling after standing for a long duration. Patients were diagnosed with neglected ankle joint dislocation talus fracture. Preoperative radiological data documentation cannot be obtained. The patient underwent a cannulated screw and stapler fusion surgery also augmentation with bone graft. Follow up radiological examination was obtained one day after surgery on November 22, 2011 (Figure 9.A-C). Radiological re-examination at one month after surgery on December 20, 2011 still did not show union of the joint yet (Figure 9.D-E). The union of the joint could be evaluated on the six months (Figure 9.F-G) and ten months (Figure 9.H-I) follow-up radiological examination. The union of the joint also showed on the latest four years follow-up evaluation (Figure 9.H-I). Clinically, the patient sometimes complaining of pain when walking away and decreasing with rest. However, patient still can work as an administrative staf until the four years after surgery.

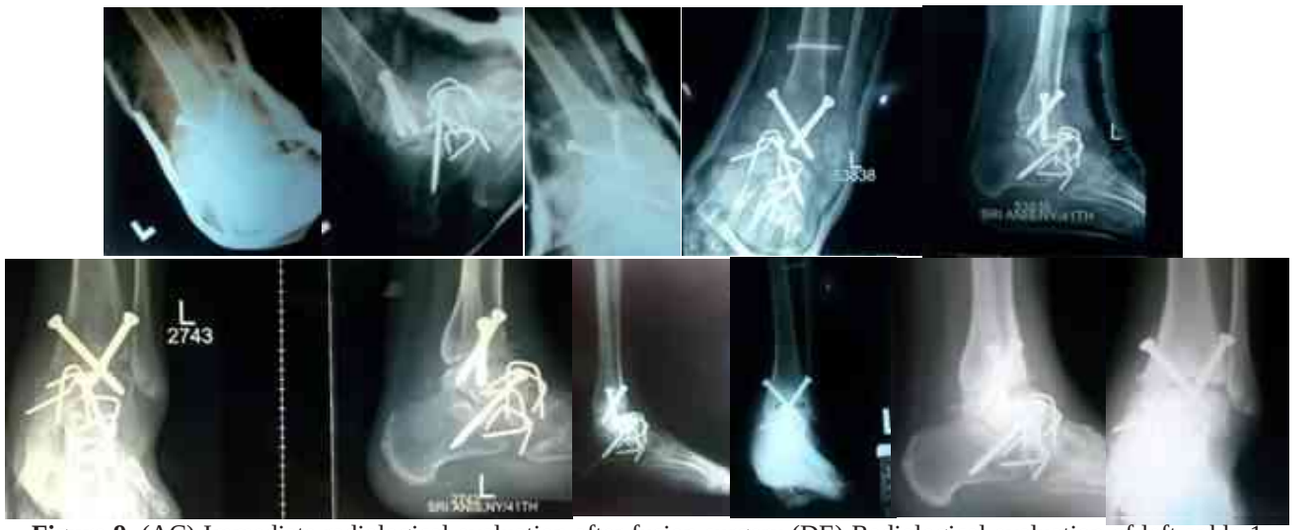

Figure 9. (AC) Immediate radiological evaluation after fusion surgery (DE) Radiological evaluation of left ankle 1 month after left ankle arthrodesis (FH) Radiological evaluation of left ankle 2 months after left ankle arthrodesis (IK) Radiological evaluation of left ankle 3 months after left ankle arthrodesis (LM) Radiological evaluation of left ankle 8 months after left ankle arthrodesis and (OP) 14 months postoperatively

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DISCUSSION

Based on the results of the SF-36 scoring covering general, physical, emotional, and social health aspects, the average score of the five patients is 76.7 with the highest score reaching 95.9 and the lowest score of 56.7. This data shows that there are patients who have achieved almost perfect result from cannulated screw ankle fusion procedures. But there is still patient who still suffer complaints after undergoing this procedure.

In a study conducted by Hendricson et al, bilateral ankle arthrodesis resulted from satisfactory results in patients through SF-36 assessment. Ankle arthrodesis was a good treatment of choice for cases of hindfoot arthritis with high satisfaction rates in postoperative intermediate reporting (Hendricson *et al.*, 2016). Concomitant conditions in the surrounding joints, especially in the subtalar joint, will have a large impact on clinical outcomes and have a significant relationship to the SF-36 quality of life assessment results in patients undergoing arthrodesis, whereas radiological results are not too important for quality of life assessment. (Fuchs *et al.*, 2003).

The condition of patient 1 and patient 4 had a low SF-36 value, most likely because in patient 1 had a long follow-up history where the initial condition of the patient with open fracture was very severe whereas in patient 4 there was a right knee osteoarthritis disease causing the low quality of life assessment results. However, most patients provide high satisfaction and arthrodesis is still the treatment of choice in ankle osteoarthritis.

From the clinical scoring of the ankle-hindfoot American Orthopedic Foot and Ankle Society, the patient's average score was 68 from a maximum of 100. The highest score reached 88, and the lowest score was 51. In this scoring, the aspects assessed included pain, function, and alignment. Thus, it can be concluded that there are patients who have relatively satisfactory clinical scores from the cannulated screw ankle joint fusion procedure. But there are still patients with lower scores which means that patients still suffer from complaints after undergoing this procedure.

Schuh et al. reported that there was no significant difference in the clinical outcome of the AOFAS score in the treatment of ankle osteoarthritis with arthrodesis and total ankle arthroplasty. So the arthrodesis procedure is chosen because the technique is more simple and doesn't take much time (Schuh et al, 2011).

Herrera-Perez et al. reported the use of cannulated screw in ankle arthrodesis giving an increased AOFAS clinical score. Compared to the Compression Staples for Subtalar Arthrodesis Fixation technique, the use of cannulated screw technique has better functional results (Herrera-Perez, et al., 2015). The combined application of the anterior contoured plate and cross screw fixation provides better stability than the technique of crossed screw fixation alone which provides a higher probability of union occurrence. In the study of Kakarala et al. provides a better picture of clinical outcomes in combination techniques (Kakarala *et al.*, 2006).

From the clinical aspect, patients who had the lowest score were patients 4. In this patient, knee osteoarthritis was obtained from the contralateral side from the ankle who underwent surgery. This becomes comorbid because reducing the patient's adherence to not loading weight sufficiently at the postoperative rehabilitation due to contralateral knee pain. So that the earlier loading of weight on the fusion of the ankle joint with cannulated screw is the main factor causing the unsatisfactory results obtained in this patient.

The advantage of our cannulated screw technique is that provides a shorter operating duration and provides easier fixation and reduction in the hindfoot area.

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Table 1. SF - 36 Scoring on patient 1,2,3,4, dan 5

No.		Patient					Average
		1	2	3	4	5	
	GENERAL CONDITION						
1.	General health status Current health level compared to 1 year ago	80	100	100	80	80	88
2.	General health status Current health level compared to 1 year ago	80	100	100	100	80	92
		80	100	100	90	80	90
	ACTIVITY BARRIER						
3.	Heavy activities (such as running, lifting heavy weights, and strenuous exercise)	0	50	50	0	0	20
4.	Moderate activity (moving tables, pushing vacuum cleaners, bowling, playing golf)	100	100	100	50	50	80
5.	Lift or carry groceries	100	100	100	50	100	90
6.	Climb up some stairs	50	100	50	50	50	60
7.	Climb up a ladder	100	100	100	100	100	100
8.	Bend, kneel, bow	50	100	100	50	100	80
9.	Runs more than 1 mile	0	50	50	0	0	100
10.	Walk a few blocks	50	100	100	50	50	70
11.	Walk one block	100	100	100	50	100	90
12.	Bathe and dress alone	100	100	100	100	100	100
		65	90	85	50	65	71
	PHYSICAL HEALTH PROBLEM						
13.	Reduced time spent on work or other activities	0	0	100	0	100	40
14.	Reach less than expected	0	100	100	0	100	60
15.	Barriers to work or do other activities	0	100	100	0	100	60
16.	Having trouble running work or other activities	0	100	100	0	0	40
		0	75	100	0	75	50

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	EMOTIONAL HEALTH PROBLEM						
17.	Reduced time spent on work or other activities	0	100	100	0	100	60
18.	Reach less than expected	0	100	100	0	100	60
19.	Do not do work or other activities as well as usual	0	0	100	0	100	40
		0	66,7	100	0	100	53,3
	SOCIAL ACTIVITY						
20.	Emotional problems affect social activities in family, friendship, neighbors, or groups?	100	100	100	100	100	100
		100	100	100	100	100	100
	PAIN						
21.	How severe physical pain is experienced in these past 4 weeks?	60	80	100	60	60	72
22.	During the past 4 weeks, how much pain affected work?	60	100	100	50	100	82
		60	90	100	55	80	77
	EMOTION AND ENERGY						
23.	Are you excited?	60	100	100	80	80	84
24.	Are you anxious?	80	80	80	80	80	80
25.	Do you feel very bad and nobody can encourage you?	60	100	80	80	60	76
26.	Do you feel calm and peaceful?	80	100	80	80	80	84
27.	Do you have a lot of energy?	60	80	80	60	80	72
28.	Do you feel low and worse?	60	100	80	80	80	80
29.	Do you feel too hard-working?	80	100	80	80	80	84
30.	Are you a happy person?	60	100	100	80	80	84
31.	Do you feel tired?	60	100	80	80	80	80
		66,7	95,6	84,4	77,8	77,8	80,5

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	SOCIAL ACTIVITY						
32.	In the past 4 weeks, how much time for your social activities is interrupted by physical or emotional problems?	75	100	100	75	100	90
		75	100	100	75	100	90
	GENERAL HEALTH CONDITION						
33.	I feel sick more easily than others	100	75	75	50	75	65
34.	I am as healthy as anyone I know	100	75	100	50	75	70
35.	I thought my health was getting worse	100	75	100	75	75	75
36.	My health is at a good level	50	100	100	75	75	80
		82,5	81,3	93,8	62,5	75	72,5
	TOTAL	**58,8**	**88,7**	**95,9**	**56,7**	**83,6**	**76,7**

Table 2. Clinical scoring of ankle-hindfoot American Orthopedic Foot and Ankle Society patients 1, 2, 3, 4 and 5

CRITERIA	**GRADE**		**Patient**					**AVERAGE**
			1	**2**	**3**	**4**	**5**	
Pain			30	40	40	30	30	34
No pain	40	40	30	40	40	30	30	34
Light, Occasionally arises	30							
Medium, every day	20							
Heavy, almost always arises	0							
Function		50	22	34	38	21	30	29
Activity barriers, assistance needs			7	10	10	7	10	8,8
There are no obstacles, no need for help	10							
There are no obstacles to daily activities, there are obstacles to certain activities, no need for help	7							
There are obstacles to daily activities, need to use a stick	4							

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There are severe obstacles to daily activities; use walkers, crutches, wheelchairs, braces	0							
Surface in walking			3	5	5	3	5	4,2
Do not experience obstacles on any surface	5							
Some obstacles on the uphill, stairs	3							
Heavy barriers on uphill and ladder roads	0							
Walking Style Abnormalities			4	8	8	4	4	5,6
Nothing	8							
Light	4							
Clearly seen	0							
Sagittal movements (flexion and extension)			0	0	4	4	0	1,6
Normal or slightly blocked (30º or more)	8							
Medium resistance (15º to 29º)	4							
Obvious obstacles (less than 15º)	0							
Hindfoot movement			0	3	3	3	3	2,4
Normal or slight resistance (75% to 100% normal)	6							
Moderate barriers (25% to 74% of normal)	3							
Clear barriers (less than 25% normal) 0	0							
Ankle-Hindfoot stability			8	8	8	0	8	6,4
Stable	8							
Very unstable	0							
Alignment			10	10	10	0	5	7
Good, plantigrade legs, ankle and hindgoot alignmet both good	10	10	10	10	10	0	5	7
Moderate, foot plantigrade, seen multiple degrees of ankle-hindfoot malalignment, without complaints	5							
Bad, feet not plantigrade, severe malalignment, complaints	0							
TOTAL			**62**	**84**	**88**	**51**	**65**	**72**

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While the weakness of this technique is that the stability of the ankle is less compared to the plate and screw technique. In full-threaded screw, there is a possibility of fewer fxation shifts that can affect the union of the ankle joint. However, in this case report there was no correlation between union and clinical outcomes or quality of life of the patients.

CONCLUSION

From this case series, the cannulated screw ankle fusion procedure had satisfactory results despite leaving complaints in one patient sample. That failure was due to patient compliance on early weight-bearing. However, fusion of the ankle joint with cannulated screw still has a role in the treatment choice for ankle joint reconstruction. Further research is still needed regarding the results of the ankle fusion procedure using cannulated screw with a larger amount of samples and a longer observation period. It is also necessary to know the factors that can determine the prognosis of cannulated screw ankle fusion procedure outcome.

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Case Report

Anatomical and sexual functions at post neovagina operation on Mayer Rokitansky Kuster Hauser Syndrome (MRKH) patients with sigmoid, amnion, and conventional methods in Dr. Soetomo Hospital

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ABSTRACT

The Mayer–Rokitansky–Kuster–Hauser (MRKH) syndrome is congenital malformation due to utero-vaginal agenesis. For many years, Dr Soetomo Hospital has been applying McIndoe technique using biomaterial amnion. Recently, in collaboration with digestive surgery, neovagina operation using sigmoid was performed. However, no data are available on the complications, anatomic, and functional results of the neovagina operation using sigmoid and amnion. MRKH patients who have performed neovagina operations from January 2011 to December 2014 were involved in this case review. The anatomical function was measured based on minimal vaginal length of more than 6 cm and width of 3 cm, while sexual performance is measured by Female Sexual Function Index (FSFI), which is above 23, and Female Sexual Distress Score Revised (FSDSR), whose score is < 11. In 4 years period, there were 6 cases of MRKH underwent neovagina (1 used sigmoid and 5 used amnion) at Dr Soetomo Hospital. All of them had a satisfying anatomical and sexual function. Even though neovagina operation signi f cantly reduces sexual distress, but it does not necessarily mean alleviate as seen by the high FSDSR score. Neovagina using amnion has faster operation time and cheaper with the same length of hospital stay than sigmoid neovagina. Sigmoid neovagina has a better vaginal length, lubrication and no need dilatation after operation, but it has higher complication risk. The Neovagina technique should be used at Soetomo Hospital depends on patient wishes and circumstances. For those who have strong f nancial support and are not willing to do manual dilatation, they should use the sigmoid neovagina, while those who are able to do manual dilatation, then the amnion neovagina is a good choice.

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INTRODUCTION

Genital organs have both reproduction and sexuality functions. But, some patients experience developmental disorders of genitalia organs, such as Mayer-Rokitansky-Küster-Hauser (MRKH) patients who do not have fully performed vagina and uterus, but their ovaries are well functioning. These patients are usually female phenotypes, in which the women have large breasts and their pubic and armpit hair grow normally, but they do not have menstrual periods, and after the examination, they do not have vagina or uterus. The women will be very di f cult to get pregnant and give birth, except with surrogacy. However, these women are still possible to enjoy sexual life, like other women, if their vaginal agenesis is reconstructed using various techniques, either surgical neovagina and non-surgical neovagina (Chandler, Machan, Cooperberg, Harris, & Chang, 2009).

The main goal of surgical neovagina for MRKH patients is not for reproductive function, but for sexual function. The operation can be said to be successful if the neovagina results are given not only adequate vaginal length, good lubrication with minimal maintenance such as the need for regular dilatation but also able to satisfy in sexual intercourse (Fedele et al., 2010).

For years, the urogynecology division in Dr. Soetomo Hospital has used surgical neovagina techniques with amniotic biomaterials. Amnion as biomaterial has several advantages in the form of the ability to prevent cicatrix and encourage epithelialization to reduce the possibility of vaginal narrowing (Rennie et al., 2012). At the end of 2014, neovagina operation is performed, using sigmoid colon, in collaboration with the department of digestive surgery. Sigmoid is a very good material for neovagina allographs because sigmoid is easy to mobilize and thick, but it can also produce lubricants and the inner part is like the original vaginal rugae (S. Robert Kovac, Carl W Zimmerman, 2012).

The report of this case is intended to evaluate the results of neovagina operation, neo vaginal operation using amnion in comparison with sigmoid allograft from anatomical aspect, sexual function, length period ready for sexual intercourse after surgery, length of operation, length of stay in hospital, operation costs and complications that may arise on MRKH patients at Dr. Soetomo Hospital between 2011 and 2014. These results will be then used in the service of choosing the type of operation that suits the needs of patients by the capability of operation at Dr Soetomo Hospital.

METHODS

This case report was taken from MRKH patients at Dr. Soetomo Hospital from January 2011 to December 2014 who had performed neovagina operation. These patients were then evaluated for neovagina anatomy by measuring neovagina length and also for their sexual function using Female Sexual Function Index (FSFI) and sexual psychological aspects by Female Sexual Distress Score Revised (FSDSR). In addition, anamnestic data was collected regarding the waiting time between the operation and its frst use for intercourse, the calculation of treatment cost and length of stay in the hospital, as well as surgical complications from medical record data.

Neovagina operation can be said to be anatomically successful if the vaginal length is at least 6 cm with a minimum width of 3 cm. (Fedele et al. 2010) Meanwhile, neovagina operation can be said to be well-functioned sexually if the FSFI score is above and the FSDSR score is less than 11.

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RESULTS

From 2011 to 2014 (3 years), seven MRKH patients had neovagina operation in Dr Soetomo Hospital (one patient was excluded from this case report due to the lost follow-up, thus only six cases in total). One patient used sigmoid (AL), while the others used an amniotic method.

Table 1. Result of MRKH Suporting Examination

	Vagina	Testosterone	Karyotyping
SIGMOID 1	3 cm	2	46 xx
AMNION 1	2 cm	< 2.0	Not performed
AMNION 2	2 cm	< 2	Not performed
CONVENTIONAL 1	1.5 cm	1.9	46 xx
CONVENTIONAL 2	1.5 cm	0.162	Not performed
CONVENTIONAL 3	2 cm	< 2	Not performed

DISCUSSION

Age for performing Neovagina operation

Most neovagina surgeries are performed at women in their 20s due to several reasons. Firstly, some techniques, like those using amnion require postoperative dilatation either by manual or continuous intercourse. The study found that vaginal length in women who were sexually active was signi f cantly longer than those who were not sexually active or who had been sexually active (6.3 cm vs. 3.6 cm vs. 3.2 cm, $p < 0.05$) (Liao, Conway, Ismail-Pratt, Bikoo, & Creighton, 2011). Manual dilatation requires psychological maturity and strong motivation, which allows the manual dilatation can be done continuously. Manual dilatation is sometimes a source of stress for patients, because they have to do it routinely in a place that requires privacy, so it is very tiring. Secondly, in order to minimize the risk of recurring narrowing due to non-compliance with manual dilatation, neovagina operation should be performed prior to sexual activity. The patients who experience neovagina narrowing postoperatively are mostly due to not manually dilated for so long or absent from for sexual intercourse. For this reason, most doctors recommend delaying the vaginal operation when the patient approaches to sexual active. Previous studies have reported that neovagina using sigmoid do not require post-surgical dilatation can indeed be done in pediatric patients (the youngest is at the age of 2 years old), but it is because the development of an imperfect vulva is often problematic in its anastomosis (Lima et al., 2010).

The patient number amnion 2, neovagina 1 dan 2, f rstly came to the gynecology center with the complaints of primary amenorrhea and they have been diagnosed with MRKH when they were still in senior high school. But, the surgery to construct the vagina was delayed until they were ready to have active sexual intercourse. Meanwhile, the patient number sigmoid 1, amnion 1 and neovagina 3 were f rst diagnosed when they were married due to their di f culty in penetrating during intercourse. This is in line with previous studies, in which the majority of MRKH patients come with their complaints of primary amenorrhea or intercourse di f culties (Fotopoulou, Neumann, Klapp, Lichtenegger, & Sehouli, 2008)

Table 2. Timetable when the Respondents Perform the Operation

Patient Name/ RM No.	Age at first visit	Age at operation	At operation
SIGMOID 1	28 yo	28 yo	3 years of marriage
AMNION 1	18 yo	18 yo	1 year of marriage
AMNION 2	27 yo	27 yo	5 months of marriage
CONVENTIONAL 1	17 yo	23 yo	1month before marriage
CONVENTIONAL 2	16 yo	26 yo	1 week of marriage
CONVENTIONAL 3	16 yo	32 yo	1 month before marriage

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Anatomical Function of MRKH Patients After Neovagina operation

Neovagina operation is said to be anatomically successful if a minimum vaginal length is 6 cm and its minimum width is two fngers at evaluation of 6 months postoperative (Fedele et al., 2010). Neovagina operation patients who use amnion method (cases amnion 1 and 2) have shorter vaginal length (averagely 6.8 cm) compared to those using sigmoid colon media (case no. 1). However, all patients have minimum vaginal length of 6 cm with a width of 3 cm; thus it can be said to be anatomically successful. Although neovagina patients with amnion method have shorter vaginal length than those using the sigmoid colon method, patients with the longest evaluation, namely four years after neovagina operation using amniotic methods, have not shown any signs of narrowing.

Patients with the amniotic method, if compared to those with sigmoid colon method, have problems with less lubrication. Patient amnion 2 and neovaginal 2 in early period after surgery require jelly lubrication before their intercourse, but they are no longer using it now. In addition, the form of neovagina rugae in post-operation using sigmoid method is even more than those in amniotic method. This is in line with previous studies of MRKH vaginoplasty patients using amniotic media that require artifcial lubrication at the beginning of sexual intercourse (Fotopoulou et al., 2008). In contrast to the amniotic method, the research on patients using sigmoid colon method will excrete the excessive vaginal discharge in the frst 8 weeks postoperative which will then decrease (Rawat et al., 2010).

Table 3. Evaluation on Post-CONVENTIONAL operation

Patient Name/ RM No.	Evaluation	Length	Width
SIGMOID 1	3 months	12 cm	3 cm
AMNION 1	3 months	7 cm	3 cm
AMNION 2	4 months	7 cm	3 cm
CONVENTIONAL 1	6 months	6 cm	4 cm
CONVENTIONAL 2	2 months	7 cm	3 cm
CONVENTIONAL 3	3 months	7 cm	3 cm

Sexual Function of Neovagina Patients based on FSFI (Female Sexual Function Index)

Patients of neovagina operation with amniotic and sigmoid method had relatively the same sexual function (FSFI of sigmoid method: 29.8, average amniotic method: 27.06) and both were in good category (above 23). Patients number sigmoid, amnion 1 and neovagina 3 who have sexual intercourse before and after neovagina operation show that neovagina operation improves their sexual function from bad to good (FSFI is less than 23 to be more than 23, p: 0.00652). The improving appearance of sexual intercourse is also felt by their spouses. From two out of three couples of patients who couples who have the surgery after marriage) state that they feel more satisfed when having sexual intercourse after the operation.

Fotopoulou's study has compared the sexual function after neovagina operation using amniotic method with those using sigmoid method and normal women, and the results are not different (total scores on those using amnion is 30.0, sigmoid is 28.1, and normal women is 30.2) (Fotopoulou et al., 2008).

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Table 4. Total FSFI (Female Sexual Function Index) Score

Patient Name/ RM No.	Total score	
	Pre	Post
SIGMOID 1	15.1	29.8
AMNION 1	16.2	28.9
AMNION 2	15.1	26.2
CONVENTIONAL 1	-	26.9
CONVENTIONAL 2	-	27.1
CONVENTIONAL 3	-	26.2

Sexual Distress Level on Neovagina Patients based on FSDS-R

Although FSFI score of all neovagina patients was good (above 23), their FSDS-R scores were not. Although there was a signifcant decrease in sexual stress level before and after surgery p: 0.015 (patient sigmoid, amnion 1, amnion 2), the average FSDS-R score in patients with amniotic methods was still high, which was 14.2 (above 11), along with one patient whose score was 11 (20%). The discrepancy between FSFI and FSDS-R scores is in accordance with Carrad's research. FSDS-R score in patients with the post-sigmoid operation and manual dilatation shows scores above 11 which indicate distress in intercourse (sigmoid method shows 21.35, in which scores below 11 are 15%, compared to manual dilatation which was 18.40, and scores below 11 are 11%). The discrepancy between FSFI and FSDs-R scores in the study was found in 39% of cases. This is because FSFI assessed the sexual function aspects, while FSDR assessed the psychological aspects of intercourse.

From Liao's research, it was found that women with neovagina MRKH have lower sexual esteem (50 %), higher sexual depression (205 %), higher sexual anxiety (172 %) and higher fear of sexual relationship (146 %) (Liao et al., 2011). Therefore, although neovaginal operation signifcantly improves the sexual function on MRKH patients, many patients still experience stress due to their physical imperfections and sadness since they cannot give birth.

Table 5. Distress Level due to Sexual Problems on Neovagina by FSDS-R (Female Sexual Distress Scale-Revised)

Patient Name/ RM No.	Pre-operation	Post-operation
SIGMOID 1	28	11
AMNION 1	30	14
AMNION 2	25	14
CONVENTIONAL 1	-	18
CONVENTIONAL 2	-	11
CONVENTIONAL 3	-	14

Waiting Period for Intercourse can be performed after Neovagina operation

There were variations in the results between one study and another, regarding the waiting time of frst intercourse after surgery and the length of time to do a manual dilatator after neovagina operation with the amniotic method. In Fotopoulou's research, neovagina patients who use amniotic method have 5.28 months for their average waiting time, between the operation and intercourse (about 2 to 7 months), and the use of dilator after operation is averagely 4.1 months (about 3-5 months) (Fotopoulou et al., 2008). In this research, the respondents are prohibited to do intercourse until 6-8 weeks after the operation and they are suggested to do dilatation in 3 to 5 months after the operation. Furthermore, in Sarwar's research, the patients, after the operation with amniotic method, are asked to use molding for three months and the next three months is only at night (Chan, Levin, Ford, Stanton, & Pfeifer, 2017). The intercourse was permitted after three months operation. Averagely, the patients had intercourse in three months after the operation. Patients who used sigmoid colon media in Imperato's study, averagely, had their frst intercourse in four months after the

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operation (about 2 months to 4 years)(Imparato, Alfei, Aspesi, Meus, & Spinillo, 2007).

The patients claimed that they did not have to wait too long between the operation and intercourse (averagely, 1.2 months). Once the surgical wound healed, they immediately had intercourse. One of the factors that influence it is that the operation is done before marriage, shortly after marriage or already married so that the patients and their spouses want to immediately enjoy the results of the operation. However, some patients claimed to continue using dilatator after the operation (averagely, 2.2 months), despite having intercourse, because of their fears of shrinking and less intercourse. Two of the patients with amniotic method complained about the painful intercourse at the beginning, so they rarely used it for sexual intercourse and chose to use dilatation. Patients with sigmoid method experienced the narrowing of vaginal introitus at the beginning of post-operation, in which the vaginal width is 2-finger narrowing. In this case, the patients had intercourse in 1 month after the operation, because they waited for a surgical wound in the abdomen to heal. These patients used their finger to widen their introitus, which in the second month of evaluation after the operation, it showed satisfactory results (2-finger widening).

Table 6. Waiting Time between Operation and Intercourse and the Length of Manual Dilatation

Patient Name/ RM No.	Waiting time between operation and	Use of dilatator
SIGMOID 1	1 month	-
AMNION 1	1 month	3 months
AMNION 2	1 month	2 months
CONVENTIONAL 1	1 month	3 months
CONVENTIONAL 2	1 month	1 month
CONVENTIONAL 3	2 months	2 months

Length of Stay in Hospital After Neovagina operation

From the data, it was found that the length of stay in the hospital was 14-15 days of treatment. The length of stay in hospital for patients with sigmoid colon method in Imparato's study was 8.3 days (about 5 to 23 days), (Imparato et al., 2007) whereas in El Sayed's study, it was 11 days (about 7 to 22 days). Meanwhile, the length of stay in hospital for the patients with amniotic method from Fotopoulou's study was 10.8 days (about 8 to 14 days) (Fotopoulou et al., 2008). One of the considerations for no difference in the length of stay in hospital between patients with amnion and sigmoid colon media is because both of them use molding with approximately the same insertion time of 10-14 days.

Table 7. Length of Stay in Hospital for Patients with Neovagina operation

Patient Name/ MR No.	Length of stay in hospital (day)
SIGMOID 1	15
AMNION 1	15
AMNION 2	15
CONVENTIONAL 1	15
CONVENTIONAL 2	14
CONVENTIONAL 3	14

Length of neovagina operation

The length of operation using amniotic media is shorter, which more or less is 54 minutes averagely, whereas those using the sigmoid colon method are about four times (3.5 hours or 210 minutes). Meanwhile neovaginal operation conventional seems faster compared to other two method.This result is in line with the results of other studies on more complex operation with colon media, by involving the expertise from department of digestive surgery that requires longer length of operation. The operation with

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amniotic method in RSDS is still around one hour. In Fotopoulou's research, it took 24.7 minutes for amniotic method (about 20-33 minutes), (Fotopoulou et al., 2008) whereas in Sarwar's study, its surgical length is less than one hour, which is between 20 to 45 minutes9. Meanwhile, the operation using sigmoid colon method, in Imperato's research, is 145 minutes (about 95 to 250 minutes), whereas in Yang's study is 279, ± 32 minutes, and in El Sayed's study, it is 184 minutes (about 160 to 210 minutes) (Imparato et al., 2007).

Table 8. Length of Neovagina operation

Name/ MR No.	Length of Operation
SIGMOID 1	3 hours 30 minutes (210 minutes)
AMNION 1	1 hour 35 minutes (95 minutes)
AMNION 2	30 minutes
CONVENTIONAL 1	1 hour (60 minutes)
CONVENTIONAL 2	45 minutes
CONVENTIONAL 3	40 minutes

Costs for neovagina operation

The costs for operation and total costs for the surgical technique are more expensive if using sigmoid colon method. This is reasonable because it involves another division (surgery). The costs for non-surgical treatment does not differ much between those who use amniotic media and sigmoid colon media.

Table 9. Costs for Neovagina operation and Treatment in BPJS era

No	Remarks	Sigmoid 1	Amnion 1	Amnion 2
1.	Operation cost	13.850 M 9.5 M	12 M	12 M
2.	Non-surgical treatment cost	4.373 M (class 3)	5.838 Mt (class 2)	5.838 M
	Total cost	27.723 M	17.838 M	17.838 M

Table 10. Complication on Neovagina Patients

Patient Name/ RM No.	Complication
SIGMOID 1	Rupture buli iatrogenic
AMNION 1	Painful → MST, Copar, Constipation → laxadine
AMNION 2	-
CONVENTIONAL 1	-
CONVENTIONAL 2	--
CONVENTIONAL 3	-

Complications from neovagina operation

A serious complication due to neovagina operation is rupture buli iatrogenic, on the patients with the sigmoid method, which has been corrected during operation. On another side, a painful complication is postoperatively experienced by patients with amniotic method but manageable by giving strong analgesics.

One patient out of six patients who used amnion in Fotopoulou's study had complications following a postoperative urinary tract infection, whereas another patient had a rectovaginal fstula due to the shortening of the vaginal canal and continued with neovagina operation using sigmoid. Another study using amnion by Sarwar had evaluated for three months postoperatively. There was 11% of the patients experiencing narrowing complications due to non-compliance with manual post-operative dilatation. Postoperative complications of the sigmoid method can be in the form of the narrowing of vaginal introitus, which in Imperato's study, as much as 8% was successfully overcome by using dilatation, and 16% of the patients in Moundoni's study also experienced a narrowing in introitus and treated with V or Y incision.

CONCLUSION

At Dr. Soetomo Hospital, it was found that anatomical and sexual functions after neovaginal operation either conventional using amniotic and sigmoid colon media were not different. Thus, which surgical technique the

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sigmoid method, depends on the needs and circumstances of the patients. Conventional and amniotic media provides the advantage of shorter surgical times and lower surgical costs. Neovagina operation with colon media does not require postoperative dilatation with better vaginal length and rugae than using amniotic media, but it has a greater risk of operation.

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Case Report

Tumour mimicking in musculoskeletal system in Surabaya: A case series

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ABSTRACT

Musculoskeletal tumors are potential causes of heavy morbidity and economic burdens for patients. There are often cases suspected as musculoskeletal tumors based on a specifc diagnostic modality because of overlapping features upon physical examination or a tumor-like appearance from the radiological examination, the more reason for triple diagnosis to be performed for an exact diagnosis. We report 5 cases of fractures tumor-mimicking lesions. The First patient, a patient with MRI revealing a primary malignant bone tumor, but with plain thorax x-ray and FNAB, the diagnosis was tuberculosis arthritis of the elbow. The second patient shows metastatic proses with plain radiographic, but from open biopsy, the diagnoses fall to chronic osteomyelitis. The third patient had a history of papillary carcinoma thyroid with pathological fracture of proximal of the left femur, but the biopsy shows a hypercalcemic state. The fourth patient, had mass size 20x15 cm at the thigh, but the biopsy shows Non-Specifc Chronic Osteomyelitis. The ffth patient with progressive swelling of the left knee for one year, 10x10 cm in size, the biopsy showed no sign of malignancy but tuberculosis of left distal femur. In conclusion, standard comprehensive diagnosis steps consisting of clinical history, imaging, laboratory and histopathological examinations are crucial to diferentiate tumor-mimicking lesions from neoplasms, thus ensuring proper treatment.

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INTRODUCTION

The reactive lesion from the bone and the soft tissue found during the histological examination, have a cellular atypical cytological fgure, similar in appearance with various nucleus and light hyperchromatic, and mitotic activity (Salter RB, 1999). Reactive lesions from the bone and the periosteum forming the bone and cartilage matrix often confused with osteosarcoma and chondrosarcoma (Solomon L, Warwick D, 2010). The cytomorphology of the bone, the uniform fgure of the cell, and the absence of atypical mitosis may aid in identifying the reactivity of the lesion (Gersch, Lombardo, McGovern, & Hadjiargyrou, 2005). The relation between the clinical and radiological appearance is paramount in order to avoid the wrong classifcation of the tumor (Hoch & Montag, 2011) because the reactive lesion is often present in the area where the osteosarcoma and chondrosarcoma are rarely found (i.e., the arm) and showing signs of malignancy (Kim, Park, Ryu, Jin, & Park, n.d.).

A retrospective observational study in RSUD Dr. Soetomo, from the data in the year 2011-2014, there are 460 new cases suspected as a musculoskeletal tumor, previously evaluated clinically, radiological, and pathologically, which was then discussed by the tumor board. Of 460 cases, 277 are males, 183 are females. Final diagnosis: 193 benign cases (41%), 251 malignant (54%), 16 infected (3%), 4 metabolic cases (0.8%), 8 inflammation (1,6%), 1 osteolysis (0.2%) and 1 bone necrosis (0,2%). There are 30 cases of tumor mimicking (6.5%).

Musculoskeletal tumor cases cost a sum amount of money, and as it progresses, and not so rarely worsen, the cost would inflate to unaffordable proportion to the patient (Ward WG, Corey RM, Watkins-Castillo SI, 2014).

Primary bone tumors are rare, thus the rare opportunity as an experience. According to the radiologic imaging and the histopathology result, and the severe consequence of the wrong surgical procedure, the proper management of the bone tumor is by a multidisciplinary approach (Madewell, Ragsdale, & Sweet, 1981). Accurate diagnostic requires clinical, radiologic, and pathologic evaluation (Binesh, Sobhan, Moghadam, & Akhavan, 2013).

DESCRIPTION

Case 1

A 52 years old male patient complained of pain in his right elbow for one year. The patient had a history of trauma seven years prior. From MRI, we found mass with 67,1 x 54,5 x 104,4cm also sunray appearance which suggested a primary malignant bone tumor (image 1). However, Radiology fnding from elbow AP/LAT 2 months after initial MRI suggested another disease (image 2), septic arthritis of Tuberculosis with osteomyelitis, and disuse osteopenia.

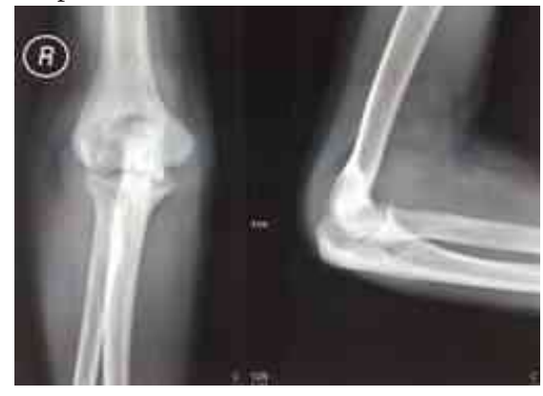

Image 1. Elbow AP/Lat, from plain radiographic, showing septic arthritis.

We diagnosed him as a septic arthritis of tuberculosis. The histopathological examination from his elbow showed granulomatous inflammation, which suggested tuberculosis (image 3). Even though the laboratory fnding not support this diagnosis with Leucocyte 6.27, CRP 2,3, Ca 5, Phosphate 4.2. The therapy we

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give for this patient is debridement, medial-lateral ligament reconstruction collateral ligament of the elbow with fascia lata, and antituberculosis drug (image 4).

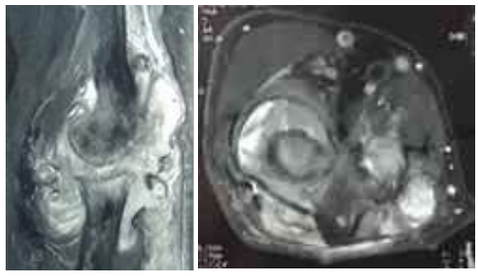

Image 2. MRI Elbow with contrast. The sun ray appearance suggesting to primary bone tumor malignant

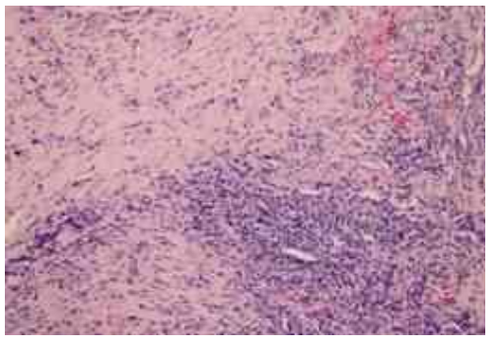

Image 3. PA Examination. The histopathological examination from his elbow showed granulomatic inf amation which suggested tubrculosis

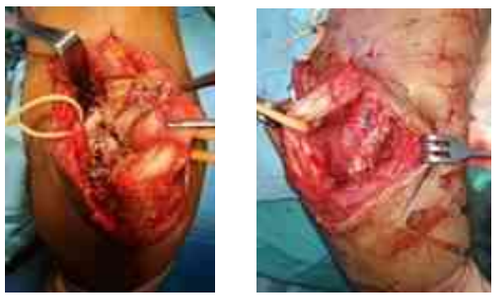

Image 4. Debridement and Ligament reconstruction

Case 2

The second patient, A 53 years old male patient complained of pain in his right thigh. The patient had a history of fell two weeks prior at the bathroom but no history

Of lump anywhere in the patient body. From the plain radiographic, there was found a lytic lesion at medulla diaphysis of 1/3 distal of the right femur (image 5), which suggested two di f erential diagnosis: a metastatic and an infection process. After an MRI examination was held, we can narrow down the diagnostic to osteomyelitis because there is no sign of metastatic proses (image 6).

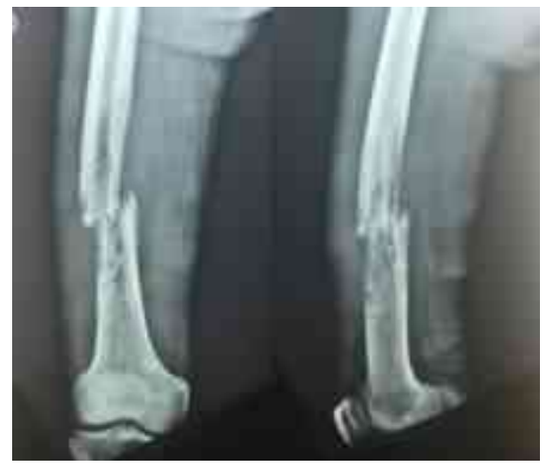

Image 5. Right Femur x-ray: showing lytic lesion with pathological fracture

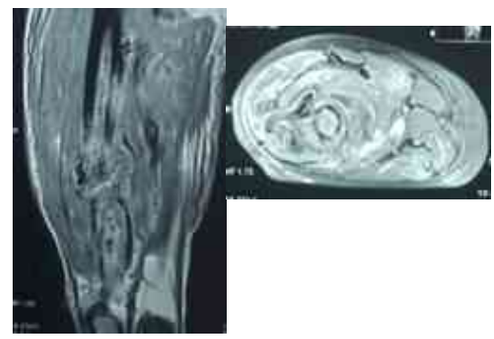

Image 6. MRI of femur of the 2nd patient.

This f nding still needs to be con f rmed to give the patient a proper therapy. From FNAB, we found there is no sign of malignancy, and with core biopsy, the de f nitive diagnosis was found necrotic with chronic suppurative in f ammation with non-speci f c in f ammation. The patient then treated with debridement sequestrectomy, f ll the gap bone of femur with bone cement with masquelet technique, gentamycin beads and external f xation (image 7).

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Image 7. (Top) Durante Operation, **(Bottom)** necrotic with chronic suppurative inflammation with non-specific inflammation

Case 3

A 60 years old male patient complained of pain in his left hip for one year ago. The patient was unable to walk for three weeks before came to the hospital. The patient had a history of thyroidectomy surgery, and the histopathological examination from his thyroid post thyroidectomy surgery showed papillary carcinoma thyroid. From his laboratory, results showed BUN/SK 33/2.4, Ca 12.8, ALP 409, CRP 2.3, PSA 7.17, Bence-Jones protein (-), PTH 1256. X-ray of the left femur (Image 8 b), pelvic (Image 8a), bone surveys (Image 9), CT scan of the left femur (Image 10) showed the lytic lesion

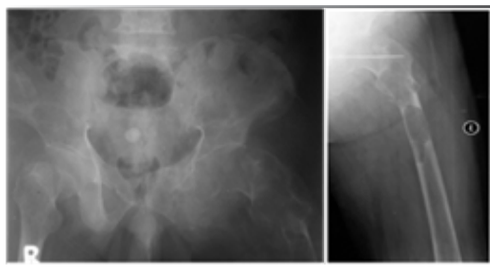

Image 8. a. Pelvic x-ray ; b. Left Femur X-ray, both a and b showed pathological fracture of the left proximal femur

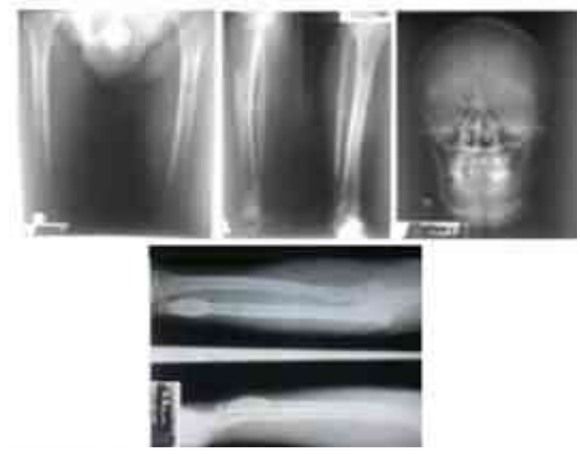

Image 9. Bone surveys showed multiple lytic lesions

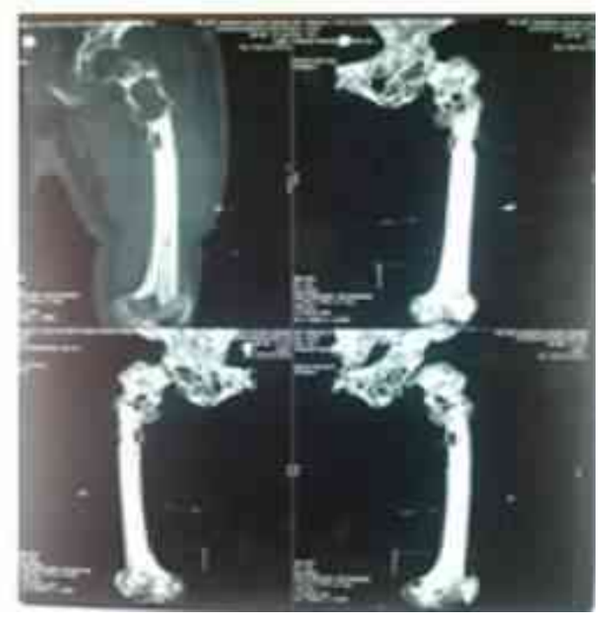

Image 10. CT scan of the left femur, showed the lytic lesions and the left proximal femur fractured

We diagnosed him as a pathological fracture of the proximal of the left femur with hyperparathyroid, and the therapy was Megaprosthesis of Left Hip. The histopathological examination of bone specimen (Image 11a) showed it was in the hypercalcemic state and no sign of neoplasm process. The evaluation of the left femur condition used the x-ray post mega prosthesis, (Image 11b) showing a good condition of the patient

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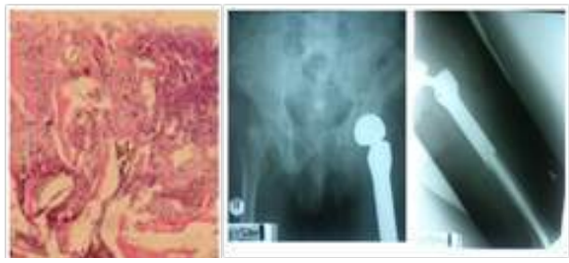

Image 11. Post Megaprosthesis of the left femur; (a.) Histopathology of the bone specimen; (b) pelvic X-Ray Post Megaprosthesis of the left femur for evaluation.

Case 4

A 19 years old male complained of swelling at his right thigh for four years ago, there were pain and warm temperature of the skin. From the physical examination of the right thigh, there was a mass size of 20x15 cm. There was tenderness, cystic, mobile warm, and smooth surfaces, also limited ROM due to the pain.

His Laboratory showed that Hb: 9,5, WBC 11.000, Plt 372.000, ESR 80, CRP 2.8, and Albumin 2.8. X-ray (Image 12) showed no deformity of the bone, while the MRI of the left knee (Image 13) showed bone abscess in the right distal femur and fuid collection in the suprapatellar region prefer to the inf ammatory process. The histopathology of the right femur specimen showed Non-Specif c Chronic Osteomyelitis (Image 14). Therefore, we diagnosed him with chronic osteomyelitis in his right femur region and gave them antibiotics for the treatment.

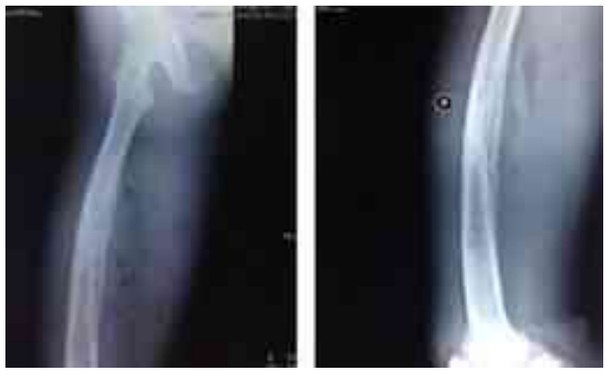

Image 12. X-ray of the right femur

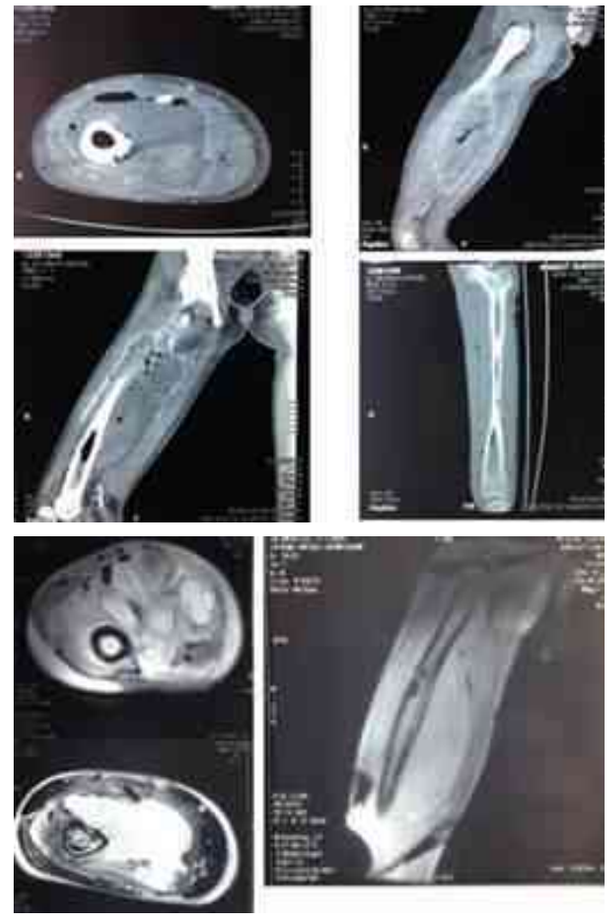

Image 13. MRI of the right femur

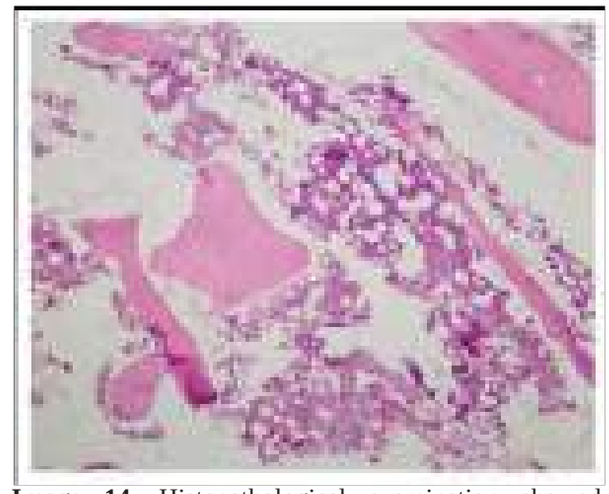

Image 14. Histopathological examination showed Chronic Osteomyelitis

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Case 5

A 15 years-old female complained of her swelling left knee for one year ago. The swelling was progressively bigger. The pain was felt especially when she was doing her knee movements. The physical examination of her left knee (Figure 15) was swelling 10x10 cm. There was tenderness, solid consistency of the swelling mass, fxed, and smooth surface of the swelling mass.

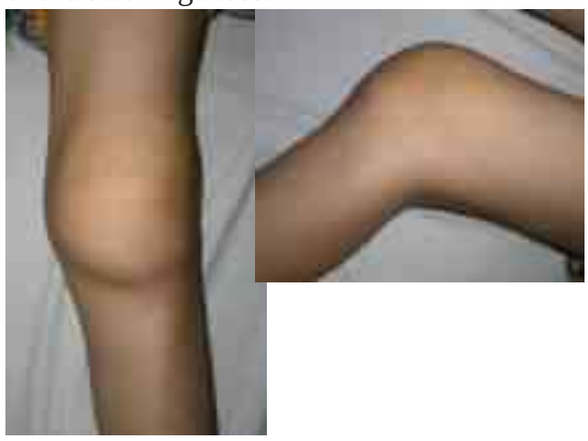

Image 15. Clinical examination of her left knee region showed swelling

The ROM was limited due to the pain. Laboratory results showed the elevation of the ESR 40-50 mm, and others were in the normal limit. X-ray of the left femur (Image 16) showed there was no sign of deformity of the bone.

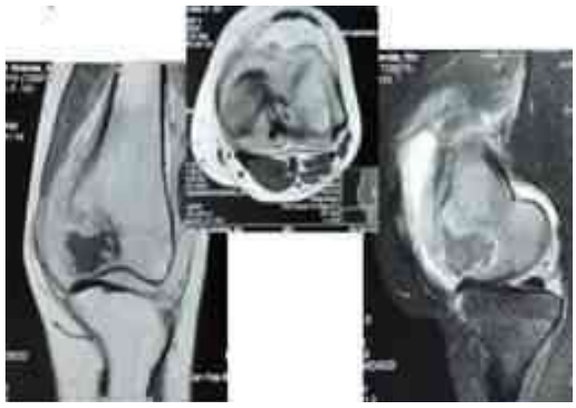

Image 16. MRI of the left knee of the patient showed bone abscess

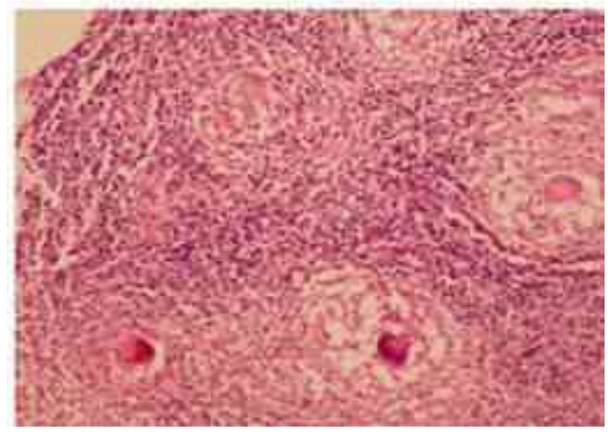

Image 17. The histopathological examination showed tuberculosis

DISCUSSION

From the frst case, the MRI result was consistent with the primary malignant tumor indicating osteosarcoma. However, the plain x-ray of elbow showing signs of the specifc infection process of septic arthritis of tuberculosis, hence by the histologically, the patient was not consistent with a primary bone tumor. With the result showing a specifc inflammation process. Therefore we can conclude that in the frst patient, even though the MRI result strongly suggested of primary malignant tumor, the other two modalities showing septic arthritis.

The second case, malignant tumor evident from plain femur x-ray obstructs the patient diagnostic. The signs are consistent with the metastatic process, the age, the lesion in lytic form. The infection process has yet to be ruled out. The bone survey showed a non-specifc chronic inflammatory process, with the periosteal reaction that could bring the diagnosis to malignancy. Osteomyelitis similar to a malignant bone tumor, both are having no specifc signs. Defning the diagnosis from the two facts are paramount in deciding the exact clinical management. But with core biopsy, we could conclude that this patient does not have a malignancy but Non-specifc chronic suppurative inflammation

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In the third case, the histopathological examination from his thyroid post thyroidectomy surgery showed papillary carcinoma thyroid, and it was in the hypercalcemic state and no sign of neoplasm process. The femur x-ray showed the lytic lesion and pathological fracture of the proximal left femur. The evaluation of the left femur condition used the x-ray post mega prosthesis showed an excellent condition of the patient.

In the fourth case, the x-ray showed no deformity of the bone, while the MRI of the left knee showed bone abscess in the right distal femur, and fuid collection in the suprapatellar region prefer to the inf ammatory process. The histopathology of the right femur specimen showed non-Speci fc Chronic Osteomyelitis (Huang et al., 2013). Therefore, the patient diagnosed with chronic osteomyelitis in his right femur region and gave them antibiotics for the treatment.

In the f fth case, laboratory results showed the elevation of the ESR 40-50 mm; others were in the normal limit. The MRI of the left knee showed that there was a bone abscess on the left distal femur and also a collection of fuid in the suprapatellar region suspected as inf ammatory processes. The histopathological examination of the left knee specimen which showed that it was Tuberculosis of the left distal femur, not a neoplasm of the bone.

The tumor-mimicking lesion in the musculoskeletal is de fned as a tumor that only looked like a tumor, due to Palpable mass, or radiologic image resembling a tumor (Miller M, 2012). In order to prove it is a true neoplasm, further diagnostic is required.

Knowledge regarding tumor-mimicking lesions will reduce unnecessary procedures (Shimose et al., 2008), relieve the patient's agitation, helps in diagnostic accuracy, and ultimately the proper management (Dirschl & Almekinders, 1993). Clinical history, underlying diseases, age, trauma, and records of surgery are required in deciding the diagnosis, Choosing the right imaging method is crucial in di f erentiating tumor-mimicking lesions from neoplasm (Rahardjo P, Utomo SA, 1998). Not rarely, the imaging leads us to believe that non-tumour is a tumor.

CONCLUSION

The proper selection of an imaging modality is important in di f erentiating tumor-mimicking lesions from true neoplasms. Pathology will conclude the diagnosis by having representative tissue (Hoch, 2011). Triple Diagnosis by an Orthopaedic Surgeon, the Radiologist, and also the Pathologist will increase the rate of proper diagnosis in di f cult cases like tumor mimics.

CONFLICT OF INTEREST

The authors con frm that there is no con fict of interest regarding the publication of this paper and signi fcant f nancial support from any company for this work that could have in f uenced its outcome.

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Case Report

Pregnancy with Myasthenia Gravis

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ABSTRACT

Myasthenia Gravis (MG) is a serious autoimmune disease, but now can be treated. Symptoms include weakness and fatigue in voluntary muscles caused by an autoantibody reaction to nicotinic acetylcholine receptor (AChR) at the post synapse of the neuromuscular junction. Pregnancy can affect autoimmune diseases so that pregnancy can aggravate MG disease. On the other hand it is also reported that pregnancy does not affect and can even improve MG disease. In this article, We report a 27-year-old woman who was diagnosed with myasthenia gravis that having a pregnancy. Initially she had no problems with pregnancy. Patients underwent pregnancy by taking the drug Mestinon four times daily and roborant. But entering the 33rd-34th week, the examination results showed that the pregnancy experienced oligohydramnios and Intrauterine Growth Retardation (IUGR), it was probably caused by malnutrition. Then we decided to end the patient's pregnancy with a Caesarean section. The operation went well, born to a baby boy / 2450grams / Apgar Score 5-7. Observation for one week the mother's condition continued to improve. Diplopia and weaknesses also improve. Likewise the baby showed a healthy condition. The patient was discharged while still taking MG drugs that had been previously consumed. This case report showed that pregnancy worsened MG disease, but MG did not affect pregnancy.

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INTRODUCTION

Myasthenia Gravis (MG) is a serious autoimmune disease, but now can be treated. Symptoms include weakness and fatigue in voluntary muscles caused by an autoantibody reaction to the nicotinic acetylcholine receptor (AChR) at the post synapse of the neuromuscular junction. The neuromuscular junction damage was first shown by Engel and colleagues in an ultrastructure study of motor endplate (Gilhus, 2016).

Pregnancy can affect autoimmune diseases so that pregnancy can aggravate MG disease. On the other hand, it is also reported that pregnancy does not affect and can even improve MG disease. A study states that 1/3 cases of pregnancy will worsen, 1/3 does not affect, and the remaining 1/3 will even improve on the state of MG disease (Téllez-Zenteno, Hernández-Ronquillo, Salinas, Estanol, & da Silva, 2004).

Myastenia crisis can occur and affect the condition of the fetus in the womb. This case reports a pregnant woman suffering from MG. For diagnosis, physical, laboratory and other supporting examinations are carried out. Furthermore, comprehensive management is carried out. Monitoring the state of the fetus while in the womb is very important, because MG can affect the growth and development of the fetus while in the womb (Hamel & Ciafaloni, 2018).

The patient was then treated with drugs for MG. Pregnancy in these patients ended with a Caesarean section at 36 weeks of gestation not because of maternal indications, but rather because of fetal indications where serial ultrasound examination began to show fetal growth disturbance accompanied by reduced amniotic fuid despite intrauterine resuscitation. The mother's condition after surgery improved. The baby was monitored after delivery, and there are no symptoms of MG. Mother and baby were sent home in

CASE REPORT

Anamnesis

A patient Mrs. M, 27 years old, came to the outpatient clinic to control pregnancy. She had three months pregnant and this was her frst pregnancy. Previously, the patient controlled in Jakarta and had been diagnosed with myasthenia gravis. For the time being, she wanted to go home to give birth in her hometown. She did not have Diabetes mellitus, asthma, hypertension, heart disease, and allergy.

Patients had weakness in the muscles since 1 year ago relapsing in both hands and feet, and could not walk since four months ago. The eyes felt heavy and partially closing. The eye closed more as the weakness in the limbs worsened. The vision appeared double, sometimes appeared vertically blurred. Other complaints were not obtained. In the past, she consumed drug Mestinon twice a day.

Physical examination

GCS: 456, Vital sign: within normal limit

Obstetric examination :

His : -

USG : Breech / Single / DJJ +

BPD : 36

CRL : 74

DJJ : + doppler

V/v : Fluxus –

Neurological examination :

Diplopia

Motoric 3 3 4 5 5 5 5 4 3 3

hypotonia

3 3 4 5 5 5 5 4 3 3

Vocal test (+)

Laboratorium Examination :

Hb : 12,2 g/dl

Leucocyte : 8870/ml

Thrombocyte : 204.000/ml

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Creatinine serum : 0,4 mg/dl (<1,2)
Potassium : 4,1 meq/l (3,8-5,0)
Sodium : 136 meq/l (135-144)
SGOT : 23 U/l (<38)
SGPT : 15 U/l (<41)
EMG : Myasthenia Gravis

Assessment

GI P_{0-0} 16/17 weeks pregnant + Myastenia Gravis

Treatment

Mestinon 4 x 1, Roboransia 1 x 1

Tabel 1. Continued Observation

	13th December 2018	15th December 2018	16th December 2018
S	contraction-, fetal movement + GCS 456,Vital sign: normal Obstetric examination : DJJ + 13-12-13 USG: H / Single / DJJ + BPD: 87,3 ~33/34 FL: 65,8 ~33/34 mgg Placenta corpus anterior /II/ AFI 9,7 ml Doppler A. umbilikalis : PI : 1,36 RI : 0,71 Non Stress Test : Baseline 130-140 Variability 2-4 FAD reactive Neurologic examination Diplopia Strength 33455 55433 33455 55433	contraction-, fetal movement + GCS 456,Vital sign: normal Obstetric examination : DJJ + 13-12-13 USG: H/ Single / DJJ + BPD: 87,3 ~ 33/34 FL: 65,8 ~ 33/34 mgg Placenta corpus anterior/II/ AFI 9,7 ml Doppler A. umbilikalis : PI : 1,36 RI : 0,71 Non Stress Test : Baseline 130-140 Variability 2-4 FAD reactive Neurologic examination Diplopia Strength 33455 55433 33455 55433	*Low Segmen Caesar Section + Tubectomy Pomeroy Bilateral* General anesthesia: Phentanyl 50 mg Morphine 2 mg Recoval 110 mg Baby boy / 2450gr / AS 5-7 20 December 2018 Motoric: 44555 55544 44555 55544
A	GI P_{0-0} 33/34 weeks + Oligohydramnion+ MG	GI P_{0-0} 33/34 weeks + Oligohydramnion+ IUGR + MG	
P	Intrauterine resuscitation USG repeated 2 days	Plan Sectio Caesarian	

Furthermore, the patient was treated for one week. The patient's condition was good. Diplopia complaints and weaknesses improved. Then the patient was discharged by continuing Mestinon 4 x 1 therapy and Methyl Prednisolone 60mg-0-0. After underwent observation, three days later, the baby was also discharged in a good condition.

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LITERATURE REVIEW

MYASTHENIA GRAVIS

Myasthenia Gravis (MG) is an autoimmune disease with symptoms of weakness and fatigue in voluntary muscles caused by an autoantibody reaction to acetylcholine receptors (AChR) at post synapses at the neuromuscular junction. MG is the most common neuromuscular junction disorder. The incidence of MG in the United Kingdom is 15 / 100,000 population with an incidence of 1.1 / 100,000 population per year (Hill, 2003), while in Virginia 1.5 / 10,000 population. MG can attack all ages but is most abundant in the 3rd decade and decades 6 and 7 (Thanvi, 2004).

The neuromuscular junction damage was first shown by Engel and colleagues in an ultrastructure study of motor endplate. The use of neostigmine, an oral anti-cholinesterase for patients with MG was first performed in 1935. Lindstrom and colleagues showed antibodies to the AChR protein in approximately 87% of MG patients. Recently found antibodies that bind to muscle specific protein kinase (MuSK), a specific protein present in muscles that can be found in patients with MG where no antibodies to AChR are found. The molecular structure of AChR and the presence of receptors in human muscles can now be studied (Thanvi, 2004). In the presence of antibodies that bind to AChR, it will cause a blockade of AChR so that it will reduce the amount of AChR that can bind to acetylcholine released from terminal nerve presynaptic (Gilhus, 2016).

The clinical picture of MG patients is a history of muscle weakness or muscle fatigue that occurs during activity and will improve with rest. Complaints will increase at dusk. Several factors will aggravate complaints, including exercise, hot temperatures, infections, emotions, some drugs (aminoglycosides, phenytoin, some local anesthetic drugs), surgery, menstruation, and pregnancy. Some of the muscles that are frequently affected by MG are the superior palpebrae levator muscle, extraocular muscles, lower movable muscles, facial muscles, and neck extensors. Ptosis due to superior palpebrae muscle weakness is usually only partial and unilateral (Gilhus, 2016).

Another complaint is the difficulty in closing the eyes, this is due to the weakness of the orbicularis oculi muscle. When the facial muscles are affected, the face will look as without expression. The mouth will always appear open and maybe the patient needs to support his jaw with a finger. The loss of sound is due to the weakness of the larynx. Voice while talking will increasingly weaker (Schwendimann, Burton, & Minagar, 2005).

The progression of muscle weakness in MG sufferers usually occurs from the top down: face → bulbar → trunkal → locomotor. Weaknesses of intercostal muscles and diaphragms can cause breathing problems when on the move even at rest. The occurrence of orthopnoea but will heal quickly on standing, and the paradoxical occurrence of the diaphragm is an important clinical sign of respiratory muscle disorders. Respiratory problems can occur suddenly in a few hours so that patients need to be monitored closely by monitoring their vital signs (Schwendimann et al., 2005).

Etiopathology Myasthenia Gravis

It is now well known that MG is a disorder caused by antibodies at the neuromuscular junction. Several explanations explain that MG is caused by an antibody process: (Thanvi, 2004)

1. Antibodies to AChR are found in 90% of patients with general MG
2. anti-AChR antibodies are found in transient MG in neonates, and their levels will decrease during the healing

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3. Passive transfer of IgG from patients with MG in mice will cause the same disease as MG.
4. Plasmapharesis will reduce the level of AChR antibodies so that it will improve the condition of patients with MG.
5. Antibodies bind to AChR at the neuromuscular junction.
6. In animal studies, MG can be caused by immunization.

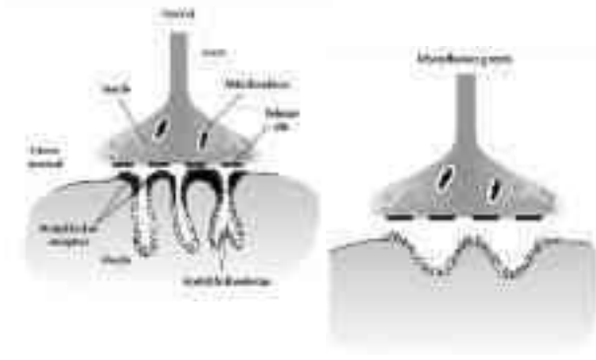

Figure 1. Neuromuscular junction normal and in MG patient (Thanvi, 2004)

Damage to AChR by antibodies caused by the mechanism:

1. Antibodies will bind to AChR with the result cause AChR degeneration of muscle cells.
2. Antibodies will block by binding to AChR
3. Complement will cause junctional fold damage from the postsynaptic membrane.

AChr antibody levels in patients with MG are not related to the severity of the disease. The gravity of MG depends on the functional activity of the antibody.

Myasthenia And Pregnancy

MG can be triggered during pregnancy or after delivery. Pregnant women with MG have several challenges in terms of treatment, so special and coordinated treatment is needed between neurologists, obstetricians, and neonatologists (Téllez-Zenteno et al., 2004).

Hormones affect autoimmune diseases. Estrogen and progesterone work by suppressing macrophages that will reduce the production of TNF-α and IL-12. High estrogen will also cause the production of IL-10. In experimental animals, estradiol (E2) will cause impaired tolerance in B cells (Yi, Guptill, Stathopoulos, Nowak, & O'Connor, 2018).

Pregnancy where hyperestrogens occur is related to the cytokine profile produced by Th2, this is important to maintain the tolerance of the mother to the fetus she is carrying. This will be different if the mother suffers from autoimmune diseases, for example in rheumatoid arthritis and multiple sclerosis, where Th1 is more dominant, the autoimmune disease will improve, but this is different for example in patients with SLE where the role of Th2 is greater, then pregnancy with conditions that are more hyperestrogens will cause lupus shock (Téllez-ZEnteno et al., 2004).

Influence Of Pregnancy In Myasthenia Gravis

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The Effect Of Myasthenia Gravis In Pregnancy

In the study, data were obtained that the effect of MG on pregnancy and childbirth was the occurrence of premature rupture of membranes and the use of obstetric measures (use of forceps and caesarean sections) was more common in patients with MG (Téllez-Zenteno et al., 2004). In pregnant women with MG the incidence of premature rupture of membranes is three times more than pregnant women who do not suffer from MG. This is thought to be possible because of treatment using corticosteroids (Bansal, Goyal, & Modi, 2018).

The Effect Of Myasthenia On New Fetal And Babies

The complication of pregnancy with MG in the fetus is the occurrence of arthrogryposis multiplex congenita (AMC) which is characterized by the occurrence of multiple contractures in the joints while the fetus is in the womb. Some cases occur due to genetic factors, but AMC is usually a complication of pregnancy in patients with MG that is thought to be caused by antibodies in the maternal circulation (Hamel & Ciafaloni, 2018). Multiple contractures occur because antibodies from the mother can penetrate the placental barrier and will attack AChR from the fetus, which will cause disruption in the movement of the fetus in the womb and will result in contractures of the fetal joints (Phillips & Vincent, 2016).

Zentenno reported an incidence of 21% occurring transient neonatal myasthenia gravis (TNMG) in newborns born to mothers suffering from MG. In this report 67% of newborns experience TNMG in the first few hours after birth and 78% experience TNMG in the first 24 hours. The occurrence of TNMG after 3 days was never reported. In MG associated with AMC, death often occurs in newborns. The mechanism that allows the occurrence of TNMG is antibodies from the mother through the placental barrier with the result of inhibition of AChR, causing paralysis in the fetus. Clinical features of TNMG look like overall muscle weakness and inadequate sucking from infants (Téllez-Zenteno et al., 2004). The severity of the mother's disease is not related to the severity of the baby TNMG it contains, TNMG can also occur in mothers with MG in the healing phase (Hamel & Ciafaloni, 2018).

Treatment Of Myasthenia Gravis In Pregnancy

Current MG treatment has very high effectiveness. Before 1958, the mortality rate was around 30% with current treatments. At present, with adequate treatment the mortality rate can be reduced to 0%. MG treatments include Acetylcholinesterase inhibitors, Corticosteroids, Immunosuppressants, Plasmapheresis, Intravenous immunoglobulins, Thymectomy. The use of drugs in MG women who are pregnant or want to become pregnant are given individually based on the severity of the disease and the distribution of muscle weakness (Bansal et al., 2018).

MG treatment can be divided into three stages, namely: (1) initial treatment, which usually uses acetylcholinesterase inhibitors. But these drugs are usually inadequate to control this disease, so additional therapy is needed. (2) Usually, direct treatment of immunological reactions

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needs to be done, starting with a thymectomy and the use of high doses of corticosteroids. (3) For long-term treatment, steroid-sparing medications need to be added at the time of steroid tappering. Short-term treatment with intravenous immunoglobulin or plasmapheresis may be effective in the early stages of treatment. (Thanvi, 2004) Plasmapharesis is safe for use in pregnant MG patients (Téllez-Zenteno et al., 2004). But in theory, plasmapheresis will increase the occurrence of preterm labor due to the loss of hormones in the circulation at the time of plasmapheresis (Bansal et al., 2018).

MG treatment using anticholinesterases and steroids did not have a significant relationship with the risk of fetal abnormalities (Téllez-Zenteno et al., 2004). Corticosteroid treatment is very effective in most MG patients and can be an option for treatment in pregnant women where immunosuppression therapy is needed to treat MG that is getting worse during pregnancy. The use of high doses of corticosteroids may be associated with premature rupture of membranes (Waters, 2019). The drug commonly used is prednisone at a dose of 1 mg / kg per day, given as a one-time dose (Chaudhry, Vignarajah, & Koren, 2012).

Because of the serious side effects of long-term use of corticosteroids, steroid-sparing immunosuppression drugs have been developed, including azathioprine, cyclophosphamide, cyclosporine, methotrexated and and new mycophenolate mofetil (Chaudhry et al., 2012). The use of immunosuppressants should be avoided during pregnancy because of its teratogenic effects (Waters, 2019). Safety of the use of intravenous immunoglobulin in MG patients who are pregnant until now there has been no report.

Thymectomy during pregnancy is out of place because with the expected effect the thymectomy is slow and increases the risk due to the surgical procedure. If there is an indication that a thymectomy is performed, it should be done before being planned for pregnancy or after delivery (Chaudhry et al., 2012).

Labor

MG usually does not affect the first phase of labor, because MG does not affect smooth muscle (Chaudhry et al., 2012), but the abdominal striated muscles. Nevertheless obstetric complications are uncommon in patients with MG. If there is muscle weakness during labor, cholinesterase inhibitors can be given intravenously, because in oral administration we cannot estimate the absorption of the drug in the digestive tract. Neostigmine can be given at a dose of 1.5 mg intra-muscular or 0.5 mg intravenously (Téllez-Zenteno et al., 2004). Surgical action on patients with MG is an act that causes very heavy stress, therefore births with sectio caesarian measures are only performed in cases that are necessary only (Waters, 2019).

DISCUSSION

In this patient the clinical symptoms that appear were muscle weakness that began one year before the patient was pregnant. The weakness felt to get heavier, along with the duration of the activity. Also visible when the patient was talking for a long time the voice will get weaker. Ptosis was found in the eye. While investigations by anti-AChR antibody examination showed normal numbers, the possibility of the patient was MG sufferers from the seronegative group. Whereas the examination of anti-MuSK antibodies is still in the research discourse, there is no commercial kit yet. Another test performed was to use electrophysiology which supported the diagnosis of MG.

The effect of pregnancy on MG varies and cannot be predicted with certainty. Approximately 1/3 of myasthenia sufferers will improve with their pregnancy and 1/3 will worsen the condition

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of myasthenia during their pregnancy, while the rest do not change the state of myasthenia. Usually, the worsening of this disease occurs in the early trimester of pregnancy and rarely occurs in the third trimester of pregnancy (Riemersma et al., 1996). It is generally thought that pregnancy is associated with immunosuppression. With the onset of depression from leukocyte function it will lead to an improvement in the condition in patients with autoimmune diseases. But some autoimmune diseases will be aggravated by pregnancy (Téllez-Zenteno et al., 2004).

In this patient, it seems that the pregnancy was exacerbating MG, because it was obtained after delivery that clinical symptoms appear to be marked by ptosis and muscle weakness improves. In infants there appears to be no motor impairment where the baby was able to breathe and suck well.

The effect of MG on pregnancy and childbirth is the occurrence of premature rupture of membranes and the use of obstetric measures (use of forceps and caesarean sections). While the influence of MG on the fetus is the occurrence of arthrogryposis multiplex congenita (AMC) which is characterized by the occurrence of multiple contractures in the joints while the fetus is in the womb. Some cases occur due to genetic factors, but AMC is usually a complication of pregnancy in patients with MG that is thought to be caused by antibodies in the maternal circulation (Chaudhry et al., 2012).

In this patient, the pregnancy problem obtained was IUGR. However, this IUGR was most likely not related to MG, but rather was caused by a lack of nutrition of the patient during pregnancy because it was recognized by the patient that she was quite stressed and worried about this pregnancy so that her appetite was reduced.

After an indication of IUGR was found in this patient, intrauterine resuscitation was initially carried out, but with serial ultrasound apparently there was no improvement in the condition of the fetus so at the age of 36 weeks it was decided to terminate the pregnancy by Caesarean section.

CONCLUSION

During pregnancy, there are significant changes in hormonal conditions where it is known that hormonal factors are associated with the occurrence of autoimmune diseases. So pregnancy can affect autoimmune diseases. Pregnancy can worsen the state of autoimmune disease.

In this case report, it was found that the pregnancy made the MG disease worse. After birth, complain of motor weakness and diplopia improved. The MG does not seem to have an effect on the patient's pregnancy. Olygohidramnions in this patient seem to be caused by low intake.

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Case Report

Collecting duct carcinoma: A rare entity

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ABSTRACT

Collecting duct carcinoma is a rare and highly aggressive subtype of renal cell carcinoma. The incidence rate is less than 1-2% of all renal tumors and usually, affect middle-aged adult, commonly in men. We reported a 76-year-old man complains of an intermittent painless gross hematuria, abdominal mass and left flank pain for approximately three months. The CT abdomen showed a slightly enhancing solid mass in the left kidney and para-aorta lymphadenopathy. Cut surfaces of the kidney showed a solid-cystic and ill-defined greyish-white tumor. Microscopically, tumor formed solid sheets and tubulopapillary structures lined by neoplastic cells, hobnailing nuclei, abnormal mitotic, and a desmoplastic stroma with lymphoplasmacytic infiltration, and the immunochemical profile were PAX8 (+) /p63 (-). Based on these findings, the diagnosis was a collecting duct carcinoma. This tumor arising from the collecting duct of Bellini in the renal medulla, accounts for less than 1-2% of all renal masses and important to be distinguished from other tumors due to differences in prognosis and therapeutic. Histopathological examination is needed to establish the diagnosis. A case of collecting duct carcinoma that occurred in a 76-year-old man has been reported. A definitive diagnosis can only be done with a detailed histopathological examination for patient management benefits.

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INTRODUCTION

Collecting duct carcinoma (CDC) of the kidney is a rare subtype of the renal epithelial cell carcinomas (RCCs), arising from the distal segment of collecting ducts of Bellini, usually located in the middle of renal sinus region. It accounts for less than l-2% of all renal masses but highly aggressive, and has a poor prognosis. They can a f ect the age range 13-83 years old with a mean age of 55 years, and there is a 2:1 male predominance. Due to its rarity, the tumor is still limited understood (Ciszewski, Jakimów, & Smolska-Ciszewska, 2015; Albadine et al., 2010; Harbin, Styskel, Patel, Wang, &Eun, 2015).

In these past two decades, paradigms that developed in the e f ort to classify pathological morphologic subtypes are aimed at the better understanding molecular origin, clinical behavior, similarities, and di f erences between RCC variants with the hope providing clinical and therapeutic opportunities to improve patient care (Shuch et al., 2015).

CASE REPORT

A 76-year-old man experiences intermittent painless gross hematuria for three months. The patient had a recent onset left f ank intermittent pain since one-month before admitted, also a history of gradual weight loss and decreased appetite for two months. A mobile palpable mass in the upper left abdominal quadrant, measuring 7x5 cm, was found during the physical examination. CT-scan with contrast at abdomen showed a slightly enhancing solid mass in the left kidney, measuring 7x6x6 cm, and para-aorta lymphadenopathy, 3.4x4.2 cm in size. Other clinical and laboratory f ndings were within normal limits. The patient underwent the left radical nephrectomy.

The resected left kidney was enlarged, measured 10x7.3x5 cm. On gross examination, the renal surface was smooth and adherent to perinephric fat. The cut surface showed an ill-de f ned greyish-white tumor, f rm in consistency, solid with a few cystic areas, measuring 7x6x6 cm, which located in the middle and lower poles predominantly involving the medulla, with minimal hemorrhages or necrosis. The tumor was seen invading the capsule and extending into the perinephric fat. The hilus was uninvolved.

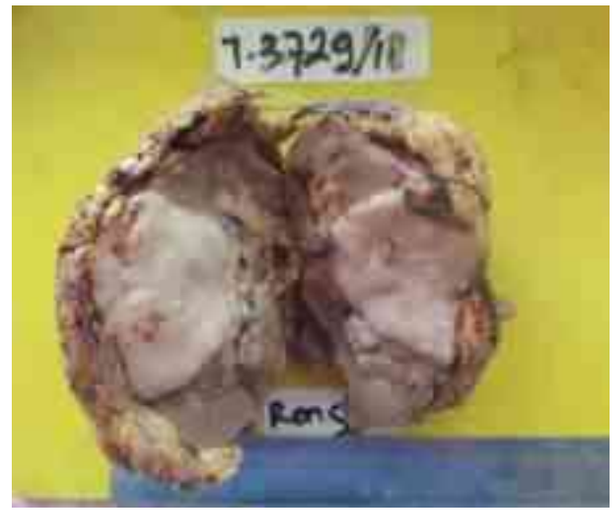

Figure 1. The rejected left kidney. Cut section showed an ill-de f ned greyish-white tumor (white arrow), solid-cystic (arrows head) minimal hemorrhages, measuring 7x6x6cm, located in the renal medulla. Renal surface smooth covered by fat (yellow arrow). The tumor invades to perinephric fat (blue arrow). (Source: Author, 2018)

Microscopically, the tumor formed solid sheets and tubulopapillary structures lined by proliferation of round to polygonal neoplastic cells with pleomorphic vesicular nuclei, prominent nucleoli, and eosinophilic cytoplasm. Many abnormal mitotic f gures were noted. The intervening stroma was desmoplastic with moderate lymphoplasmacytic in f ltration. A few tubules were also seen lined by atypical cuboidal cells with evidence of hobnail nuclei. The tumor cells showed nuclear expression of PAX8 but were stained negatively for p63.

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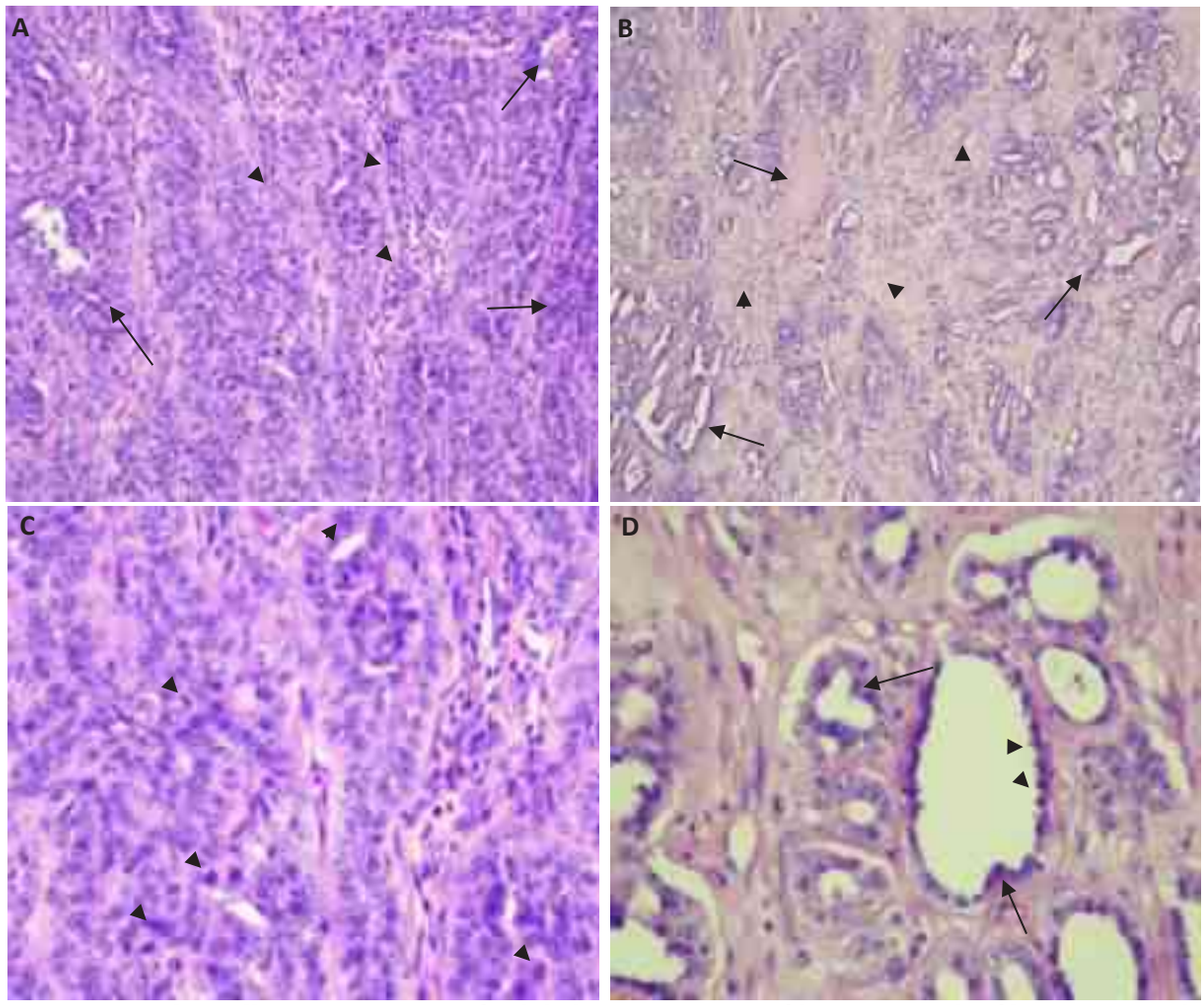
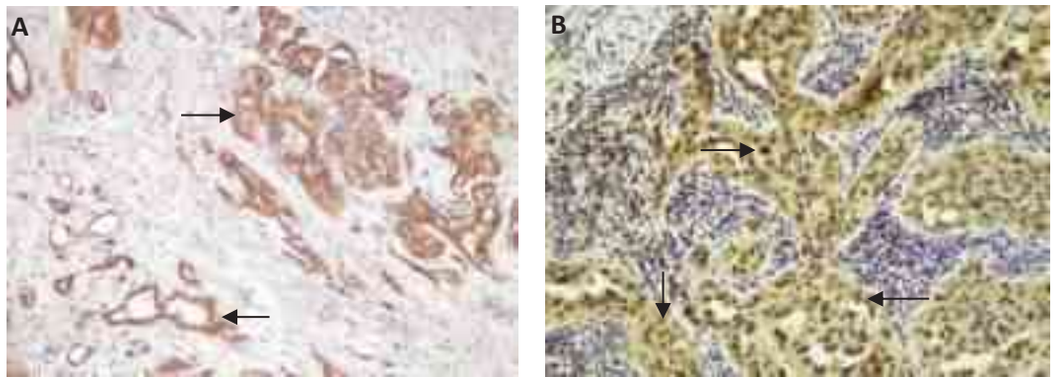


Figure 2. Histologically. A. Formation of solid sheets (arrows), infiltration into the fibrous stroma that infiltration by lymphoplasmacytic cells (head arrows, x20), B. Predominantly tubulopapillary structures (arrows), sometimes content material like mucin, with reactive stromal desmoplastic (arrowhead, x20), C. A few of abnormal mitotic figure (head arrows) (x20), D. Tubules lined by high-grade eosinophilic, basophilic cells (arrows) with hob-nail nuclei features (arrows head, x40). (Source: Author, 2018)



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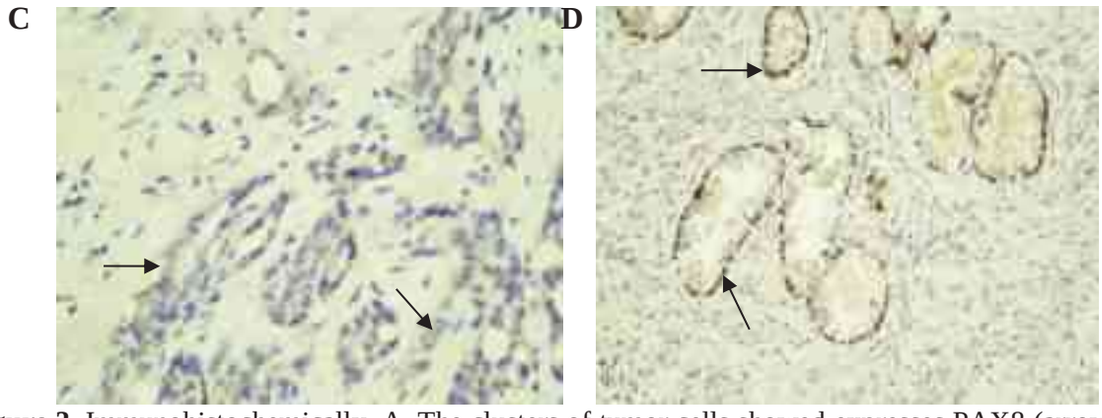

Figure 3. Immunohistochemically. A. The clusters of tumor cells showed expresses PAX8 (arrows, x20), B. Positif stained for PAX8 at nuclei of tumor cells (arrows, x40) C. Nuclei of tumor cells not express p63 (arrows, x40) D. p63 control: showed positive stained at basal cells nuclei of the ducts (arrows, x20) (Source: Author, 2019)

DISCUSSION

Many factors are believed to be related to the risk of kidney cell carcinoma such as demographics, smoking, the use of fenacetin, obesity, lack of physical activity, exposure to industrial or environmental agents, hypertension, hyperglycemia and hyper-triglyceridemia, and also blood concentrations of vitamin D-binding protein (VDBP). The risk of RCC increases in obesity, approximately 20-35% higher for every 5 kg /m2 of higher BMI (Petejova & Martinek, 2016).

CDC is de f ned as a malignant epithelial tumor arising from the lining cells of the collecting ducts of Bellini in the renal medulla. This is di f erent from most RCCs, which occur due to malignant proliferation of the proximal tubular of nephron cells, and from urothelial carcinoma (UC) which arises from the transitional epithelium lining of the mucosa of the bladder, renal pelvis and ureters (Mishra, Manikandan, Dorairajan, Mittal, & Rekha, 2016).

Fleming and Lewi frst introduced CDC in 1986 as a new entity that di f ers from other subtypes of renal cell cancer. The study by Pepek and colleagues found that the incidence rate was only 1-2% of all renal tumors, generally a f ected people ages 13-83 years with an average age of 55 years. The male to female incidence ratio is 2:1 and found mostly in white patients, African-American, and some other races (Seo, Yoon, & Ro, 2017; Harbin et al., 2015; Mishra et al., 2016).

Similar to our case, most of patients complain some symptoms such as hematuria, f ank pain, palpable abdominal mass or distant metastases, weight loss, but some cases might be asymptomatic (Harbin et al., 2015; Liu J, Li Y, Su Z, Duqun Chen, Ni L, Mao X, 2016; Albadine et al., 2010). Usually, polycythemia (erythrocytosis) in patients with RCC is caused by the production of ectopic erythropoietin by cancer cells. Symptoms such as fever, weight loss, and general fatigue in many malignancies, are thought to be mediated by cytokines, especially TNFα and IL-6 (Petejova&Martinek, 2016). More than 30% of CDC patients present with metastasis at the time of diagnosis, most commonly in regional lymph nodes (about 80% of cases), lung, adrenal gland, and liver, and about 60-70% of them die within a two-year period (Muglia &Prando, 2015; Dall'Oglio et al., 2008; Wu, Zhu, Zhu, Chen, & Wang, 2015).

The literature mentioned that on the CT-Scan

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examination, the tumor is usually located in the medullary, with weak enhancement (hypovascular pattern), renal sinus involvement and infiltrative growth pattern. It usually still maintains the renal contour and has cystic components. The para-aortic lymphadenopathy is also indicated (Mishra et al., 2016). The hyperdense appearance of tumors on unenhanced CT refers to a minimal intratumor hemorrhage (haemosiderin deposition) (Wu et al., 2015). These findings were also found in our case.

In this case, macroscopically, tumors are generally firm, gray-white, with poor margins but without extensive necrosis or hemorrhage. The tumor invasion into perirenal fat was found. The presence of tubular or tubulopapillary infiltrative patterns, intense stromal desmoplasia, and infiltration of chronic inflammatory cells in and around tumors, help to establish a definitive diagnosis. The tumor cells usually moderate to severe eosinophilic, basophilic, or amphophilic nuclear pleomorphism and mitosis, with hobnails nuclei feature. Lymphovascular invasion can be seen, and metastases can occur in regional lymph nodes, bones, adrenal glands, lungs, and skin (Konjengbam & Singh, 2017; López, Larrinaga, Kuroda, & Angulo, 2015). The other patterns include a variable admixture of solid cords, sheets, papillary formations, and cystic dilated spaces. The tubules, glands, or cysts showed focal to prominent intra-luminal basophilic to amphophilic mucin in other cases (Gupta et al., 2012).

The guidelines for diagnosing CDC are based on the criteria established by the International Society of Urological Pathology (ISUP) on the conference of renal neoplasia in Vancouver 2013, and the WHO classification 2016, as follows: (1) at least a portion of tumors involving the medullary region, (2) formation of dominant tubules, (3) desmoplastic stromal reaction, (4) high-grade features, (5) infiltrative growth patterns, (6) and no other RCC subtypes or urothelial carcinomas were found (Seo et al., 2017; Harbin et al., 2015).

CDC needs to be distinguished from other renal neoplasms such as papillary renal cell carcinoma, renal medullary carcinoma, and high-grade urothelial carcinoma, also the possibility of metastatic carcinoma, especially from GIT. Papillary RCCs usually shows a well-demarcated lesion on a cut surface, yellow or brown color, and lack of stromal desmoplasia on the histological feature. Immunohistochemically, papillary renal cell carcinoma shows frequent positivity for CK7 and, occasionally, CD9 (Konjengbam& Singh, 2017). Renal medullary carcinoma commonly shows islands of anastomosing tubule, and cords forming irregular microcystic spaces and usually occur in young black patients with sickle cell trait, with a different history and age of patients, and the INI-1 retention is strictly able to rule out the possibility of medullary carcinoma (Konjengbam & Singh, 2017; Zheng et al., 2017; Gupta et al., 2012).

Although the CDC behavior and immunohistochemical properties are similar to urothelial carcinoma (UC), both have a distinct genetic pattern. The cytogenetic profiles of the CDC are associated with the chromosomal DNA losses at 8p, 16p, 1p, and 9p, and gains at 13q (Shuch et al., 2015; Harbin et al., 2015; Petejova & Martinek, 2016). Both macroscopically and microscopically, the invasive UC growth pattern gives an appearance similar to the CDC. The UC mostly forms nests and cell cords, pseudo-glandular patterns, and squamous metaplasia, and in particular, shows intraepithelial neoplasia in the pelvic mucosa, which is not found in CDC cases (Kobayashi et al., 2008). As the CDC tumor cells spread in the cortical collecting tubule, the lesion develops characteristics similar to those of upper tract urothelial carcinoma (Jung, Oh, & Shin, 2017). The high-grade UC does not express p63 and GATA-3 (Konjengbam& Singh, 2017; Zheng

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et al., 2017) Most CDC tumor cells express PAX8, High Molecular Weight Cytokeratin, sometimes also CK7, and strongly positive for epithelial membrane antigen (EMA), focal reactive with vimentin, but they do not express CK20, CD117, CD10, GATA3 and p63 on immunohistochemistry staining (Hu et al., 2015; López et al., 2015; Zheng et al., 2017).

PAX8 is consistently positive towards the CDC, normal collecting ducts, and differentiating nephrons. Immunohistochemistry is particularly useful in the differential diagnosis, where panels of GATA3, p63, and PAX8 are good guidelines for differentiating the CDC from invasive urothelial carcinoma. When the tumor showing immune-profile PAX8 (+) / p63(-) and/or GATA3 (-) are favor to CDC, while a profile of PAX8 (-)/p63 (+) and/or GATA3 (+) tends to UC diagnosis (Seo et al., 2017; Harbin et al., 2015). A research by Albadine and colleagues found all 21 (100%) CDCs were positive for PAX8, and p63 was positive in 3 of 21 (14%) CDC cases (PAX8 + / p63 +). In CDC lesions with urothelial differentiation, it can be observed that the tumor cells express p63 focally (Albadine et al., 2010)

As in our case, that immunohistochemical staining shows tumor cell positivity for PAX8 and negative for p63 (PAX8 + /p63 -), where this scenario has a specificity of 100% and a positive predictive value of 100% in the diagnosis of Collecting Duct Carcinoma (Jung et al., 2017).

Current treatment options for CDC are based on standards set for renal cell carcinoma, but due to their aggressiveness and also with metastasis, the intervention such as cytoreductive nephrectomy is less useful for the survival of this case and more suitable for the management of RCC cells (ccRCC), which is known resistant to systemic chemotherapy (Sui et al., 2017). Majority of CDC with metastases have a very poor prognosis, but pathological similarities with UC are the main reason to use sophisticated chemotherapy agents such as Gemcitabine plus Cisplatin; therefore CDC may be chemosensitive/radiosensitive (Sui et al., 2017; Kawaguchi, Ito, Shimazaki, & Asano, 2017).

Pathological diagnosis is needed to establish a definitive diagnosis of the CDC, but imaging techniques can help to lead to early diagnosis (Harbin et al., 2015). To increase the survival rates, it is important to establish an early diagnosis, treatment, and surgery performed on patients with organ limited small tumors (Ciszewski et al., 2015).

CONCLUSION

A case of collecting duct carcinoma that occurred in a 76-year-old man has been reported. Collecting ductal carcinomas is a rare entity that must be distinguished from other renal neoplasms because of the differences in prognosis and therapy. A definitive diagnosis can only and must be done with a detailed histopathological examination for patient management benefit.

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Case Report

Synovial chondromatosis in woman with symptoms mimicking early stages osteoarthritis

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ABSTRACT

Synovial chondromatosis is a case that rarely found epidemiologically. It is a process which is benign in the synovial lining of joints, synovial sheaths, and bursae. It is the metaplastic process of synovium, which converts it into the cartilage and gets detached to become a loose body. Methods of this study are describing a case report of patient of Airlangga University Hospital that has synovial chondromatosis. A 38 years old woman, with a one-year history of pain, edema, and restriction of the left knee joint. Patient symptoms were insidious in onset, which gradually progressed. Decreased range of motion of her knee. The symptoms were mimicking of osteoarthritis. Considering the extensive involvement with multiple nodule masses inside the knee joint, we planned surgical management and open procedure. Total synovectomy was done, synovium and the masses were sent for histopathological examination which con f rmed the diagnosis of synovial chondromatosis. In our case, the patient has clinical symptoms mimicking osteoarthritis of genu. Some study reported similar cases. Although synovium osteochondromatosis is a rare case and it should be kept as a di f erential diagnosis with chronic knee pain with swelling. Synovial chondromatosis is a rare case in the orthopedic patient. Diagnosis of synovial chondromatosis is often made following a thorough history, physical examination, and radiographic examination and histopathologic. In our case report, we present synovial chondromatosis in woman mimicking osteoarthritis. Patient treated by surgical removal of the loose bodies

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INTRODUCTION

Synovial chondromatosis is a benign process involving the synovial lining of joints, synovial sheaths, and bursae. Its synovium becomes metaplasia, which changes over it into the cartilage and gets segregated to ended up as a loose body (Ho and Choueka, 2013).

It is found more often in men than women, about two to four times more frequent, happening at any age group, most frequently between the third and fifth decades of life (Wolfgang, 2011). All joint can be affected by synovial chondromatosis , but the knee is the most frequent site to be affected about 50-65% from the total cases, followed by elbow, hips, and shoulder in decreasing order of frequency (Terazaki, 2014). The disease is commonly mono-articular. Pain is usually the main complaint from the patient, followed by swelling, effusion, crepitus, and restriction of movements that were found in physical examination (Mackenzie & Gulati, 2010).

The purpose of this case report is reporting synovial pathology, which followed by early stages OA required total synovectomy and debridement and physiotherapy.

CASE REPORT

A 38 years old woman with a year history of pain, edema, and restriction of the left knee joint. Patient symptoms were insidious in onset, which gradually progressed. There was a history of trauma eight years ago at her left knee, then she felt pain in that time, but the pain is gone not long after the injury. A year ago, the symptom appeared, the pain came when the patient did some activity, especially when she works as a chef at her restaurant which needs a long time standing. The pain subsided when the knee is flexed, and she took a rest. Edema knee sometimes appeared at her knee. It also subsided by taking some rest. In the past few months, the patient said that it was hard for her to extend her knee. The patient also complained about having a fever for a couple of days since a year ago.

Body mass index of this patient is overweight (BMI=27,3). On Inspection, her left knee was edema, and quadriceps muscle of her left leg was wasted. On palpation, effusion was present and felt warm. There was also crepitus at the anterior of the knee. Multiple mass palpated at the anterior of the knee measured each 0.5 x 0.5 cm. Diffuse tenderness was found all around her knee. Range of motion of her left knee was still normal, but she felt severe pain when we extend the knee. Instability tests were negative, and there was no abnormality upon examination of distal neurovascular status.

Multiple calcifications in suprapatellar, infrapatellar recess and fossa popliteal were found in plain X-ray of the left knee joint. Osteophytes also found in lateral et medial condyles, margo posterosuperior, and inferior patella. CT scan shows multiple intra-articular calcified loose bodies.

Considering the extensive involvement with multiple nodule masses inside the knee joint, we planned surgical management and open procedure. A medial parapatellar incision was done, and the knee joint was exposed. Multiple nodule masses were found inside the joint capsule around 0,5 x 0,5 cm. The masses had an irregular border and cartilaginous consistency. Total synovectomy was done, synovium and the masses were sent for histopathological examination which confirmed the diagnosis of synovial chondromatosis. Postoperatively patient was instructed about knee mobilization and strengthening exercises and followed up at one, three, and six months.

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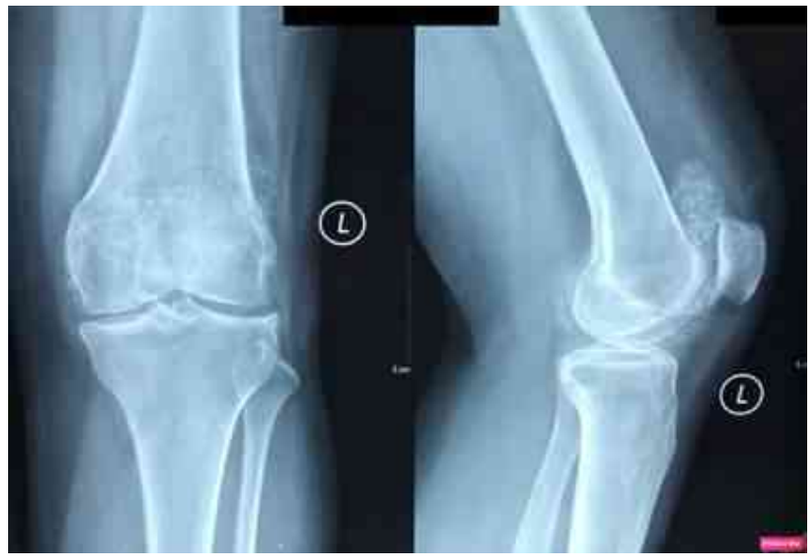

Figure 1. X-ray of left genu

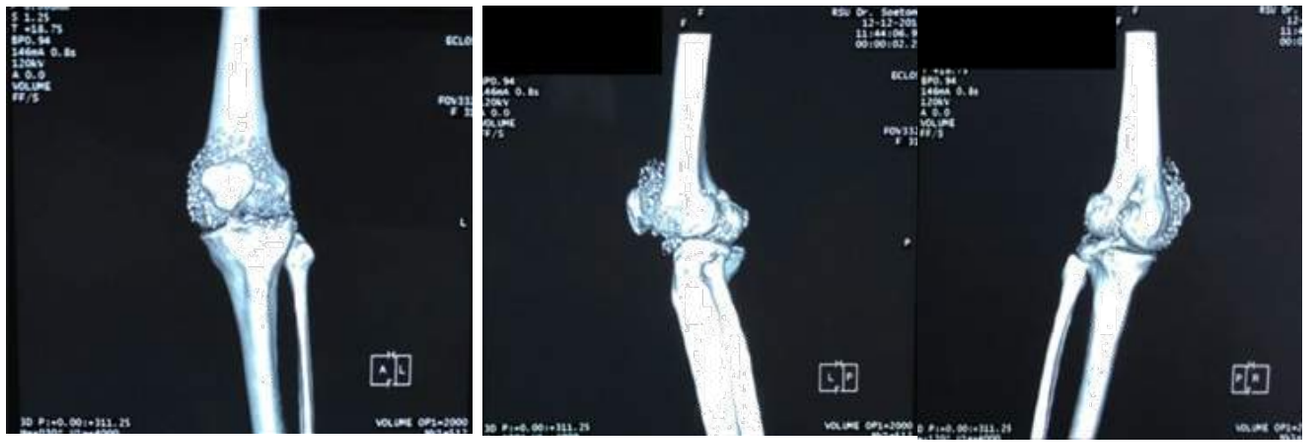

Figure 2. CT-scan of left genu

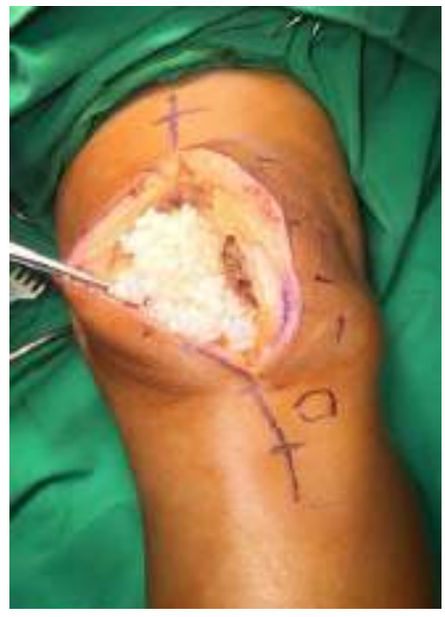

Figure 3. Synovial chondromatosis durante op

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DISCUSSION

Synovial chondromatosis is a metaplasia process involving the synovial lining of joints, synovial sheaths, and bursae which can occur with trauma or without trauma. It can be divided into two forms, primary and secondary forms; the primary form is uncommon, has unknown causes, and generally monoarticular (Wolfgang,2011). Synovial chondromatosis can a f ect all joints, but the knee is the most frequent site to be a f ected (Terazaki,2014). The secondary form is a more common condition caused by mechanical injury of the intraarticular hyaline cartilage triggered by joint anomalies such as osteoarthrosis, osteonecrosis, osteochondritis , neuropathic osteoarthropathy, trauma, and rheumatoid arthritis. When found in elderly patients, it generally involves multiple joints and may be related to degenerative joint disease, more frequently in the knees, hips, and shoulders (Shaaibu et al., 2018).

Synovial chondromatosis presents with decreased range of motion, palpable swelling, e f usion, crepitus, and locking of joints. The disease can be intra-articular and extra-articular; the form which involves bursae, tendinous sheath, and surrounding soft tissues are rare (Sarangi and Kumar, 2017).

The main cause of this disease is unknown, but the pathophysiology is cells in the synovial membrane become metaplasia, they become look like chondroblast and produce a deposit of cartilage tissue within the membrane. Cartilaginous deposit become vascularized and then become ossi f ed. While osteochondral grows, it becomes pedunculated, and loose from the synovial membrane to be free bodies in the synovial cavity and becomes osteochondral loose bodies. The ossi f ed nucleus has been died because of losing its blood supply but remains in its co f n of cartilage. The cartilaginous being nourished by synovial f uid, then it survives and grows (Salter, 1999).

History taking, physical examination, and radiographic examination are very important to make the diagnosis of this disease. Many conditions can mimic synovial chondromatosis like Pigmented villonodular synovitis, synovial hemangioma, and lipoma arborescent (Shearer, 2007). It can be di f erentiated between them with radiological and pathological examination. Characteristically, radiographs show evenly distributed innumerable intra-articular calci f cations of similar shape and texture throughout the joint space. Typical “dot-and-comma/ring-and-arc,” “popcorn-like” pattern of mineralization is common signifying chondroid origin. On ultrasonography, synovial chondromatosis shows heterogeneous mass containing foci of hyperechogenicity with or without posterior acoustic shadowing depending on the mineralization or endochondral bone formation. CT scan is the optimal imaging modality for detection and characterization of calci f cation and extrinsic erosion of bone. Histological examination of the synovial tissue is the de f nitive diagnosis (Sarangi, 2017).

The extent of the disease and the presence of osteoarthritis also presented a challenging management problem. The combination of synovial chondromatosis and degenerative arthritis is a common f nding in the advanced stage of the disease. Primary synovial chondromatosis over time can lead to cartilage degeneration by mechanical wear via the loose bodies and through nutrient deprivation to the articular cartilage. However, degenerative arthritis can lead to secondary synovial chondromatosis (Ackerman, 2007).

Surgical management is the main treatment for synovial chondromatosis. Open and arthroscopic procedures can be used to treat this condition. Synovectomy gives better results as compared to loose body removal alone. Total

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knee arthroplasty is also an option if synovial chondromatosis is coexistent with osteoarthritis. Complications of synovial chondromatosis can be secondary osteoarthritis, malignant transformation, and recurrence (Kukreja, 2013).

In our case, the patient has symptoms mimicking osteoarthritis of genu. Pain increases while she is inactivity when fexed and extend the knee. There is also edema sometimes. Her BMI is overweight, and from radiograph also found narrowing joint space. There is also a case reported with similar symptoms by Shaaibu A et al. in 2018. The pain also aggravated with weight-bearing activity, long-distance walking. But from radiograph, they found not only joint space narrowing but also multiple ossi fed loose bodies. In their case, the patient also treated by surgery. Grace M. et al., 2018 also reported a similar case. At this point, the clinical message that we can get is before we diagnose a patient, osteoarthritis in our case, we have to think about any other cause and also the epidemiology. Although synovium osteochondromatosis is a rare case, it should be kept as a di f erential diagnosis with chronic knee pain with swelling.

CONCLUSION

Synovial chondromatosis is a rare case in the orthopedic patient. Diagnosis of synovial chondromatosis is often made following a thorough history, physical examination, and radiographic examination and histopathologic. In our case report, we present synovial chondromatosis in woman mimicking osteoarthritis. Patient treated by surgical removal of the loose bodies followed by total synovectomy.

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