



## LITERATURE REVIEW

# Effect of viral, reservoir, host, and environmental factors on viral evolution that affect morbidity and mortality of COVID-19 disease

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### ABSTRACT

The COVID-19 pandemic has been going on for more than two years. The number of sufferers of this disease continues to increase as well as those who die. The number of disease and death cases varies in each country and even in one country in certain seasons and certain tribes. This is triggered by the evolution of viruses that create new variants with different virulences so that they can affect the transmission of the COVID-19 virus. Several factors can trigger the evolution of the virus, one of which is the ability to mutate to create new variants and/or new strains that cause differences in morbidity and mortality due to early COVID-19 strains. Other factors that favor viral evolution are the reservoir, host immunity, and extreme environmental conditions. This is supported by differences in the percentage of morbidity and mortality in various countries. This literature review aims to determine the effect of viral, reservoir, host, and environmental factors (season and rainfall, temperature, sunlight, materials around the environment, animal habitat, water, and wastewater) on the evolution of viruses that affect morbidity and mortality in COVID-19 disease.



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### INTRODUCTION

The COVID-19 pandemic emerged due to the coronavirus, which was first detected in the Chinese city of Wuhan at the end of 2019 (Jia & Gong, 2021). This coronavirus is a zoonotic type, and bats are considered the first reservoir of the virus. The virus that causes COVID-19 is called SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) (da Silva et al., 2021). The morbidity and mortality of the first coronavirus case in China (in December 2019) were different in several countries during the pandemic. This difference indicates that the virus mutates and gives rise to new variants (Banoun, 2021). Variant B.1.1.7 is found in the UK, B.1.351 in South Africa, and P.1 in Brazil (Jia & Gong, 2021).

Some researchers and journals estimate that this virus had spread and mutated before the pandemic emerged. Several studies in 2020 analyzed the alleged spread of this virus in early October 2019, or even earlier, before the first cases of this virus appeared. The circulation of this virus was accompanied by the evolution and mutation of the virus. Still, the virus was not detected because, at that time, the virus had not yet caused disease (Banoun, 2021).

The time required for the evolution of the virus into a virus that is pathogenic to humans and causes the disease is still not known. However, an epidemiological approach can explain what factors can trigger the evolution of a virus to become more dangerous or not. Control of these factors can prevent future outbreaks and reduce morbidity and mortality when an epidemic occurs. These factors are viral, host, reservoir, host, and environmental.

### Virus characteristic

The COVID-19 virus belongs to the Coronaviridae family and is named SARS-CoV-2 because of its 79% similarity in genome structure to the 2003 SARS-CoV virus. (Ha, John, & Zumwalt, 2021). Coronaviruses are a family of enveloped positive-sense RNA viruses (V'kovski et al., 2021). RNA viruses have the ability to replicate and evolve rapidly, which causes the emergence of new variants continuously (Jaag & Nagy, 2010). The ability of these RNA viruses to trigger an increase in mutations of up to a million times, and these mutations correlate with increased virulence and evolutionary ability (Duffy, 2018). One of the evolutionary capabilities of RNA viruses is the ability to recombine RNA. This ability also facilitates viruses to attack new reservoirs or host species, increases virus resistance and forms new strains/variants (Jaag & Nagy, 2010; Duffy, 2018).

These variations/mutations cause different levels of infectivity. In Europe, from March to April, there was a decline in the number of people with and deaths from the virus. The virus is thought to have evolved into a benign strain since late May 2020 (Banoun, 2021). Three viral components have been identified as contributing to the virulence and pathogenicity of SARS-CoV-2 (Alsobaie, 2021):

#### 1) *RBD protein S*

The receptor-binding domain (RBD) on the SARS-CoV-2 S protein must bind to the host cell's ACE2 receptor for docking and entry. The binding between RBD and ACE2 is the initial stage of virus transmission from one species to another (da Silva et al., 2021). The SARS-CoV-2 S protein has a stronger binding affinity

compared to other coronaviruses caused by previous outbreaks (SARS-CoV and MERS-CoV), so the morbidity and mortality rates caused by SARS-CoV-2 are also higher during the pandemic (Alsoabaie, 2021).

### 2) Different types and functions of accessory proteins and nonstructural proteins

Accessory proteins ORF33a, ORF8b, ORF6, and E, play a role in the innate immune system, namely the NLRP3 inflammasome, which triggers the secretion of proinflammatory cytokines. Many protein accessories' functions are unknown (Alsoabaie, 2021).

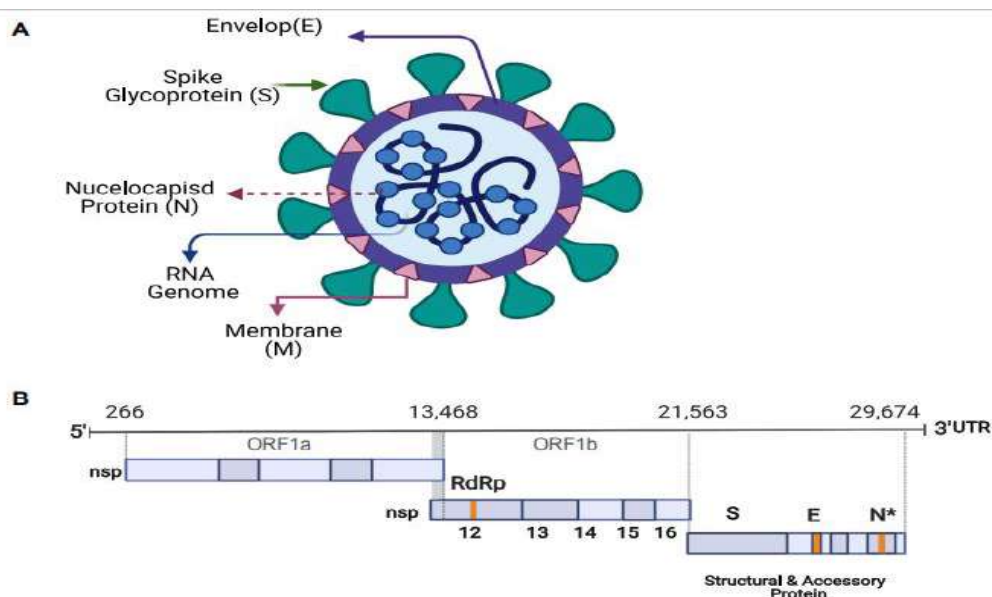
### 3) Polybase cleavage site

The addition of polybase sites at the S1 and S2 junctions can alter the virulence of the virus, but it has not been shown whether it increases or decreases SARS-CoV-2 transmission (Alsoabaie, 2021).

The illustration of SARS-CoV-2 below shows the shape pattern of the virus in relation to the

role of viral components in viral pathogenicity. The SARS-CoV-2 viral RNA complex also triggers a high virus mutation rate.

The emergence of new variants was triggered by two factors: the low fidelity of RNA-dependent RNA polymerase (RdRp) and the high ability of RNA recombination. Coronavirus has a high mutation rate due to its low RdRp precision. The extremely high mutation rate allows the coronavirus to evolve according to new environmental stresses and changes, i.e., adapt to different environments. In the case of coronavirus, mRNA synthesis occurs discontinuously, replicative RNA complexes are located within the genome, and high template turnover during replication triggers recombination events. All these factors give more plasticity to evolve (da Silva et al., 2021). The mutation rate of viruses is much higher than that of other organisms. This ability is especially true in RNA viruses such as SARS-CoV-2 because the hydroxyl group in the genome serves as a catalytic group for



**Figure 1.** (A) SARS-CoV-2 illustration. (B) the open reading frame (ORF)1a/b is composed of 16 non-structural proteins (nsp1–16) and RNA-dependent RNA polymerase (RdRp) (Source: Alsoabaie, 2021).



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mutations. This high mutational ability in COVID-19 affects virus virulence and can make the virus more virulent than the initial COVID-19 strain. The molecular epidemiology approach allows researchers to determine specific variants and integrate their transmission. It can be an essential tool in controlling outbreaks (Ansori et al., 2020).

### Reservoir

Bats are animals that were first suspected of being a reservoir of the coronavirus. This virus is carried by reservoirs and transmitted to humans or other animals that have close contact with humans (pets or pets for consumption of food sold in the Chinese market) (Valencak et al., 2021). Genetic viral mutations occur during the transmission process in animals and produce new variants through recombinant mechanisms. This new variant can adapt and cross species boundaries. Genetic mutation in RBD protein S, polybasic sites, and functional roles of accessory proteins play a role in trans-species transmission (Alsobaie, 2021), and this happened in the case of the SARS-CoV and MERS-CoV pandemics (Wu, Chen, & Chan, 2020; Shereen et al., 2020).

The coronavirus isolated from the Malay pangolin had amino acid similarities in E, N, and S proteins by 100%, 98.6%, 97.8%, and 90.7% compared to SARS-CoV-2 (Xiao et al., 2020). Another study found that SARS-CoV-2 RBD amino acid similarity to pangolin coronavirus was higher (97.4%) bat coronavirus (89.2%) (da Silva et al., 2021). This information suggests that pangolins may be an intermediate reservoir for SARS-CoV-2 (Xiao et al., 2020).

Some data have found that SARS-CoV-2 infects mammals and other bird species, including livestock and pets (V'kovski et al., 2021). Data show that there are types of

animals infected with SARS-CoV-2, but not all infected species are symptomatic (da Silva et al., 2021). Some data have found that SARS-CoV-2 can replicate and cause symptoms in ferrets and cats and is transmitted through the respiratory tract, but the virus does not replicate in dogs, pigs, chickens, and ducks (Shi et al., 2020). Infected animals can trigger new strains of the virus and possibly spread these new strains to other people or animals (Valencak et al., 2021). A study in 2021 found that mink infected with the virus by humans or other reservoir animals can transmit the virus back to humans (Prince et al., 2021). The above report indicates that mammals are the species most likely to bridge the entry of the COVID-19 virus in humans. This information can be a strategy to prevent future transmission of COVID-19 and other coronaviruses (Rothan & Byrareddy, 2020).

### Host (human)

COVID-19 infection has spread globally, but Europe and American countries had higher morbidity and mortality rates from December 2019 to April 2020 (European Centers for Disease Prevention and Control, 2020; Garg et al., 2020; Sarangarajan et al., 2021). Differences in mortality and morbidity in various ethnicities indicate that the infectivity of the COVID-19 virus is different in certain ethnicities (Ha et al., 2021). Several studies have tried to analyze the host factors that influence differences in the morbidity and mortality of COVID-19 among specific populations. They can even prevent the spread of new virus variants (Sarangarajan et al., 2021).

A person infected with COVID-19 cannot transmit the virus directly to other people. The infectious dose of COVID-19 is still unclear, but the viral load of the infected patient's sputum is  $10^8$  copies/mL. Viral load increases at the onset of infection up to 12 days after the onset of symptoms, so COVID-19-positive patients can transmit the virus for about two weeks



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after initial symptoms appear (Wu et al., 2020). Angiotensin-converting enzyme 2 (ACE2) is the main receptor that binds to the COVID-19 virus, and infection causes decreased ACE2 expression. The binding of COVID-19 to ACE2 may enhance the response to ACE and Angiotensin II signaling and is further enhanced by genetic polymorphisms in ACE, where the effect is on COVID-19 symptoms. The presence of ACE polymorphisms in certain ethnic groups plays a role in increasing morbidity and mortality in these ethnic populations due to COVID-19, for example, in the African-American race (Sarangarajan et al., 2021). Comparative rates of COVID-19 infection in the main black country are three times higher than in the largest white country (Ha et al., 2021). An *in silico* study examining the variability of human ACE2 found polymorphisms that could make these individuals more susceptible or protect them from SARS-CoV-2. The variants of ACE2 polymorphism that increase the affinity of ACE2/S-protein are S19P, I21V, E23K, K26R, K26E, T27A, N64K, T92I, Q102P, and M383T. The variants of ACE2 polymorphism that decrease the affinity of ACE2/S-protein are thought to be protective polymorphisms, namely K31R and E37K (Suryamohan et al., 2021).

This difference in the severity of the disease can be caused by the individual's immune system (Banoun, 2021). Several studies have explained the relationship between immunogenicity and individual resistance to emerging new variants (Alsobaie, 2021).

The presence of antibodies provided cross-protection with early case COVID-19 strains, but protection was slightly reduced in variants B.1.1.7 and B.1.351 (Garcia-Beltran et al., 2021). Sex differences provide different immunity where the X chromosome is associated with the

gene coding for adaptive and innate immunity. Females with an XX chromosome allow for a stronger immune response than males who do not have a "spare" X chromosome. This makes females have stronger immunity, while males tend to be more susceptible to pathogens. Differences in immunity between sexes are also influenced by differences in sex hormones. Some immune cells have varying amounts of sex hormone receptors; females show a higher number of receptors than males. Gender was not associated with ACE2 expression levels, although more males were infected and died by SARS-CoV-2 during the pandemic (Ha et al., 2021). ACE2 expression correlates with age, i.e., increases in renin-angiotensin II signaling with age. This can exacerbate COVID-19 symptoms in the elderly (AlGhatrif et al., 2021). Morbidity and mortality increase in individuals aged > 50, especially those with comorbid hypertension, obesity, and diabetes (Sarangarajan et al., 2021).

Viral proteins that trigger the host immune response continue to mutate. Host immunity is triggered to overcome the new viral strain. People who are exposed but whose immune system does not fight the virus effectively will become seriously ill. This differs in those who are exposed but not because the immune system destroys the infecting virus or is able to induce disease in a less efficient (replicated less efficiently) form of the virus. This mechanism is predicted to be one of the factors causing the mild severity of the symptoms of a disease (Banoun, 2021). One of the efforts to stop a pandemic is to obtain groups with the highest immunity among the population through natural immunity or vaccines, which are very important in preventing and reducing infectious diseases, and stopping the evolution of viruses (Alsobaie, 2021).



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### Environment

Changes in the environmental factors studied can disrupt the stability of the virus so that it can trigger the evolution of the virus or can kill the virus. Environmental factors that contribute to the mutation (evolution) of the COVID-19 virus are season and rainfall, temperature, sunlight, materials around the environment, wildlife habitat, water, and wastewater.

#### *Season and rainfall*

Seasons play a role in viral mutation. Epidemiological analysis of the SARS-CoV-2 genome found that the virus's spread and evolution rate is lower in summer than in other seasons because high summer temperatures affect virus viability (Jia & Gong, 2021). This is also seen in Australia, where the incidence in winter is six times higher than in summer (Kifer et al., 2021). The more varied the environment experienced by the RNA virus, the lower the virus's resistance in that environment, but the higher the mutation rate triggered so that the virus can adapt to that environment. Mutations of this virus can increase or decrease its virulence (Duffy, 2018). Seasonal changes also affect individual susceptibility, namely the interaction between changes in temperature and dysfunction of airway defense mechanisms that lead to an increased incidence of viral infections and a higher susceptibility to the nasal mucosa under low temperature and humidity (McMullin et al., 2019). Breathing air with low humidity will reduce the mucociliary transition time of the nose, thereby prolonging viral exposure to the nasal mucosa (Kifer et al., 2021). Rainfall is an important factor to consider. Countries with high rainfall show an increase in positive COVID-19 patients, with an additional 56.01 cases / inch increase in average rainfall/day (Saputra, Susanna, & Saki, 2021).

### Temperature

Cities with temperatures higher than 25°C experience a decrease in positive COVID-19 cases (Mozumder et al., 2021). This suggests that the increase in temperature contributed to the easing of the outbreak (Saputra et al., 2021). Rising temperatures increase the number of positive COVID-19 cases in Pakistan (Basray et al., 2021). The same thing happened in Oman, United Arab Emirates, and Qatar (Meo et al., 2020). This proves that other factors besides the influence of temperature trigger an increase in COVID-19 transmission, namely human mobility. Increased human mobility can support the spread of disease if a person carries the disease or acts as a carrier (Findlater & Bogoch, 2018).

#### *Sunlight*

Ratnesar-Shumate et al. found that ultraviolet (UV) B sunlight can inactivate viruses in aerosols rapidly (Saputra et al., 2021). Coronavirus virulence decreased by 90%/6.8–12.8 min of UV B exposure time (Schuit et al., 2020). Sunlight can reduce the risk of transmission from aerosols (Azuma et al., 2020).

#### **Materials around the environment**

The COVID-19 virus only survives 4 hours on copper surfaces. This has led to the use of copper in metal combinations as a strategy to reduce the risk of transmission. Copper ions can destabilize proteins in viruses and have the effect of inactivating viruses by causing aggregation of viral particles (Azuma et al., 2020).

#### *Wildlife habitat*

Deforestation and ecosystem changes that result in the destruction of viruses in nature and encourage the evolution of viruses to adapt to new environments are the basis of the zoonotic process (da Silva et al., 2021). Continuous habitat destruction by humans and animals



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will cause all zoonotic events (Prince et al., 2021). Continuous monitoring of wildlife at the urban-rural boundaries, trade, livestock, and food distribution is needed to prevent further epidemics (da Silva et al., 2021).

### **Water and wastewater**

The COVID-19 virus was detected and can survive in wastewater (Eslami & Jalili, 2020). RNA viruses can be found in the mucus, phlegm, blood, and feces of COVID-19 patients, and all of these are included in medical waste (Wu et al., 2020). Insects using medical waste technology can act as reservoirs and infect other species. Virus adaptation in new reservoirs can induce new variants and complicate the prevention of COVID-19 transmission. This can be used by improving environmental hygiene, such as putting waste into bags and landfills, controlling disposal, sanitation of toilets, and creating a good waste disposal system (Eslami & Jalili, 2020).

### **CONCLUSION**

This literature review aims to determine the effect of viruses, reservoirs, hosts, and environmental factors (season and rainfall, temperature, sunlight, materials around the environment, animal habitats, water, and wastewater) on the evolution of viruses that affect morbidity and mortality of COVID - 19 diseases. Factors from the virus, reservoir, host, and environment can trigger viral mutations and alter virulence to increase or decrease the morbidity and mortality of COVID-19. Epidemiological approaches and biomolecular research are needed to control the causative agents (viruses, bacteria, etc.), reservoirs, humans, and the environment to prevent the occurrence of new pandemics in the future.

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### LITERATURE REVIEW

## Community-based psychosocial rehabilitation model for people with schizophrenia

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### ABSTRACT

Schizophrenia is a mental disorder that triggers the occurrence of impaired function in the human brain, behavior, cognitive, and emotional functions. This disorder has become a problem in the study of mental health, which must be treated comprehensively by using empirical treatment combined with rehabilitation. Hopefully, increasing the maximum level of healing and reducing recurrence rates can improve social function and quality of life. Thus, this review aims to narrate the model and effective community-based psychosocial rehabilitation center. The articles of the studies published from 2017-2021 were collected and analyzed in this literature review. The keywords used were community-based rehabilitation for schizophrenia. The results show that in addition to pharmacological therapy, six community-based psychosocial non-pharmacological therapy methods are considered effective for intervention in patients with schizophrenia. The methods are club methods in elderly schizophrenic patients, community-based methods, direct patient decision-making methods, case and club management methods, psychoeducational and social skills methods, and community care unit methods. All of the above methods analyzed showed significant effectiveness in community-based psychosocial rehabilitation treatment in developing countries.



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### INTRODUCTION

Schizophrenia is a mental illness that is a problem in the world of health. Schizophrenia is a problem or mental disorder that can cause impaired function in the human brain, behavior, cognitive, and emotional functions of sufferers. Schizophrenia also often occurs in developing countries and usually occurs in low economic groups. In general, patients with schizophrenia have different or varied symptoms that confuse many people, the symptoms that appear are usually hallucinations, delusions, delusions, bizarre behavior, and a general decline in abilities (Zuraida, 2017).

According to the World Health Organization (2017), about 50 million people worldwide have schizophrenia and 6.5 million in Southeast Asia. The number of people with schizophrenia in Indonesia is 0.3-1% of the total population. Meanwhile, in East Java Province in 2016, the number of people with mental disorders reached 2.369 and increased compared to 2015 with the number of sufferers 1.619. Cases of mental disorders will continue to increase if there is no concern from the community regarding their mental health and those of others around them (Rusdianah *et al.*, 2021). In addition, people with mental disorders often get stigma and bad behavior from society. Various ways or actions of the community to respond to people with mental disorders, such as taking them to the hospital, avoiding, imprisoning, mocking, and even beating them. Actions or behaviors like this worsen and complicate the patient's healing (Farhan, 2020).

The management of schizophrenia can be done in two ways: pharmacology and non-pharmacology. Pharmacology is giving medication according to the symptoms suffered by the patient. The non-

pharmacology management is rehabilitation, one aspect of therapy that is very important for treating schizophrenic patients and even becomes support so that patients have abilities according to their interests and talents after recovery. Mental rehabilitation is all activities or actions to restore function and improve physical conditions and social relations with the surrounding community (Widianingsih and Astanto, 2020). There are various rehabilitation models, one of which is a community-based psychosocial rehabilitation model. Many countries have applied the model with various methods, so we are interested in analyzing the effectiveness of these methods.

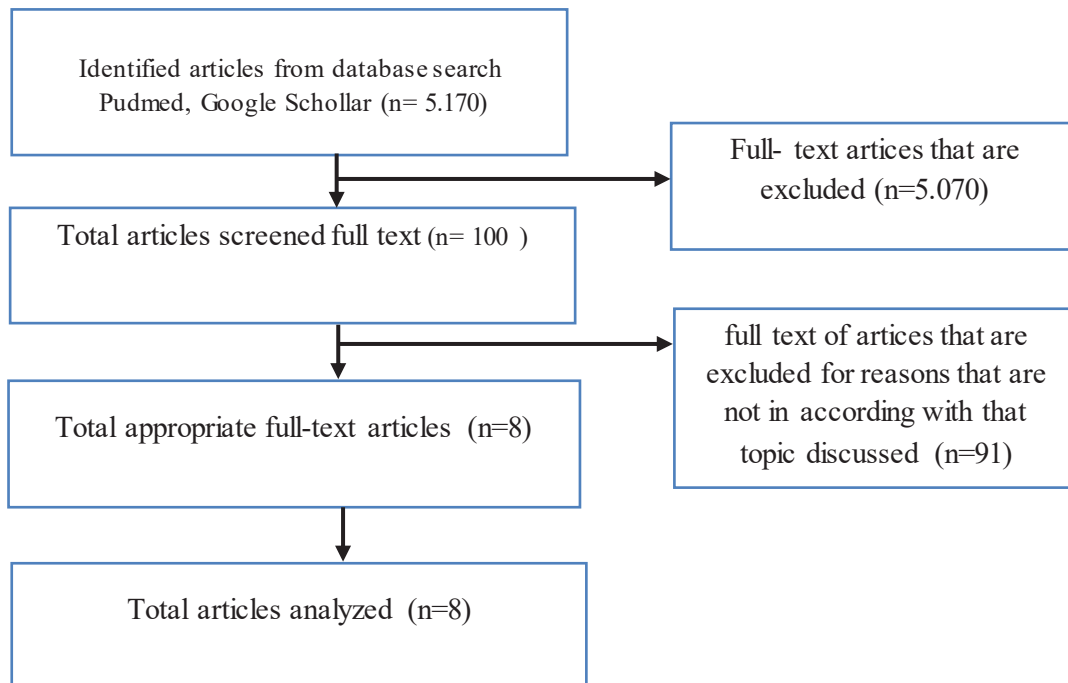
### METHOD

The method used in this paper is a literature review study. *The databases* used in the source search are PubMed, Science Direct, and Google Scholar. The article search collected topics on the correlation between schizophrenia and psychosocial rehabilitation. The range inclusion of the literature used was published from 2017 until 2021 in English or Indonesian language by choosing the full article journal and literature review. The search keyword is *community-based rehabilitation for schizophrenia*. The total number of articles used for analysis was 8 out of several that met the inclusion criteria.

### LITERATURE REVIEW

#### Schizophrenia

Schizophrenia is a group with mental limitations (psychosis) known as positive symptoms and negative symptoms characterized by major disturbances in thoughts, emotions, and behavior of disturbed thoughts, various thoughts are not connected logically; wrong perception and attention; flat or inappropriate affect; and various motor activity disorders as well as hallucinations, illusions, and delusions



**Figure 1.** Information Analysis

(Sembiring, 2020). The leading cause of schizophrenia is still unknown. However, there are several theories about schizophrenia, namely the *diathesis-stress model theory*, biological factors, the dopamine hypothesis related to the hyperactivity of the dopaminergic system, the serotonin hypothesis, and genetics.

### Symptoms of Schizophrenia

According to DSM-IV-TR Schizophrenia, the characteristic symptoms are two (or more) of the following, each occurring significantly over one month (or less if successfully treated): 1) delusions, 2) hallucinations, 3) speech chaos, 4) very disorganized or catatonic behavior, and 5) negative symptoms, namely flat affect, alergia or loss of interest (Sadock, B. J., Sadock, V. A. & Ruiz, 2017).

### Schizophrenia Treatment

The drugs used in the pharmacological therapy of schizophrenia are antipsychotic drugs. Anti-psychotic drugs are the main element in

pharmacotherapeutic treatment in treating schizophrenic patients. Antipsychotic drugs are classified into two groups, typical and atypical antipsychotics. Typical antipsychotics work more effectively to treat positive symptoms. The following are typical antipsychotic drugs: Chlorpromazine, Flupenthixol, Fluphenazine, and Haloperidol, Antipsychotics. This atypical or APG 2 works in overcoming both positive and negative symptoms (Andari, 2017).

Considering the functioning of social cognition is a treatment target in schizophrenia. Although classified as treatment as the main anti-psychotic drug, it was not significantly able to improve social cognition (Kucharska-Pietura, David, Masiak, & Phillips, 2005). At the same time, psychosocial treatment programs have been developed specifically to accompany psychotic drugs in restoring social cognition. One of the psychosocial therapies that can be applied in treating schizophrenia is a community-based intervention approach.



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The National Institute of Clinical Excellence Guidelines in the UK emphasizes the need for community-based psychiatric interventions, such as cognitive therapy, counseling, and family interventions, in addition to standard treatment (Widianingsih and Astanto, 2020). In the last five years, in several countries, there have been many uses and, at the same time, developing community-based psychosocial therapy methods.

### Club method in elderly schizophrenic patients

A systematic review of the effectiveness of community-based psychosocial therapy models in several countries will provide a detailed summary using the evidence already available in Amsterdam. Findings refute the ancient belief that disorders such as schizophrenia fundamentally impede adequate social interaction (Meesters *et al.*, 2019). Today, social engagement is considered as one of the critical positive psychosocial factors in recovery-oriented practice (Jeste, Palmer, and Saks, 2018). Community-based psychosocial therapy in Amsterdam called *The New Club* for old age has the aim of fostering independence and social participation in groups in order to be able to recover personally and socially for its members. On a personal level, attending the facility, activation, and feeling welcome were rated positively. On a social level, engaging with others, experiencing a sense of community, and learning from each other's social skills are positive contributors.

Furthermore, various environmental factors proved to be necessary. The New Club demonstrates the feasibility of creating a facility that offers an environment receptive and non-demanding social living in an older community with severe mental illness. Many patients with schizophrenia are confined to their homes due to psychological limitations

(such as paranoia or anxiety) or physical limitations. Receiving and reaffirming the social climate experienced by participants in the facility challenge this self-stigmatization and can restore self-esteem and prominent identity apart from psychiatric patients (Wong, Sands, and Solomon, 2015). This process proves the importance of social relationships for psychological empowerment and positive psychosocial key in recovery-oriented practice (Christens, 2012; Jeste, D. V, Palmer, BW and Saks, 2018). However, it is essential to realize that a large group of elderly people with severe mental illness remains out of the reach of The New Club. Severe chronic psychosis (either due to positive psychotic symptoms or negative ones) can lead to climate-fighting behavior in social facilities. The physical suffering that requires attention intensive does not match the number of facility staff. Facility location is community-based; avoiding connections to health institutions mentally can strengthen the character of facilities that are not stigmatized and lower the threshold for participation (Meesters *et al.*, 2019). Explained by Meesters *et al.* that *The New Club* can be implemented successfully if several organizational requirements are met, including adequate funding, qualified personnel on duty, and ongoing consultation by skilled psychiatric health workers to be ensured (Meesters *et al.*, 2019).

### Community-based Method

Asher *et al.* describe community-based psychosocial therapy (CBR) such as family support; community-based rehabilitation; and/or self-help groups, and support should be provided for people with schizophrenia in low- and middle-income countries (Asher, Patel, and De Silva, 2017). The CBR emphasizes community engagement, which may require raising awareness or mobilizing practical support from community members. Community mobilization is the primary key to creating



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a sustainable CBR program (World Health Organization, 2010). Provide limited evidence from low- and middle-income countries supporting the feasibility and effectiveness of community-based psychosocial interventions for schizophrenia. Therefore, community-based psychosocial interventions should be provided in these settings as an adjunct service to facility-based care for persons with schizophrenia.

Recently, community-based psychosocial therapy by Asher *et al.*, 2021 redeveloped in Ethiopia as community-based psychosocial therapy (CBR) using the Rehabilitation Intervention for people with Schizophrenia in Ethiopia (RISE) method. The method was through training lay people with little or no previous experience to provide psychosocial interventions for people with schizophrenia in low-income countries with multimodal training, including role play, fieldwork, and group discussion, contributing to early competency development. The CBR is a promising intervention to address the complex health, social and economic needs of people with schizophrenia and is recommended as an adjunct to facility-based care, including the prescription of antipsychotic drugs. The RISE CBR intervention consisted of home-based psychosocial support, awareness-raising, and community mobilization. At RISE, interventions are delivered by lay people who are trained in fundamental problem-solving and counseling skills to become CBR workers. The pilot study shows that the CBR for schizophrenia is mainly acceptable and feasible. The combination of 'expert' and 'friend' suggests that lay health workers not only 'fill the gap' in services but may offer something unique in terms of social relationships during the care of people with schizophrenia so that it can increase the success of psychosocial therapy for schizophrenic patients and have physical, socio-economic, and cultural closeness with the recipient.

Further developed by Chen *et al.* (2021) in their research entitled *Metacognitive training: a valuable complement to community-based rehabilitation for schizophrenia patients in China*, confirmed the superiority of the combination of MCT (metacognitive training) and CBR with a control group receiving only CBR. Moritz and Woodward developed MCT as an intervention for patients with schizophrenia (Moritz, S. and Woodward, 2010). Recent studies have confirmed that MCTs are attractive and can effectively alter patients' delusional ideas (Moritz *et al.*, 2013; Moritz *et al.*, 2014; Balzan, Delfabbro, and Galletly, 2013; Vitzthum, Veckenstedt and Moritz, 2014; and Moritz and Woodward, 2007). The effectiveness of MCTs in schizophrenic patients has been carried out in several randomized controlled studies (Moritz, Andreou, *et al.*, 2014). The primary outcome of MCT, such as a reduction in positive symptoms, would meet the requirements of community rehabilitation for chronic schizophrenic patients (Spaulding *et al.*, n.d; Kumar, 2010). This study specifically wants to know the feasibility of MCT in community rehabilitation and for the government to adopt community services by taking MCT as a regular complementary strategy to CBR. Furthermore, this study provides preliminary evidence for the usefulness of MCT as a complementary measure for the community-based rehabilitation of schizophrenic patients (Chen *et al.*, 2021).

### Patient-directed decision-making method

Another development in Ethiopia by Souraya, Hanlon and Asher (2018) is community-based psychosocial therapy that provides opportunities for the involvement of people with schizophrenia in decision-making regarding their care. The study is the first to explore the involvement of people with schizophrenia in decision-making regarding



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their care in a low-income country setting. However, in his research, Souraya explained that the implementation of the involvement of people with schizophrenia in decision-making regarding their care in rural Ethiopia is limited, and there is still coercion in the process of treating people with schizophrenia (Souraya et al., 2018). Involvement in decision-making is considered a fundamental component of a person-centered and recovery-oriented care model that rests on the assumption that care must respect the needs, experiences, and rights of individuals with mental health problems, in developing and high-income countries. Interventions designed to involve people with schizophrenia in treatment-related decisions have been associated with better outcomes, improved long-term medication adherence, decreased readmissions, improved social functioning, and increased satisfaction with community programs. Souraya et al. also explained that there is evidence that people with schizophrenia are interested in and can participate in decision-making, especially concerning the choice of psychotropic drugs (Souraya, Hanlon, and Asher, 2018). Thus, to increase the involvement of people with schizophrenia in rural Ethiopia, there needs to be greater empowerment of service users, wider availability of treatment options, and a facilitating policy environment.

### **Psychoeducational methods and social skills**

Indonesia is a developing country in research. It has also been shown to effectively improve the quality of life of people with schizophrenia in the Yogyakarta community. Community-based psychosocial therapy in low-resource settings can effectively overcome economic, geographic, and cultural barriers to rehabilitating people with schizophrenia (Puspitosari, Wardaningsih, & Nanwani, 2019). The study was a quasi-

experimental study on schizophrenic patients aged 18-56 years for 12 weeks. The two main activities used in the study as community-based psychosocial therapy are psychoeducation and social skills training. This intervention is in line with the intervention recommended by Psychopharmacological Treatment (PORT). The study explains previous research that psychoeducation can increase knowledge, reduce family burden, reduce relapse rates, and improve the quality of life and clinical symptoms of people with schizophrenia, while social skills can improve communication skills and social functioning. This is supported by the research results, where subjects who received community-based psychosocial therapy experienced a more significant improvement in quality of life than those who did not receive community-based psychosocial therapy (Puspitosari, Wardaningsih, and Nanwani, 2019).

### **Community care unit method**

A study in Australia was conducted with different methods for community-based psychosocial therapy with a community care unit model of psychiatric rehabilitation. The model was a psychiatric rehabilitation model that aimed to improve the independence and community functioning of people with severe and persistent mental illness (Parker et al., 2020). This study used data from a retrospective cohort (n = 501) of all patients admitted to five Community Care Units (CCU) in Queensland, Australia, between 2005 and 2014, proving a significant predictor of improvement in mental health and social functioning due to longer duration of stay. Length of stay at CCU, lower baseline mental health and social functioning and disability, and lower pre-admission to psychiatric-related bed use. Contemporary CCU is a treatment that provides clinically oriented residential psychiatric support over a period of time that focuses on improving various





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aspects of personal functioning – particularly the development of life skills and community integration – within the context of overall mental health, and providing rehabilitation support 24 hours to people with serious mental illness (Meehan et al., 2017; Parker and Siskind, 2019). At the individual level, CCU treatment followed by RCS demonstrated improved mental and functional health in 43% of patients. It can also be used in patients with poor mental and social health with longer episodes of treatment showing improvement in RCS. The group level showed an increased reduction in hospitalizations in patients before and after CCU on mental health and social functioning. While the results of this study corroborate the positive trend in readmission rates found in previous research, it is essential to recognize that system-related factors, such as access, availability, and lack of alternative services, influence service usage. Assessment of individual changes in CCU consumers revealed improvements in accommodation instability that were not detected at the group level.

### Case and club management methods

The last study we analyzed was the study conducted in Hungary by Varga *et al.* in 2018. The study compared prospective changes in social cognition and functional outcomes in two groups of schizophrenic patients involved in two forms of community-based psychosocial care, namely case management and community-based clubs with a group of regular patients. Case management is important for patients and helps them develop coping mechanisms to deal with the seemingly insurmountable challenges of everyday life. This program provides various trainings for patients with the participation of family members or friends at the patient's home. The long-term goal of CM is to develop and maintain skills to cope with the difficulties of daily living and improve the relapse index, social functioning, and the patient's standard of

living (Holoway and Carson, 1999; Thornicroft, 1991). In comparison, CC or Community-Based Club or community-based club is a daycare service formed based on the concept of the Psychosocial rehabilitation Clubhouse Model for chronic schizophrenic patients over the age of 18 years (Mckay *et al.*, 2016). Patients have the opportunity to participate in a variety of social interactions and community programs, including various cultural programs and leisure activities. Their main goal is to help people with mental illness, usually living in social isolation; they struggle to find their way into the community. The results show that the most notable changes in social cognition function were detected in the community-based club group. The functional outcomes improved significantly in the community-based club and case management group compared to the treatment-as-usual (TAU) group. According to the findings, Varga *et al.* believed that community-based psychosocial care was able to facilitate functional outcomes in schizophrenia (Varga *et al.*, 2018).

Regarding social cognition, Varga *et al.* found that community-based club programs can achieve the most prominent perspective changes. The results of this study suggest that this is due to a supportive social environment in which various social interactions can be practiced and new social roles can be learned, which exerts a specific enhancing effect on social cognition and helps patients find their way into society (Varga *et al.*, 2018). Moreover, the current results clearly show that they need to engage in community-based clubs to improve patients' social cognitive performance significantly.

### CONCLUSION

The methods analyzed in this literature review showed significant effectiveness in community-based psychosocial rehabilitation treatment



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in developing countries, including Indonesia. Community-based psychosocial therapy is believed to improve the social functioning and quality of life of schizophrenic patients. It is also reasonably effective in developing countries or low-income communities, and this is due to the minimal resources that can be used in community-based psychosocial therapy models compared to primary home treatment. It can also reduce the level of patient care in the hospital. However, several things need to be considered in its implementation, among others, improving the quality of the assistant staff working in it and the material. This article is expected to be helpful and can be used as an insight into planning and providing community-based psychosocial therapy for schizophrenic patients.

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### Literature Review

## The influence of the quality of Tuberculosis services with adherence to taking Anti-tuberculosis drugs

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### ABSTRACT

Indonesia was the second world's highest TB case in 2021. Tuberculosis therapy that takes a long time can cause patients to drop out of treatment. Hospitals conduct quality evaluations regularly and improve the quality of health service personnel to realize excellent health services. This literature review aims to determine the effect of the quality of tuberculosis services on patient compliance with anti-tuberculosis drugs. This literature review was written using a systematic approach. The databases used were Google Scholar, Science Direct, Proquest, and Scopus. The total number of articles obtained was 8 out of 64 based on inclusion criteria. The things that affect the regularity of taking medication based on the eight journal articles above are as follows: 1) the assurance dimension is 50%, 2) the dimensions of empathy and reliability amounted to 37.5%, 3) the responsiveness dimension is 25%, 4) patient satisfaction, direct evidence and service quality amounted to 12.5%. Adherence to taking medication is influenced by: 1) the presence of supporters of taking medication, 2) difficulty taking the medication regularly, (3) perceived benefits of taking anti-tuberculosis drugs, and 4) self-perception related to healing. The dimensions of assurance, empathy, and reliability have the most influence on the regularity of taking anti-tuberculosis drugs.



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### INTRODUCTION

The number of tuberculosis cases worldwide was estimated at 9.9 million in 2020, equal to 127 per 100,000. The number of TB cases in Indonesia will be 824,000 in 2020 (World Health Organization, 2021). Indonesia is in second position with the highest number of TB cases in the world after India, followed by China, the Philippines, Pakistan, Nigeria, Bangladesh, and the Democratic Republic of the Congo, respectively. In 2020, Indonesia was in third place with the highest number of cases, so 2021 is no better. TB cases in Indonesia are estimated at 969,000 (one person every 33 seconds). This figure is up 17% from 2020, namely 824,000 cases. The incidence of TB cases in Indonesia is 354 per 100,000 population, meaning that for every 100,000 people in Indonesia, 354 suffer from TB. Tuberculosis cases in Indonesia were only 443,235 (45.7%) of the estimated 969,000 cases, while 525,765 (54.3%) other issues had not been reported and reported. The total number of patients with drug-resistant tuberculosis in Indonesia is 8,268 cases, with 5,234 people starting treatment for drug-resistant tuberculosis (World Health Organization, 2022).

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. The bacteria attack the lungs as much as 85% and can also attack the extra lungs. Treatment of drug-sensitive tuberculosis takes six months, and for drug-resistant tuberculosis, the duration of treatment reaches 9-24 months. Therapy failure increases after the patient starts treatment until the fourth week (Dheda et al., 2016). The management of tuberculosis cases is (1) treatment and management of drug side effects, (2) monitoring of medication adherence, (3) monitoring of treatment progress and treatment outcomes; and (4) tracking of lost patients. The procedure is

carried out by established national standards (Peraturan Menteri Kesehatan Republik Indonesia Nomor 67 Tahun 2016 Tentang Penanggulangan Tuberkulosis, 2017).

The empathy of health workers toward tuberculosis patients will build Trust so that patients will become obedient in completing tuberculosis treatment (Zainaro & Gunawan, 2020). Poor communication between staff and tuberculosis patients is the most common cause of non-adherence to patients taking anti-tuberculosis drugs. This is because health workers do not explain tuberculosis, drug side effects, length of treatment, and effects of patients dropping out of treatment (Anggraini et al., 2018).

Adherence to taking anti-tuberculosis drugs is related to the quality of health facilities' services. The research was conducted at the Labuhan Maringgai community health center in 2018 (Dian Utama Pratiwi Putri, 2020). Dissatisfaction with tuberculosis services in Armenia is associated with non-adherence to treatment, hospitalization, drug-resistant tuberculosis, higher Education, marital status, i.e., unmarried, family income, dissatisfaction with consultation, empathy of officers, and place of residence (Yarimoglu, 2014).

Routine evaluation and improvement of the quality of health service workers need to be carried out to realize excellent service. Management of health facilities surveyed patients to determine the quality of tuberculosis clinic services. The survey is essential to improve health facility services (Merzistya et al., 2021). The objective measure of universal health is that patients can access quality health services in every government and private health facility. The goal of universal health can be achieved by seeking quality diagnostic services, good treatment rooms, current data, and the skills of health workers. (Stallworthy et al, 2020).



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The influence of the quality of tuberculosis services assessed according to patient perceptions and medication adherence is essential for healthcare facilities. This article aims to determine the effect of the quality of tuberculosis services according to patient perceptions in health facilities on patient compliance in taking anti-tuberculosis drugs. This review literature used a systematic review method where the articles to be discussed are limited to five years before 2022.

### METHOD

This paper is a literature review using a systematic approach (systematic review). Science Direct, Proquest, Google Scholar, and Scopus are the databases used. The keywords used are “quality services,” “tuberculosis,” “adherence to tuberculosis treatment,” “quality of tuberculosis services,” adherence to taking TB drugs,” and “patient perspective.” The article search process was carried out in August-October 2022.

The inclusion criteria used were: 1) English or Indonesian articles, 2) articles published on January 1, 2018 - September 30, 2022, 3) full text, 4) Open access, and 5) articles that wrote about service quality from the patient’s perspective. Tuberculosis in health care facilities, 6) articles about the quality of tuberculosis services based on service quality, and 7) articles about the relationship between service quality and adherence to tuberculosis drugs. The exclusion criteria were: 1) duplication of articles, 2) Tuberculosis articles with Co-infection and other co-morbidities such as TB-DM, TB-HIV, and TB-COVID-19, 3) articles published before January 1, 2018-September 30, 2022, 4) the quality of tuberculosis services is not based on patient perceptions, 5) articles on medication adherence that are not related to service quality, 6) articles are not literature reviews, and 7) articles use quantitative methods.

The articles obtained from the initial search amounted to 67 themes consisting of 21 pieces from Google Scholar, ten from Proquest, 16 from Science Direct, and 20 from Scopus. Researchers selected articles containing duplicates, the theme of TB-COVID-19 co-infection, and articles published before January 1, 2018, so we obtained 63 reports. Researchers decided on 21 articles because the piece of the writing discussed the quality of tuberculosis services that were not according to patient perceptions; researchers obtained 42 articles. The author found 23 articles because they contained the theme of tuberculosis drug adherence unrelated to service quality. We got 19 pieces. A total of 5 papers were excluded due to the writing method using a literature review, 14 articles to be analyzed, and eight articles using quantitative methods were selected.

Things that affect the regularity of taking medication based on eight articles are as follows: 1) the dimensions of assurance are 4 out of 8 articles (50%), 2) empathy and reliability are 3 out of 8 articles (37.5%), 3) power response as much as 2 of 8 articles (25%), 4) patient satisfaction, direct evidence and quality of service as much as 1 of 8 articles (12,5%). Other factors that affect adherence to swallowing drugs are: 1) support for taking medication, 2) difficulty taking the medication regularly, 3) perceived benefits of taking anti-tuberculosis, and 4) self-perception related to healing. The article above says things related to the satisfaction of tuberculosis patients, namely: Communication, Information, and Education delivered by doctors, long waiting time for doctor services, where communication, information, and Education by doctors  $p$ -value = 0.000 OR value of 41.43 (95% CI 5,09-337.11) and the waiting period for Doctor services with a  $p$ -value of 0.000, OR value of 27.88 (95% CI 4.77-162.92).



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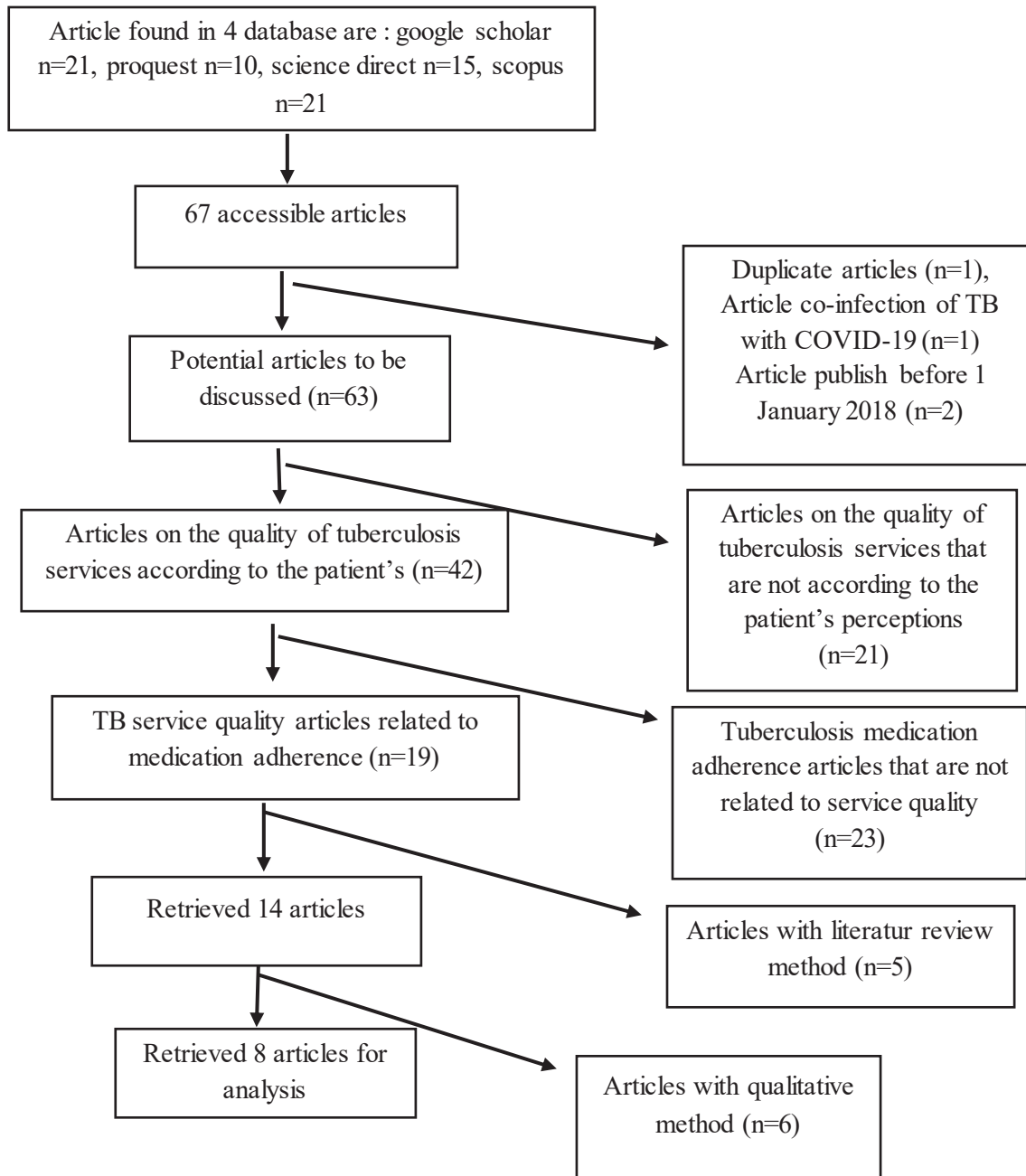


Figure 1. Prisma Diagram





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**Table 1.** Characteristic Article

Authors	Journal	Year	Title	Method	Sample	Result
Mayang Sari ayu (Ayu, 2019)	<i>Jurnal Jumantik</i>	2019	<i>Analisis Pelayanan Terapeutik Pada Pasien Tuberkulosis Resisten Obat di Kota Medan</i>	Cross-Sectional Research	32 samples with non-random sampling	Variables that affect adherence to drug-resistant TB drugs are medical services, pharmaceutical services statistically, and nursing services statistically
Yulin Mustika Sari, Juliandi Harahap, Masnelly Lubis (Sari et al., 2020)	<i>Media Publikasi Promosi Kesehatan Indonesia, Jurnal UNISMUH Palu</i>	2020	<i>Faktor Penentu Minat Berkunjung Ulang Pasien Tuberkulosis Di Poliklinik Paru Di Rumah Sakit Pirngadi di Medan</i>	Cross-Sectional Research	93 samples with the purposive sampling technique.	Assurance, empathy, responsiveness, and patient satisfaction influence the regularity of treatment or repeat visits for TB patients
Sri Ratna, Lukman F, Chatila M, Aufiena Nur Ayu Merzistya, Hima Sakina Firdhausy, Tika Dwi Cahyani, and Fina (Rahayu et al., 2021)	<i>Turkish Journal of Physiotherapy and Rehabilitation</i>	2021	<i>Patients' perspectives on tuberculosis services in the urban area, Indonesia: An assessment using quote tb light. Turkish Journal of Physiotherapy and Rehabilitation</i>	Cross-Sectional Research	138 samples, with purposive sampling	Staff service standards, interactions, solutions to problems, TB-HIV relationships, available drinking water, toilets, patient care, competent health workers, and support need to be improved



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Demisu Zenbaba, Mitiku Bonsa, Biniyam Sahiledengl (Zenbaba et al., 2021)	Heliyon	2021	Trends of unsuccessful treatment outcomes and associated factors among tuberculosis patients in public hospitals of Bale Zone, Southeast Ethiopia	Quantitative research using retrospective data	1281 samples, with total sampling	Hospital level, patient, age, and human immunodeficiency virus status significantly relate to failure TB patient treatment outcomes
Resom Berhe Gebremariam, Maereg Wolde and Aykerem Beyene (Gebremariam et al., 2021)	Journal of Health, Population, and Nutrition	2021	Determinants of adherence to anti-TB treatment and associated factors among adult TB patients in Gondar city administration, Northwest, Ethiopia	Cross-Sectional Research	265 samples with random sampling	Patient supporters, difficulty taking TB medication regularly, perceived benefits, and self-perception of healing related to adherence to anti-tuberculosis treatment
Ragil Sekar Kinanti Hutabarat (Hutabarat, 2018)	<i>Jurnal Ilmu Kesehatan Masyarakat</i>	2018	<i>Faktor-faktor yang Berhubungan dengan Kepuasan Pasien Tuberculosis di Puskesmas Padang Bulan Medan</i>	Cross-Sectional	122 samples with accidental sampling	Doctors' explanations and waiting times for TB patients have a relationship with patient satisfaction



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Dian Utama Pratiwi Putri (Dian Utama Pratiwi Putri, 2020)	<i>Masker Medika</i>	2020	<i>Hubungan Mutu Pelayanan Kesehatan dengan Keteraturan Berobat Penderita TB Paru di Puskesmas Labuan Maringgai Lampung Timur Tahun 2018</i>	Cross-Sectional	68 samples with random sampling.	Reliability, responsiveness, assurance, direct evidence, empathy, and quality of service are related to routine tuberculosis treatment.
Muhammad Arifki Zainaro, Ahmad Gunawan (Zainaro & Gunawan, 2020)	<i>Holistik Jurnal Kesehatan</i>	2020	<i>Kualitas pelayanan kesehatan rawat jalan dengan tingkat kepatuhan minum obat penderita tuberkulosis paru</i>	Cross-Sectional	49 samples with a total sampling	The empathy of health workers related to adherence to taking anti-tuberculosis drugs has a significant relationship

**DISCUSSION**

Hospital managers need to pay attention to essential aspects related to the quality of hospital services, namely: (1) timely service, (2) attentive hospital staff, (3) accurate service prices, (4) providing information about the right time of service, (5) punctuality, (6) employees who are ready to serve patients with heart (Meesala & Paul, 2018). Patients can assess tangibles (physical appearance), the availability of adequate parking space, comfortable patient waiting rooms, and maintained hospital cleanliness. Examples of reliability are compliance with existing standard operating procedures, health facility employees who serve professionally, and implementing services as promised. An example of responsiveness (dexterity in service) is responding to every

patient’s complaint quickly and accurately. Assurance (intelligence), for example, is good communication by health workers to convince patients to complete treatment and the accuracy of doctors in making diagnoses. Empathy, for example, is listening to all patient complaints and giving positive responses and the officers feel what the patient is feeling (Alim et al., 2019).

The side effects of anti-tuberculosis drugs include nausea, vomiting, weakness, palpitations, tingling, and others (Dirjen P2P Kementerian Kesehatan RI, 2020). Medication adherence is higher in patients who experience mild drug side effects than in those with severe side effects (Wulandari, 2015). Officers’ empathy is always needed to provide solutions to patients to continue treatment until completion. Good



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communication by health workers also helps patients complete their treatment; on the other hand, if the communication between officers is terrible, the patient does not understand his illness and stops taking medicine (Anggraini et al., 2018).

Timeliness of service is essential to increase patient Trust in health workers; with belief, patients will be committed to obeying the advice officers give. Trust will also motivate the patient to recover from his illness. Doctors educating patients about curable tuberculosis, the transmission of tuberculosis, and the regularity of taking anti-tuberculosis drugs will convince patients to take medication regularly (Ayu, 2019).

The dimensions of SERVQUAL (Service Quality) that need to be improved to increase the visits of tuberculosis patients in hospitals are tangibles, assurance, and empathy. Health service management can improve the completeness of facilities and infrastructure, such as parking lots, waiting rooms, checking rooms for drinking water availability, and the fullness of inspection equipment. Patients will feel comfortable when they are in the hospital. Physical aspects, aspects of employee knowledge and behavior that can build patient Trust can also improve medication adherence in tuberculosis patients; the empathy of health workers is also essential (Noviyanti & Widiastuti, 2021).

Factors influencing tuberculosis patients' desire to return to health facilities are the responsiveness of assurance, empathy, and patient satisfaction (Sari et al., 2020). Health workers play a crucial aspect in establishing a diagnosis, giving medicine, and motivating patients to want to take medication; therefore, health workers need to master interpersonal communication and counseling skills (Colvin et al., 2019). Attitudes of health workers,

access to health services, side effects of drugs, attitudes of tuberculosis patients, and family support influence taking medication (Tukayo et al., 2020). Good staff attitudes such as practical communication skills, empathy, and responding to every complaint of tuberculosis can help patients complete treatment. Drug side effects that are handled optimally and recording and reporting tuberculosis drug side effects can improve service quality. Access to health services that are not accessible to patients can be overcome by collaborating with cross-sectoral organizations both government and non-government to deal with these problems. Family support is also a factor that can affect medication adherence, hospital staff can provide education to the patient's family regarding tuberculosis, good family understanding regarding tuberculosis will support patient compliance in completing treatment.

The failure rate to take medication was higher in TB patients with smear-positive than in TB patients with smear-negative and extrapulmonary tuberculosis (Zenbaba et al., 2021). The factors that influence patient adherence to taking anti-tuberculosis drugs are: (1) Supporters of swallowing drugs, (2) difficulty swallowing drugs regularly, (3) perceived benefits, and (4) perceptions of patient confidence to take medication. completed treatment (Gebremariam et al., 2021). Patients' understanding of TB disease and its treatment, beliefs about TB, trusted TB healthcare facilities, and their responsibilities in completing treatment are the most common factors influencing patients to complete treatment. The main driving factors were the support received from health facilities, family, and friends, the desire to avoid TB-related stigma, and good tolerance for TB drugs (Grigoryan et al., 2022). Research conducted at an integrated health home hospital revealed that TB patients' perception of their disease,



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drug side effects, and drug-taking supervisors was most related to medication adherence (Wulandari, 2015).

Pharmacists' knowledge will also affect their performance in educating patients. Verification, explanation of drug indications, effectiveness, safety, and compliance are points that should be explained to patients. Pharmacists' skills can provide patients confidence in understanding, hope, attention, and adherence to drug therapy regimens (Priyandani et al., 2022). Pharmacists are expected to be able to update knowledge about tuberculosis so that it is easy to invite patients to comply with their treatment.

The weakness of this review is that the research method uses a literature review limited to 8 articles discussed. Only a few literature reviews discuss the effect of service quality in health facilities on adherence to the treatment of tuberculosis patients. It only concerns the quality of service from the patient's perspective, which is associated with adherence to TB drugs.

### CONCLUSION

The dimensions of SERVQUAL (Quality of Service) used to assess service quality according to patient perceptions are reliability, responsiveness, tangibles, assurance, and empathy. Other factors that influence patient adherence to taking anti-tuberculosis drugs are: 1) Supporters of taking drugs, 2) difficulty swallowing drugs regularly, 3) perceived benefits, 4) perception of patient confidence to complete treatment, 5) trust in health workers, 6) support health facilities, family and friends, and 7) the affordability of TB services. The dimensions of commitment, kindness, and reliability influence the regularity of taking anti-tuberculosis drugs. Healthcare facilities that serve tuberculosis patients should improve the quality of service on five dimensions: assurance, empathy, reliability, responsiveness, and tangibles.

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### Research Article

## Development of Android-based health media applications as promotional media in improving COVID-19 preventive behavior in the community

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### ABSTRACT

Corona Virus Disease 2019 (COVID-19) caused by SARS-CoV-2 became a worldwide pandemic. The spread of wrong information causes people to misperceive the information. The massive spread of the virus shows the lack of public knowledge about preventing the transmission of COVID-19. Intrapersonal factors, namely changes in individual behavior, are the main focus of breaking the chain of the spread of COVID-19. This study aims to develop an Android-based health education application for COVID-19 prevention behavior in the community. This research method used an *exploratory design* with an R&D approach which consists of 2 stages. The first stage was making a *prototype* application through 1) Evaluation of public knowledge and attitudes about COVID-19 prevention with a questionnaire in the form of a *google form* to find strategic issues; 2) Development and mapping of *prototype* content through Focus Group Discussions with nurses and expert consultations. The evaluation used a simple random sampling technique on 193 respondents. The second stage was socialization and application feasibility testing on 193 respondents. The results of the first stage were an overview of the implementation of health education that had not been maximized due to the risk of transmission, sufficient knowledge (52.8%), and negative attitudes (63.2%) toward the prevention of COVID-19, as well as a *prototype* system of health education in applications that include prevention COVID-19 prevention. It was followed by the second stage of socialization and application feasibility testing for users. This study concludes that the development of an android-based application supports effective health promotion efforts in conveying information to increase knowledge and attitudes toward COVID-19 prevention.



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### INTRODUCTION

*Corona Virus Disease* (COVID-19) was first reported in Wuhan, Hubei, China, in December 2019, and on March 11, 2020, the *World Health Organization* (WHO) declared that COVID-19 had become a worldwide pandemic (Bedford et al., 2020). The biomedical function of the best curative and preventive treatments for COVID-19 is currently limited (Prompetchara et al., 2020). The current healthcare infrastructure cannot clinically manage the onset of COVID-19 disease (Eaton & Kalichman, 2020). The distribution of health information and the slow disclosure of cases of positive COVID-19 patients causes public perceptions of the risk of virus transmission to be low (Eaton & Kalichman, 2020). The spread of wrong information through social media also causes people to misperceive information (Li et al., 2020). The importance of public understanding of COVID-19 is the main focus of breaking the chain of spread because until now, there has been no proven effective drug or vaccine. The massive spread of the virus shows the lack of public knowledge about preventing the transmission of COVID-19 (Jaga et al., 2020).

Data on the distribution of COVID-19 based on the WHO report as of January 25, 2021, Global as many as 224 countries, confirmed 98,794,942 patients and 2,124,193 died. Positive COVID-19 in Indonesia as of January 25, 2021, as many as 999,256 people, 809,488 recovered, and 28,132 died (WHO, 2021). Based on a survey conducted by SC Nielsen in collaboration with UNICEF to try to explore public attitudes regarding COVID-19 prevention practices in daily life. It shows that only 31.5% of the 2,000 respondents carried out all 3M behaviors (washing hands, wearing masks, keeping a distance), on a

disciplined basis. The remaining 36% did two of the 3M behaviors, and 23.2% did one of the 3M behaviors. The increase in COVID-19 sufferers in Indonesia from day to day shows the lack of public knowledge caused by the implementation of providing health education to the public about COVID-19 has not been carried out optimally (Djalante et al., 2020).

Our public health in dealing with COVID-19 is highly dependent on social approaches and behavior change as strategies to stop transmission (Lotfi et al., 2020). Intrapersonal factors, namely change in individual behavior, as a preventive basis in preventing the transmission of COVID-19. Interventions to change personal behavior patterns are essential in reducing disease spread, including self-isolation and *social distancing* (Eaton & Kalichman, 2020). Behavior consists of knowledge, attitudes, and practices. Knowledge is measured by whether the respondent can identify the causes of disease, transmission, general symptoms, risks, and prevention of COVID-19. Attitude is measured by awareness of social distance in work and worship and learning from home. Practices related to the ability to bring prevention such as washing hands, avoiding not touching the face, procedures for coughing and sneezing, wearing masks and using disinfectants to prevent COVID-19 (Jaga et al., 2020).

*The World Health Organization* (WHO) states that the best way to prevent and slow down transmission is to obtain information about SARS-CoV-2, the disease it causes, and how it spreads (Gray et al., 2020). Prevention activities are very important to break the chain of transmission of COVID-19 (Jaga et al., 2020). Prevention of COVID-19 transmission can be delivered through the provision of health education. Education is an effort of persuasion or learning to the community so that they are willing to take actions (practices) to maintain



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(solve problems) and improve their health (Gray et al., 2020).

With advances in software and mobile technology, mobile applications have become an important element in everyday life. The use of mobile health applications makes health information easily accessible (Ming et al., 2020). Health education efforts need an attractive strategy to be easily accepted, one of which is health education with android-based media. One of the studies using smartphones during the COVID-19 pandemic is a smartphone-based COVID-19 self-test study using respiratory sounds. Telemedicine can be the key to controlling the COVID-19 pandemic, and the development of smartphones as self-testing respiratory monitoring applications, where users can check respiratory sound patterns through the application (Faezipour & Abuzneid, 2020). Research conducted on the application of smartphone technology during the pandemic as an extension of telemedicine has significantly impacted the COVID-19 pandemic, playing a key role in medicine, patient referral, consultation, and other health care (Iyengar et al., 2020).

The provision of health education media based on Android as an alternative to promotive and preventive efforts to address the lack of knowledge, attitudes, and practices of the community in the prevention COVID-19. It is expected to increase the awareness and interest of respondents so that respondents can adopt the behavior. The digital era is access that can be used as a learning method to provide knowledge about COVID-19, because access is affordable and easy to operate. Through an Android-based health education application, it is expected to increase knowledge and attitudes toward preventing COVID-19. Therefore, this study aims to develop an Android-based health education application for COVID-19 prevention behavior in the community.

## METHOD

### Research methods

This study used an *exploratory design* with a *research and development* (R&D) approach. Research and development (R&D) served to validate and develop products. The development research model was the development of health education applications based on the Android system. This study also used a research design that consisted of two stages. The first stage was an exploratory, descriptive survey of the development of an intervention model. The second stage was socialization and testing to prepare recommendations.

In the first stage, the researchers explored information from the informant's point of view to evaluate the factors that led to the lack of knowledge and attitudes toward preventing COVID-19 in the community and what interventions had been carried out before to improve preventive behavior. Followed by compiling and developing a health education model to enhance COVID-19 prevention behavior.

The researcher started by finding strategic issues regarding evaluating COVID-19 prevention behavior in the community. In this stage, the researcher aims to explore, understand and collect information and data about: (1) The evaluation of community knowledge and attitudes about COVID-19 prevention, (2) The evaluation of interventions that have been implemented by health services to improve COVID-19 prevention behavior, (3) The process of compiling and developing an android system-based health education model for COVID-19 prevention behavior. The second phase of the research flow is (1) The socialization of Android-based health education applications about COVID-19 prevention behavior, (2) Trial and



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assistance to the community in using the application. The research instrument was a questionnaire evaluation sheet in the form of a *google form* about knowledge and attitudes of preventing COVID-19, a questionnaire evaluating the implementation of health education interventions at the Mulyorejo Health Center. Data analysis used descriptive analysis.

### Inclusion and Exclusion Criteria

Inclusion criteria (1) People aged 31 – 45 years, (2) Can communicate verbally well, (3) Can read and write and speak Indonesian well, (4) Have an *Android smartphone* and be able to operate it. Exclusion criteria (1) The patient is sick with COVID-19 or other aggravating diseases, (2) Has severe cognitive impairment, (3) Has impaired consciousness.

### Population and Sample

People in the Mulyorejo Health Center area who have android and are able to operate it. Aged 31-45 years and a sample of 193 respondents using the G-Power Analysis technique, (2) The population of participants in the first phase of FGD activities consisted of multidisciplinary (Head of Mulyorejo Health Center, COVID-19 Nurse, IT Expert), (3) The population of participants in expert consultation activities are experts in the field of COVID-19 in Indonesia (Lung Specialist Doctors).

## RESULTS

### Characteristics of stage I respondents

This research was conducted at the Mulyorejo Public Health Center in Surabaya, East Java Province. The initial stage in research phase I is to evaluate and examine the strategic issues contained in the research site. The characteristics of the respondents in this study were obtained by descriptive analysis of the

respondents' demographic data from March to April 2021. This phase I research involved people with health conditions in the working area of the Mulyorejo Health Center, namely in Mulyorejo Village, Kejawan Putih Tambak Village, and Manyar Sabrangan Village as many as 193 respondents. Characteristics of respondents from male gender 106 respondents (54.9%) and female 87 respondents (45.1%). The age of respondents 31-38 years 59.6% and 39-45 years 40.4%, last education did not go to school 2.6%, elementary school 8.3%, junior high 28%, high school 48.1%, and college 13%.

### Characteristics of FGD participants

Participants consisted of 1 Head of the health center, 3 nurses who handled COVID-19, and 1 IT expert. Most of the participants were female (80%), aged 31-45 years (80%), with last education D3/Diploma (60%), years of work 10-20 years (60%), and contract employment status (60%). This shows that FGD participants have sufficient work experience, so they are expected to be able to provide education and advice to meet the needs in the preparation of developing Android-based health media applications as promotional media to improve COVID-19 prevention behavior in the community.

Results of the evaluation of the health education system

Evaluation of the health education system at the Mulyorejo Health Center was carried out on 193 respondents using a questionnaire in the form of a *google form*. Assessment of the implementation of the provision of health education related to COVID-19 carried out by the Mulyorejo Health Center Surabaya found that the provision of health education by the lecture method (16.6%), the highest respondents explained that they had never received health education about COVID-19 from the health center (83.4 %). The media used



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were leaflets (13%), and the highest number of respondents explained that they had never received health education media about COVID (87%). Implementation time < 1 time a month (16.6%) duration < 15 minutes (11.9%). The place of implementation is in the health center (13%) and in the market (3.6%).

Most of the respondents explained that they had never received health education about COVID-19 from the health center. The health education method found that nurses did not provide health education with lectures, discussions, or direct demonstration methods due to the risk of COVID-19 transmission. Respondents also received information about COVID-19 from social media (WhatsApp, Facebook, Instagram, Twitter), television and radio. A small number of respondents received health education when they were at the health center with loudspeakers or when they were in markets and crowded places where nurses went around in ambulances and explained about COVID-19 with loudspeakers.

Results of the evaluation of knowledge and attitudes of preventing COVID-19

Evaluation of community knowledge and attitudes towards COVID-19 was carried out on 193 respondents who were in the Mulyorejo Health Center working in Mulyorejo Village, Kejawan Putih Tambak Village, and Manyar Sabrangan Village. The evaluation of respondents' knowledge and attitudes towards COVID-19 used a questionnaire in the form of a google form. Most respondents have sufficient knowledge (52.8%) and a negative attitude (63.2%) toward COVID-19 prevention.

### **Android-based health education media application development**

Based on the results of the evaluation of the implementation of the health education intervention system, knowledge and attitudes of the community towards the prevention of

COVID-19 disease that has been carried out, several findings of strategic issues will be discussed in the FGD. (1) The implementation of health education is still not maximized for all communities. The health education method found that nurses did not provide health education by lecture, discussion, or direct demonstration methods due to the risk of COVID-19 transmission. So that most respondents did not receive health education regarding COVID-19, (2) There is no effective media in providing health education, the media used such as leaflets are at risk of COVID-19 transmission. (3) Most of the respondents showed sufficient and insufficient knowledge and negative attitudes related to the prevention of COVID-19 disease.

### **Focus Group Discussion (FGD) and Expert Consultation**

Recommendations from the FGD related to the development of Android-based health education media applications as promotional media in improving COVID-19 prevention behavior in the work area of the Mulyorejo Health Center Surabaya are (1) Health education methods about COVID-19 prevention with the proper method without gathering mass or meeting face to face to minimize the transmission of COVID-19, (2) Effective and efficient health education media, easy to obtain and easy to understand, are needed in providing health education interventions so that they can improve COVID-19 prevention behavior in the community, (3) Health education materials are made in a language that simple, planned according to the needs of the community, (4) The method of developing an Android-based health education media application as a promotional media is deemed appropriate as an effort to increase public knowledge and attitudes regarding COVID-19 prevention. After conducting the FGD phase I, the researchers then arranged the development of an Android-



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based health media application through literature study and expert consultation.

Expert consultations were carried out to obtain input from the results of literature studies, field studies and FGDs that have been carried out and implemented into the development of Android-based health education media applications as promotional media in improving COVID-19 prevention behavior. The expert consultation activity was carried out with one expert lecturer who is an expert in the field of COVID-19, namely dr. Afrita Amalia Laitupa, Sp.P through the whatsapp application and zoom meeting was held on 26-31 April 2021. The results of expert consultations (1) Development of android-based health education media applications must be easy to obtain, understand and apply. The systematics used are according to standards, the descriptions are explained in detail in easy-to-understand language, (2) the nature of the program must be in the form of information that can be updated or updated according to scientific developments, (3) the user guide module is made in easy-to-understand language, systematic in accordance with writing rules that have been set along with relevant references, (4) Android-based applications can be accessed by everyone and applications can be downloaded for free, (5) Using points so that they are interesting and easy to understand such as the understanding of COVID-19, risk groups that need to be monitored, how to prevent COVID-19, 5 important things to prevent COVID-19, increase immunity/immunity, apply cough and sneeze etiquette, keep distance/limit physical interaction, self-isolate, avoid stress and stay optimistic, prevention of COVID-19 in transportation public, prevention of COVID-19 in educational institutions, prevention of COVID-19 in religious activities, prevention of COVID-19 in shopping malls.

Test the validity of android-based health education media applications

The trial of developing an Android-based health education media application as a promotional medium in improving COVID-19 prevention behavior in the Mulyorejo Health Center Surabaya work area based on a questionnaire filled out by respondents in phase 2 research. The components of quality *functionally, reliability, usability, efficiency, and portability* inform that all respondents (100%) stated that the feasibility of the Android-based health education media application regarding the prevention of COVID-19 from the respondent's point of view is good in terms of function, efficiency, feasibility and ease of use. The application is considered to be able to achieve the goal of increasing knowledge and attitudes to prevent COVID-19. The features presented by the application help make it easier for patients to get information regarding the prevention of COVID-19 disease. Using the application is very easy, it can be downloaded for free on the play store.

## DISCUSSION

### Evaluation of Health Education Implementation

Evaluation of the implementation of health education provided by Mulyorejo Health Center Surabaya was carried out using a questionnaire in the form of a google form which had been tested for validity and reliability. The evaluation of the implementation of health education based on six components, namely the method, the media used, the time of performance, the place of implementation, and the content of health education, has been carried out by the Mulyorejo Health Center but the evaluation results illustrate that the provision of health education to the community has not been carried out optimally due to the risk of COVID-19



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transmission so that the method used is not with discussions, lectures or demonstrations directly orally or face to face due to the prohibition on gathering mass and the high number of COVID-19 transmissions. The provision of health education still does not use effective media that can minimize the risk of COVID-19 transmission. Education on the prevention of COVID-19 was only given at the beginning of the pandemic by distributing leaflets, masks and hand sanitizers. The health center nurse provides education by using loudspeakers in an ambulance. The public explained that they got information from social media such as Facebook, Twitter and Instagram.

Health education interventions are defined as helping patients gain the knowledge, skills, tools, and confidence to be active in their care so that they can achieve their self-identified health goals (Gray et al., 2020). The results of previous studies indicate the successful implementation of the mobile health application that supports health workers by providing education about COVID-19, self-assessment, and the ability to monitor their own health (Timmers et al., 2020). The results of the observational cohort study showed that between April 1 and April 20, 2020 a total of 6,194 people downloaded the application, the self-assessment functionality was frequently used to check health status, a total of 5,104 people answered questions and 242 of them showed severe symptoms, 102 users contacted service providers, health which then resulted in 91 contacts. Application users said they were satisfied with the information in the application (mean scale 8.0-10) and appreciated the application's functionality from the symptom assessment (mean 8.0-10) (Timmers et al., 2020).

### Evaluation of Public Knowledge on COVID-19 Prevention

The research shows that the results of respondents' knowledge of COVID-19 prevention before being given an android-based application intervention are mostly classified as sufficient knowledge (52.8%). This knowledge includes general knowledge about the meaning of disease, clinical signs and symptoms, modes of disease transmission, and COVID-19 prevention behavior. This level of knowledge can be influenced by several factors, including the education level of most respondents and having a secondary education background related to the ability to seek and understand information. Knowledge is the result of knowing, which occurs after people sense certain objects; sensing occurs through the human senses, namely the senses of sight, hearing, smell, taste, and touch. Most of the knowledge is obtained from the eyes and ears. Knowledge is a guide in shaping one's actions (Notoatmodjo, 2014). Knowledge can be categorized as good, sufficient or less (Nursalam, 2017).

Low knowledge can make it difficult for someone to form behavior because knowledge or cognitive is a very important domain in shaping a person's actions that are influenced by the learning process (Lee et al., 2021). Behavior that is based on knowledge will be more lasting than behavior that is not based on knowledge. One factor that influences the health education process is the media used to convey messages. If there are no media, the results achieved in health education are less than optimal (Alrasheedy et al., 2021).

Based on the description above, respondents' insufficient knowledge and lack of knowledge



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about COVID-19 prevention prior to intervention based on android applications was due to the lack of attractive health media use strategies and the use of media that pose a risk of COVID-19 transmission, resulting in a lack of public understanding about COVID-19 prevention.

### Evaluation of Public Attitudes towards COVID-19 Prevention

The research shows that the results of respondents' attitudes towards preventing COVID-19 before being given an android-based application intervention are mostly classified as negative (63.2%). Social attitudes can influence a person's negative attitude because social attitudes are formed from the social interactions experienced by individuals. Social interaction means more than just social contact and relationships between individuals as members of social groups. In social interaction, there is a mutually influencing relationship between individuals and one another. There is a reciprocal relationship that also affects the behavior patterns of each individual as a member of society (Azwar, 2015).

This is in accordance with the opinion of Allport (1954) that attitude is a kind of readiness to react to an object in certain ways. The readiness in question is a potential tendency to react in a certain way when an individual is faced with a stimulus that requires a response. After someone knows the stimulus or object, the next process will assess or behave towards the stimulus or health object. A person's negative attitude toward an object is a feeling of being unsupportive or *unfavorable* to the object (Alrasheedy et al., 2021).

Based on the description above, the negative attitude of respondents before the intervention

of android-based applications was caused by a lack of knowledge and could affect a person's attitude. In addition to knowledge, the methods or methods used in conveying messages or programs also affect a person's attitude change, coupled with the lack of interaction between the community and health center staff due to the risk of COVID-19 transmission. The lack of interaction causes respondents to receive less stimulus regarding the prevention of COVID-19 disease, the stimulus in question is the provision of health education regarding the prevention of COVID-19. The existence of a positive attitude before being given an intervention could be because respondents previously received information from social media and mass media.

### Application Development for Android-Based Health Education Media Applications

Compilation of the development of an Android-based health education application regarding the prevention of COVID-19 in the community in the working area of the Mulyorejo Health Center by finding strategic issues presented in FGDs with professional health workers at the health center. This strategic issue was obtained from filling out a questionnaire evaluation sheet regarding the implementation system of health education interventions at the Mulyorejo Health Center Surabaya, as well as evaluating community knowledge and attitudes toward COVID-19 prevention. The results of the FGD showed that there were several strategic issues raised, including: the implementation of health education is still not optimal for all communities, the methods used are one-way and conventional and there is a risk of COVID-19 transmission if gathering mass or explaining directly orally to the community without social distancing, the media used is still limited due to the risk of transmission if distributing leaflets or media in paper form, the material provided is not planned, current health education carried





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out by the health center is delivered orally using loudspeakers with a mobile ambulance or when the community comes to the health center, there is no effective media in providing health education that minimizes the risk of COVID-19 transmission, most of the respondents show sufficient and insufficient knowledge and negative attitudes regarding the prevention of COVID-19 disease, this is because the community almost never gets Health education related to the prevention of COVID-19 from the health center, the public gets information from social media and mass media whose truth is not guaranteed.

Along with the development and advancement of technology, many applications in smartphones can be used as a medium for providing health education to improve health behavior (Timmers et al., 2020). The successful implementation of a *mobile health* application supports health workers by providing education about COVID-19, self-assessment, and the ability to monitor their own health (Timmers et al., 2020).

Researchers developed an Android-based health education media application based on the results of literature studies, FGDs, and expert consultations. Recommendations from the FGD for efforts to improve community behavior toward preventing COVID-19 by developing an effective and efficient method, easy to obtain and easy to do, so as to provide information to the public on the importance of preventing the transmission of COVID-19. The interactive application of how to prevent COVID-19 is deemed appropriate to meet health education needs and improve preventive behavior by considering the risk of COVID-19 transmission. The development designed by the researcher was presented and offered to the respondents. This application is an android-

based application that can be installed on smartphones up to Android version 9. This application is already available on the *google play store*, by doing search by typing ways to prevent COVID-19 and can be downloaded for free with a memory size that is not too large. This application contains information about COVID-19, understanding the disease, clinical signs and symptoms of the disease, modes of transmission, and methods of disease prevention.

## CONCLUSION

The implementation of health education at the Mulyorejo Health Center has been running but has not been maximized and does not have special media due to the high risk of transmission of the COVID-19 disease. The method of implementing health education is carried out by traveling around using an ambulance assisted by loudspeakers. The respondent's knowledge about COVID-19 is in the sufficient category, and the respondent's attitude towards COVID-19 is in the negative category. Android-based health education media applications were developed through literature studies, FGDs, and expert consultations to produce media that provide more effective and efficient health education interventions. This application consists of a health education menu that contains the understanding of the disease, clinical signs and symptoms of the disease, modes of disease transmission, and methods of disease prevention. The use of this application is installed on an Android-based smartphone. This application can be used as a medium for health promotion and as a guide for preventing COVID-19 in the community.



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## Research Article

# Association between the degree of Osteoarthritis and pain level of patients at Baptist Hospital, Batu City

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## ABSTRACT

Osteoarthritis is a chronic disease characterized by the destruction of cartilage in the joints, causing stiffness, pain, and impaired movement. The condition most commonly affects the joints of the knees, hands, feet, spine, and often the shoulders and hips. Knee osteoarthritis is a major public health problem that causes chronic pain and reduces physical function and quality of life. This study determined the relationship between the degree of Osteoarthritis and the pain level in patients at Baptist Hospital, Batu City. This research used a cross-sectional study with 31 respondents. Data collection was conducted directly using the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) questionnaire, modified in Indonesian. To determine the grade of Osteoarthritis using the Kellgren-Lawrence system. The results showed that out of 31 respondents, there were nine patients (29%) who had grade 1 osteoarthritis, 12 patients (38.7%) had grade 2, and 10 patients (32.3%) had grade 3. There were 22 patients (71%) who had a mild pain level, four patients (13%) had a moderate level, and five patients (16%) had a severe pain level. The Spearman correlation test showed no significant relationship ( $p > 0.05$ ) between the degree of Osteoarthritis and the level of pain in patients. This study concludes that there was no relationship between the increasing degree of Osteoarthritis and the level of pain.



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### INTRODUCTION

Osteoarthritis is the most common degenerative joint disease. The disease causes progressive pathological changes in osteoarthritis joints, including articular cartilage damage, subchondral bone thickening, osteophyte formation, synovial inflammation, ligament degeneration, and knee meniscus and joint hypertrophy (Chen *et al.*, 2017). Osteoarthritis can affect any joint but most commonly affects the knees, hands, hips, and spine. This disease considerably impacts the patient, resulting in pain, disability, and social impact. In addition, the economic burden of Osteoarthritis on patients and society is quite significant (Kloppenborg & Berenbaum, 2020).

Knee osteoarthritis contributes to >80% of the total burden of Osteoarthritis, which is directly caused by joint tissue damage, but specific causes of the high prevalence of Osteoarthritis remain unclear. Recently, two dominant factors causing knee osteoarthritis were found to be increasing age, which causes the tissue to age and accumulate more burden, and the second factor, a high body mass index (BMI), resulting in joint overload and inflammation caused by excess fat (Wallace *et al.*, 2017). Determination of the degree of knee osteoarthritis using the Kellgren-Lawrence method based on X-ray images of the knee joint. Each picture will be assigned a value from 0 to 4. Grade 0 indicates there is no osteoarthritis and grade 4 shows severe Osteoarthritis (Sukhikh *et al.*, 2020).

Approximately 654.1 million people (aged >40 years) with knee osteoarthritis in 2020 worldwide. The prevalence of Osteoarthritis in Indonesia is still high, with 1.69 million females and 1.39 million males. Osteoarthritis is the most common type of arthritis and is one of the causes of disability worldwide (Budiman & Widjaja, 2020).

The main symptom of Osteoarthritis is pain (Bacon *et al.*, 2020). Pain is a sensory or emotional discomfort associated with potential or actual tissue damage (Kumar & Elavarasi, 2016). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) test is used to assess knee osteoarthritis patients' pain levels and severity. It has three subscales: pain (5 items), stiffness (2 items), and physical function (17 items) (Seifeldin *et al.*, 2019).

This study aimed to determine the association between the degree of Osteoarthritis and the pain level in patients at Baptist Hospital, Batu City. This study hypothesizes that there is a significant association between the degree of Osteoarthritis and the pain level.

### METHODS

This research used a cross-sectional study. The participants in this study were osteoarthritis patients at Baptist Hospital's Orthopaedic and Traumatology Department from April to May 2020. Sampling used a total sampling technique, where all of the population was sampled (Sugiyono, 2017). The inclusion criteria for this study were patients with knee osteoarthritis who had radiological results confirmed by a Baptist hospital radiologist and were willing to be interviewed. Exclusion criteria were patients with knee pain caused by other diseases such as infection, rheumatoid arthritis, or gouty arthritis. The Kellgren-Lawrence system is used to assess the degree of knee osteoarthritis through radiographs of the patient. The Kellgren-Lawrence system has four grades (0-4); the higher the degree of Osteoarthritis, the higher the severity (Sukhikh *et al.*, 2020). The WOMAC test was used to determine 3 dimensions of pain, stiffness, and physical function with questions 5, 2, and 17, respectively. The Likert version of WOMAC was rated on an ordinal scale of 0 to 4 according to severity (none, mild, moderate, severe, and



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extreme). Each subscale is summed with a maximum score of 20, 8, and 68, respectively (Seifeldein *et al.*, 2019). The research data was analyzed using the Spearman correlation test.

## RESULTS

The total respondents in this study were 48 patients. Based on the inclusion and exclusion criteria, the appropriate criteria were 31 respondents (Table 1).

Based on age characteristics, the majority of osteoarthritis patients were >60 years old (68%), and based on gender, most of the patients were female (71%). Based on the degree of Osteoarthritis, it was most commonly found in grade 2 (38.7%), followed by grade 3 (32.3%). In addition, most of the osteoarthritis

patients were found to have mild pain levels (71%) (Table 1). Patients in grades 1, 2, and 3 most experienced mild pain levels, at 22.5%, 26%, and 22.5%, respectively (Table 2). In this study, there were no patients with grade 4 osteoarthritis.

Analysis of the relationship between the degree of Osteoarthritis and the level of pain in patients was measured using the Spearman Rank test with a P-value of 0.911, which indicates a probability value > significant value ( $\alpha$ ). The interpretation of these results is that there is no significant association between the degree of Osteoarthritis and the level of pain in knee osteoarthritis patients at Baptist Hospital, Batu City.

**Table 1.** General characteristics of respondents

Characteristics		n	%
Age	<60	10	32%
	>60	21	68%
	Total	31	100%
Gender	Males	9	29%
	Females	22	71%
	Total	31	100%
Degree of Osteoarthritis	Grade 1	9	29%
	Grade 2	12	38.7%
	Grade 3	10	32.3%
	Grade 4	0	0%
	Total	31	100%
Pain level	Mild (0-40%)	22	71%
	Moderate (40-70%)	4	13%
	Severe (70-100%)	5	16%
	Total	31	100%



**Table 2.** Characteristic relationship between the degree of osteoarthritis and the level of pain

Degree of Osteoarthritis	Pain Level						Total		P-value
	Mild		Moderate		Severe		n	%	
	n	%	n	%	n	%			
Grade 1	7	22.5%	1	3.2%	1	3.2%	9	29%	0.911
Grade 2	8	26%	0	0%	4	12.9%	12	38.7%	
Grade 3	7	22.5%	3	9.7%	0	0%	10	32.3%	
Grade 4	0	0%	0	0%	0	0%	0	0%	
Total	22	71%	4	12.9%	5	16.1%	31	100%	

## DISCUSSION

This research uses a cross-sectional study with 31 respondents. Based on the results of the study, the distribution of respondents by age showed that most of the respondents were elderly people who were more than 60 years old. There were 21 patients. These results are in accordance with the research of Subroto *et al.* (2021), which states that patients with ages more than 60 years are at high risk for knee osteoarthritis. According to Supartono *et al.* (2018), anyone over the age of 65 is at a high risk of developing calcification of the knee joint. The aging process causes tissue swelling and the release of cartilage-toxic chemicals, leading to increasing deterioration.

The gender distribution of respondents showed that most respondents were females, with 22 patients (71%) (Table 1). These findings, similar to Subroto, Supartono, and Herardi's (2021) research, found that females were more likely than males to suffer from knee osteoarthritis. Females are more susceptible to knee osteoarthritis, particularly after menopause, which is caused by the regulation of estrogen (Johnson & Hunter, 2014). The majority of the respondents (48.6%) had knee Osteoarthritis grades 2 and 3, according to the distribution depending on the degree of knee osteoarthritis (Table 1). According to Ali (2017) research, patients diagnosed with

knee osteoarthritis were more usually detected in grades 3 and 4.

Osteoarthritis is characterized by pain and interruption of joint function as a result of cartilage damage (Enohumah & Imarengiaye, 2008). In individuals with knee osteoarthritis, activities including ascending stairs, getting out of a chair, and running create pain (Felson, 2006). The findings revealed that 22 of the 31 patients had mild pain levels, 4 had moderate pain, and 5 had severe pain (Tables 1 and 2). These results are similar to the research by Bacon *et al.* (2020), who explained that the loss of cartilage thickness has a weak correlation with knee pain. The association with pain may be partly mediated by changes in synovitis and may have a greater effect on those without previously had knee pain than on patients with existing knee pain. According to research by Neogi *et al.* (2010), the variability of pain in osteoarthritis patients might be explained by daily adaptations to overcome pain and avoid activities that cause pain.

Osteoarthritis occurs because it involves many factors, such as trauma, inflammation, biochemical reactions, and metabolic disorders. In addition, it is known that cartilage tissue is not the only one involved, given the lack of blood vessels and nerves in cartilage, so it is unable to produce inflammation or pain. Therefore, the source of pain comes from changes in the





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non-cartilaginous components of the joint, such as the joint capsule, synovium, subchondral bone, ligaments, and periarticular muscles. As Osteoarthritis progresses, these structures are affected and change, including bone remodeling, osteophyte formation, weakening of the periarticular muscles, ligament laxity, and synovial effusions that become more pronounced (Mora *et al.*, 2018). The occurrence of inflammation plays an essential role in the development of Osteoarthritis in some patients and is also a cause of chronic pain. This triggers a series of events driven by inflammatory mediators such as proteases, prostaglandins, neuropeptides, and cytokines (Fu *et al.*, 2018).

In a univariate analysis of a cohort study of patients with knee osteoarthritis, we discovered that several variables, including psychosocial, sociodemographic, disease, and medication, were all significantly associated with higher knee pain scores. Following multivariate analysis, higher pain scores were found to be associated with Hispanic or Native American ethnicity, opioid use, and depression. This demonstrates that, even if there is no relationship between pain scores and the severity of Osteoarthritis, discrepancies in results have been observed in previous studies. Hispanic or Native American ethnicity, age, opioid prescription, fibromyalgia, drug use, antidepressant prescription, alcohol use, gabapentinoid prescription, health insurance status, smoking, previous knee injections, and treatment recommendations are all associated with knee osteoarthritis pain levels. The surgical versus nonsurgical treatment of Osteoarthritis, as a result, age, gender, BMI, race/ethnicity, substance abuse, and psychological variables such as depression, hopelessness, overall well-being, and social stress have all been studied about reports of osteoarthritis-related pain (Eberly *et al.*, 2018).

According to Arendt-Nielsen (2017), significant and continuous nociceptive input might cause

central nervous system sensitization. High levels of sensitization are linked to increased discomfort, disability, and a decreased quality of life. There is frequently a weak or no link between tissue damage and the degree of pain in the corresponding tissues in people with Osteoarthritis. Other factors that influence the use of the WOMAC questionnaire can cause this. The WOMAC questionnaire is a validated pain scale, but it only measures pain over a short period, whereas pain in Osteoarthritis is chronic pain associated with an activity that changes over time (Wu *et al.*, 2020). There are several causes of pain, such as synovial inflammation, capsular fibrosis, and muscle fatigue (Sampiere, 2010). Osteoarthritis pain is heterogeneous, varying between individuals and with different phases of the illness. The mechanisms underlying osteoarthritis pain are complicated, and they are influenced by a variety of psychosocial factors (Fu *et al.*, 2018). The basis for the progression of Osteoarthritis and the neurophysiological correlations are still not fully understood. In recent years, the nervous system's role in the development and manifestation of Osteoarthritis has become clearer. As the disease progresses, neurological changes that occur as the disease progresses will eventually lead to sensitization, resulting in the patient having more pain than expected compared to the actual structural joint damage (Arendt-Nielsen, 2017).

The Spearman correlation test was used to determine the relationship between the degree of Osteoarthritis and the level of pain suffered by patients in this study. The research revealed a P-value of 0.911, indicating that there is no statistically significant association between the degree of Osteoarthritis and the level of pain in patients at Baptist Hospital, Batu City. According to another study by Khairina *et al.* (2018), the pain level is unrelated to Osteoarthritis's radiological grading.



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This study had various flaws, including a small sample size because it was conducted during the COVID-19 outbreak, which limited the number of participants. Nonetheless, this study can be used as a guideline in the treatment of knee osteoarthritis, allowing patients with Osteoarthritis to improve their quality of life through their activities and motions.

### CONCLUSION

From the results of this study, it can be concluded that there is no association between the degree of Osteoarthritis and the level of pain in patients at Baptist Hospital, Batu City.

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### Research Article

## The differences of parasitemia in *Plasmodium berghei* infected mice treated with extract of mango parasite leaves with Artemisinin combination

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### ABSTRACT

Malaria is a disease transmitted through the bite of a female *Anopheles* mosquito caused by the *Plasmodium* parasite. *Plasmodium* has been reported to become resistant to artemisinin. Thus, the study on the ethanol extract of mango parasite leaves/*Dendrophthoe pentandra* (MP) on *P. berghei*-infected BALB/c mice with and without artemisinin combination (MP+A) was conducted. This study is experimental laboratory research with a post-test only design. The percent parasitemia in mice treated with ethanol extract of MP and MP+A leaves decreased. There was no difference in the spleen index in mice given ethanol extract of MP, and MP+A leaves with  $p = 0.203$  and the spleen weight of mice with  $p = 0.134$  (significance:  $p < 0.005$ ). Pearson Correlation test showed a correlation between spleen index with parasitemia and spleen weight with parasitemia; however, there was no correlation between body weight and parasitemia. The ethanol extracts of MP and MP+A leaves had significant antimalarial activity, and the difference in the percent parasitemia between groups was significant but not so far. The spleen index value was not affected by the ethanol extract of MP and MP+A leaves, but the percent parasitemia was affected.



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### INTRODUCTION

Malaria is a life-threatening disease caused by a parasite transmitted through the bite of a female Anopheles mosquito infected with the *Plasmodium* parasite. In 2016 there were 451,000 deaths caused by malaria, then in 2017, there were 435,000 deaths globally. Although there was a decrease in mortality due to malaria in 2016-2017, it was not significant and still relatively high (World Malaria Report, 2018). However, in 2020, there was a 12% increase in cases from the previous year due to service disruptions during the COVID-19 pandemic (World Malaria Report, 2021). Malaria treatment encounters various problems, including parasite resistance to antimalarial drugs (Harijanto, 2006). In Indonesia, there has been resistance to antimalarial drugs such as chloroquine in East Kalimantan since 1973, and it is increasingly spreading to several places (Baird et al., 1996; Kemenkes, 2013). Efforts to overcome the resistance have been carried out in Indonesia by recommending drugs other than chloroquine and sulfadoxine-pyrimethamine against *Plasmodium*, namely the combination of artemisinin (Tjokropawiro et al., 2015). WHO recommends that the use of artemisinin is not given alone but in combination with antimalarial drugs or other supportive drugs (Noedl et al., 2008).

Based on the facts explained above, alternative treatments are needed in dealing with malaria cases, for example, using plants with antimalarial properties. Mango parasite leaves/*Dendrophthoe pentandra* (MP) contain active flavonoid compounds which are antimalarial. According to Yulianti, Dahlia, and Ahmad (2014), mango parasite leaves have a total flavonoid compound of 2.48%. The leaves of the mango parasite were extracted by

maceration using 96% ethanol solvent. This study was conducted on BALB/c mice infected with *P. berghei*. Several studies on parasite leaves have revealed that parasite leaves can function as anticancer agents and antibacterial (Ikawati et al., 2008; Anita, Khotimah, and Yanti, 2014).

### METHODS

#### Research type and design

This study is an experimental laboratory research with a post-test only design. This study was used to determine the antimalarial activity of the ethanol extract of the mango parasite (MP) leaves and MP+A (mango parasite leaves combined with artemisinin) on the percentages of parasitemia and the spleen index. The percent parasitemia in mice infected with *P. berghei* was calculated before treatment.

#### Sample, sample size, and sampling

The sample consisted of white male mice (*Mus musculus*) strain BALB/c. The mice were acclimatized for a week prior to the study. The mice had to meet the inclusion criteria (male white mice, weight 20-30 g, age 6-8 weeks, and in healthy condition) and did not meet the exclusion criteria (anatomical abnormalities in mice; sick or dead during research). Sampling consisted of peripheral blood smears taken on day one to day four after treatment, the spleen was taken on day four after treatment, and body weight was measured before the mice were dissected. The controls used for comparison were positive and negative controls. The positive control used artemisinin at a dose of 0.52 mg/gBW, and the negative control used 0.5% Na-CMC as much as 0.5 ml.

#### Research variables

The independent variables in this study were the doses of ethanol extract of MP leaves



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consisting of 10, 100, and 200 mg/kgBW/day and artemisinin with a dose of 0.52 mg/gBW/day. The control variables in this study included experimental animals (strain, age, body weight), food and drinks given to experimental animals, cages, cage sanitation for experimental animals, and tools used for conducting research in the laboratory. The dependent variables in this study were the percent parasitemia and the mean of splenomegaly of BALB/c mice treated with the ethanol extracts of MP and MP+A leaves.

## RESULTS

The highest percentage of parasitemia was found in the group treated with MP leaves+A ethanol extract at a dose of 10 mg/kgBW. The lowest percentage of parasitemia was found in the group treated with MP leaves+A ethanol extract at the dose of 200 mg/kgBW. The data on the percent parasitemia of MP and MP+A leaves ethanol extracts are shown in Table 1 and Figure 1.

The analysis of parasitemia at the group level using the Anova test showed  $p < 0,005$ , which means that there was a significant difference in all groups, both given the ethanol extract of MP leaves and MP leaves +A. The group of ethanol extract of MP leaves with the lowest dose showed the highest percentage of parasitemia. The higher the dose of ethanol extract of MP leaves, the lower the percentage of parasitemia. In the MP leaves+A ethanol extract group, the higher the dose, the lower the percentage of parasitemia. The percentage of parasitemia in the MP and MP+A groups with the control group also differed. The positive control group showed a lower percentage of parasitemia, while the negative control group showed a higher percentage of parasitemia compared to the MP and MP+A groups.

The highest growth percentage was found in the group treated with ethanol extract of MP leaves at a dose of 10 mg/kgBW. On the contrary, the lowest growth percentage was found in the group treated with MP +A leaves ethanol extract at a dose of 200 mg/kgBW (as shown in Figure 2).

The higher the extract dose, the higher the inhibition percentage. In contrast to the growth percentage, the higher the extract dose, the lower the growth percentage. Positive control showed a negative growth percentage, which was because artemisinin caused a decrease in parasitemia since the second day after treatment.

The highest inhibition percentage was found in the group treated with MP+A leaves ethanol extract at a dose of 200 mg/kgBW. On the other hand, the lowest inhibition percentage was found in the group treated with ethanol extract of MP leaves at a dose of 10 mg/kgBW (shown in Figure 3). The higher the dose of ethanol extract of MP leaves, the higher the inhibition percentage. Likewise, in the MP+A leaves ethanol extract group, the higher the dose, the higher the inhibition percentage.

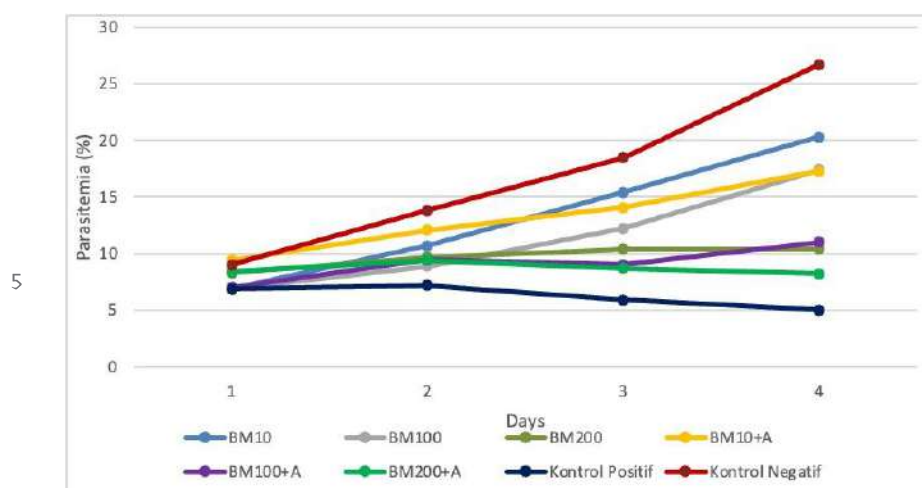
The paired simple t-test analysis showed a significant difference between the weight of the mice before and after treatment ( $p < 0,005$ ). The analysis of the difference in spleen weight after the administration of MP and MP+A leaves ethanol extracts using ANOVA showed no significant difference in the spleen weight of each group ( $p = 0.134$ ). The results indicate that the ethanol extract of the leaves of MP and MP+A had no effect on the spleen weight of mice.

The highest spleen index was found in the group treated with MP +A leaves ethanol extract at a dose of 10 mg/kgBW, and the lowest

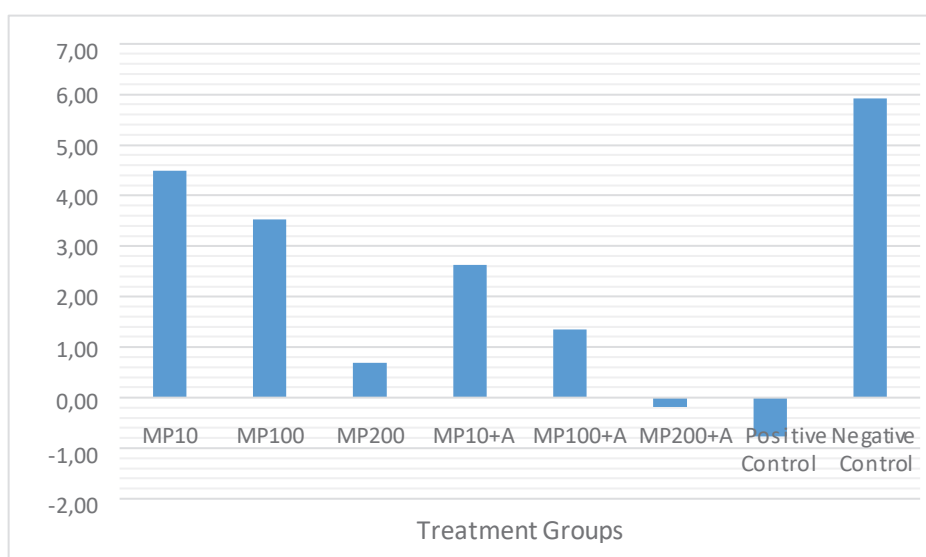


**Table 1.** Mean of parasitemia (%) in *P. berghei* ANKA-infected mice given the ethanol extracts of MP leaves, MP leaves + A, and control.

Treatment Groups	Parasitemia (%)				Mean
	Day 1	Day 2	Day 3	Day 4	
MP10	6,9	10,7	15,4	20,3	13,3
MP100	6,9	8,9	12,2	17,4	11,4
MP200	8,3	9,7	10,4	10,4	9,7
MP10+A	9,4	12,1	14,1	17,3	13,2
MP100+A	7	9,5	9	11	9,1
MP200+A	8,4	9,4	8,7	8,2	8,7
Positive Control	6,9	7,2	5,9	5	6,3
Negative Control	9	13,8	18,5	26,7	17



**Figure 1.** Graph of the relationship between extract dose and percentage parasitemia

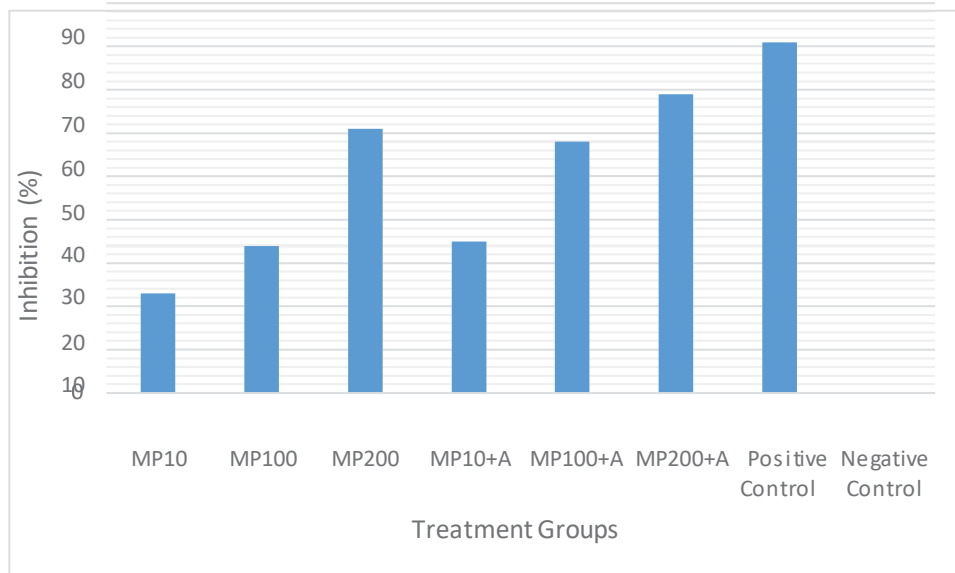


**Figure 2.** Diagram of the relationship between extract dose and growth percentage





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**Figure 3.** Diagram of the relationship between extract dose and inhibition percentage

**Table 2.** Mean of body weight (g), spleen weight (g), spleen index (%), and parasitemia (%) after administration of MP and MP+A leaves ethanol extracts

Treatment Groups	BW (g)	Spleen Weight (g)	Spleen Index (%)	Parasitemia
MP10	26,7	0,59	0,022	13,3
MP100	27,3	0,57	0,021	11,4
MP200	26	0,47	0,018	9,7
MP10+A	26,7	0,53	0,020	13,2
MP100+A	25	0,44	0,018	9,1
MP200+A	26,3	0,42	0,016	8,7
Positive Control	26,7	0,43	0,016	6,3
Negative Control	25,7	0,64	0,025	17

spleen index was in the group treated with MP +A leaves ethanol extract at a dose of 200 mg/kgBW. The higher the dose of ethanol extract of MP leaves, the lower the spleen index value. Likewise, in the MP+A leaves ethanol extract group, the higher the dose, the lower the spleen.

The normality test of the spleen index using

Shapiro-Wilk showed that the data were normally distributed. Analysis of the spleen index between groups using the Anova test showed  $p= 0.203$ , which means that there was no significant difference in all groups, either given MP or MP+A ethanol extract.



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### DISCUSSION

Compounds contained in MP leaves, including flavonoids, are also found in several species used as antimalarial drugs, such as extracts of *Thespesia populnea* (L.) *Soland Ex Correa* leaves (Nurchayanti et al., 2014) and *Kawista* extract (*Limonia accidisima* L.) (Tjahjandarie and Tanjung, 2015). The percentage of parasitemia in Table 1 shows that the ethanol extract of the leaves of MP and MP+A had antimalarial activity. Parasitemia in the MP+A leaves ethanol extract group showed lower parasitemia than the MP leaves ethanol extract group. It means that the ethanol extract of MP+A leaves has better antimalarial activity than the ethanol extract of MP leaves without artemisinin. The MP+A leaves ethanol extract showed lower parasitemia than the group given MP leaves ethanol extract. Tukey's test showed a significant difference in parasitemia in the two treatment groups ( $p < 0.05$ ), except for some groups. However, the difference was not significant. The flavonoid compound in the leaves is the same or lower; however, it was not measured in this study. Based on several studies, many other compounds in MP leaves and the ability to reduce parasitemia depend on the levels of flavonoids in the leaves. In addition, several studies using experimental animals also show that individual responses from experimental animals affect the test results (Gamber and Wayne, 2011).

The results of some studies on flavonoids and artemisinin show that flavonoids and artemisinin have a synergistic effect that can be seen from the interaction between flavonoids and artemisinin, showing that the combined use of flavonoids with artemisinin can increase the effectiveness of artemisinin (Ferreira et al., 2010; Wei et al., 2015; Zhou et al., 2020). Flavonoids have effective inhibitory characteristics similar

to artemisinin (Wei et al., 2015) and, in total administration, provide advances in malaria therapy through dual transcriptional regulation of artemisinin (Zhou et al., 2020). The effect is shown by the dissolved flavonoids that have the same dose effectiveness as artemisinin (Suberu et al., 2014). Based on the growth percentage, it was found that the extract dose is directly proportional to the inhibition percentage and inversely proportional to the growth percentage. It is because the mice given the ethanol extract of the leaves of MP and MP+A with a higher dose had a higher inhibition percentage and a smaller growth percentage.

Spleen index is related to body weight, and spleen weight of mice after administration of ethanol extract of MP and MP+A leaves. The relationship between body weight and parasitemia analysis showed no significant relationship ( $p = 0.947$ ). This was because *P. berghei* infection reduced appetite in mice; therefore, their body weight decreased. Lack of appetite in mice resulted in weight loss. This decrease in body weight in mice is in line with the increase in red blood cells in infected mice (Syamsudin, Dewi, and Marlina, 2008). The weight loss is also in line with the increased number of red blood cells in the infected mice. Weight loss in mice is caused by organ systems damage, impaired metabolic function, and hypoglycemia disorders (Shimada et al., 2019). The impacts after *Plasmodium* infection include acute fluid and nutrient loss resulting from increased activity of the permeability of the digestive tract (Wilairatana et al., 1997). In addition, there is also a reaction to fever and decreased or reduced appetite (Karney and Tong, 1972). Thus, the weight loss of the infected mice results in increased gastrointestinal permeability and disturbances in growth and nutrition (Sowunmi et al., 2007).



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The spleen index and parasitemia showed a significant relationship with  $p < 0,005$ , although weight was not associated with parasitemia. Spleen index analysis in each group using the ANOVA test showed no significant difference ( $p = 0.203$ ). This result is because the ethanol extract of MP and MP+A leaves had no effect on the spleen index but did have an effect on parasitemia. It also resulted in the spleen weight between groups showing no significant difference ( $p = 0.134$ ).

In this study, mice given artemisinin also showed splenomegaly, although there was a decrease in parasitemia (Table 1). This is because artemisinin is a schizonticide in the blood that acts very quickly on all malaria species and does not affect tissues such as the liver and spleen (Katzung, Masters, and Trevor, 2012). There is no effect on the spleen index on the fourth administration of the drug (Windasari, Maslachah, and Rahardjo, 2016). Spleen tissues infected by *Plasmodium* macroscopically cause spleen enlargement (Intan et al., 2017). The enlargement is caused by the immune response in the body which produces inflammatory cells and causes the size of the spleen to enlarge (Kemenkes, 2013). Splenomegaly occurred in all mice given the test extract; thus, the ethanol extract of MP leaves works the same way with artemisinin in that it affects parasites in the bloodstream but not tissues.

### CONCLUSION

The percentage of parasitemia in mice given MP and MP+A leaves ethanol extracts decreased. There was no difference in the spleen index and body weight in mice given MP, and MP+A leaves ethanol extracts.

The analysis of the relationship between BW and parasitemia did not show a significant relationship. However, there was a significant relationship between spleen weight and parasitemia and spleen index with parasitemia.

Further research is needed to identify and isolate the type of active compound that acts as an antimalarial in more detail from the ethanol extract of MP leaves so that it can be developed as an antimalarial.

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### Research Article

## Relationship of mid-parental height, Calcium intake, and intensity of physical activity with body height growth of high school students in Malang

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### ABSTRACT

Stunting is one of Indonesia's problems, as portrayed in RISKESDAS 2018. This means the growth of Indonesian children was not optimal. Some factors that might affect body height growth were genetic factors, represented by mid-parental height, nutritional factors, especially calcium, and physical activity, which could activate pathways to stimulate growth. These factors were known to have a huge role in body height growth, especially if these factors were optimized in adolescence, as in high school students. This research aimed to explain the relationship between body height growth and the factors that might affect it: mid-parental height, calcium intake, and the intensity of physical activity. This research was observational analytic, using purposive sampling as the sampling method and collecting data using a cross-sectional questionnaire. Statistical analysis between variables shows that mid-parental height was positively related ( $p < 0.05$ ,  $r: 0,356$ ), while calcium supplementation was not associated ( $p < 0.05$ ,  $r: -0.165$ ), and intensity of physical activity was not related ( $p = 0.059$ ,  $r: 0.089$ ) with the body height growth of the students. In conclusion, among the factors that were analyzed, mid-parental height was the only one that had a relationship with body height growth.



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### INTRODUCTION

Stunting was one of the problems in Indonesia portrayed in RISKESDAS 2018. It shows that 4,5% of teenagers (16-18 years old) were still very short, and 22,4% of the population was classified as short. This problem means that the growth of Indonesian children was not optimal (Riskesdas Jatim, 2018). Mid-parental height is a tool that is used in clinical practices to determine the potential final height that could be attained by a child based on the height of the parents (IDAI, 2017). This measurement represents genetic factors, in a very simple way, which have a huge role in a child's growth (Garza et al., 2013). The nutritional factor was also known to have critical roles in the growth process. Without sufficient nutrition, the growth could be stunted (Gat-Yablonski & Phillip, 2015). One of the most important nutrients in body height growth is calcium, whereas this nutrition is one of the main components of bone (Sherwood, 2016). Besides those factors, physical activity was also publicly known to affect body height growth. This happened because physical activity could activate pathways by increasing the hormones and growth factors that stimulate growth (Bajer et al., 2015). The growth process itself mainly happens in adolescence, around the age of 16-18 years old, depending on the gender of the child (Guyton & Hall, 2019), and in Indonesia, children this age attend high school. It was publicly known that optimization of the factors described above in this phase was vital to achieving optimal final adult height. This research aimed to explain the relationship between mid-parental height, calcium intake, and intensity of physical activity with the growth of high school students.

### METHODS

This research was cross-sectional observational analytics research. The data was collected using a questionnaire with two data collection instruments: SQ-FFQ (Semi Quantitative-Food Frequency Questionnaire) to collect calcium intake data of the students, and GPAQ (Global Physical Activity Questionnaire) to assess the intensity of physical activity of the students. The population of this research was students of 10 state and private high schools in Malang that agreed to participate in the study. Based on the calculation, the minimum number of samples was 116, and purposive sampling was used as the sampling method. The relationship of every variable was analyzed using the Spearman correlation test. This research was approved by the Health Research Ethic Committee of University of Muhammadiyah Malang through ethical approval No.E.5.a/020/KEPK-UMM/I/2022.

### RESULTS

This research involves 152 students as the samples. The profile of the samples containing minimal, maximal, and average values of age, body height percentile, mid-parental height percentile, calcium intake, and intensity of physical activity is shown in table 1.

The data from every variable is then classified into categories. In the "body height" variable, 19 students, or 12% of the total sample, was classified as "very short". While 41 students or 27% of students, was "short". 88 students or 58% have "normal" body height. 4 students or 3% of the total sample was "tall", and none of them were classified as "very tall". The result was also shown in Figure 1.

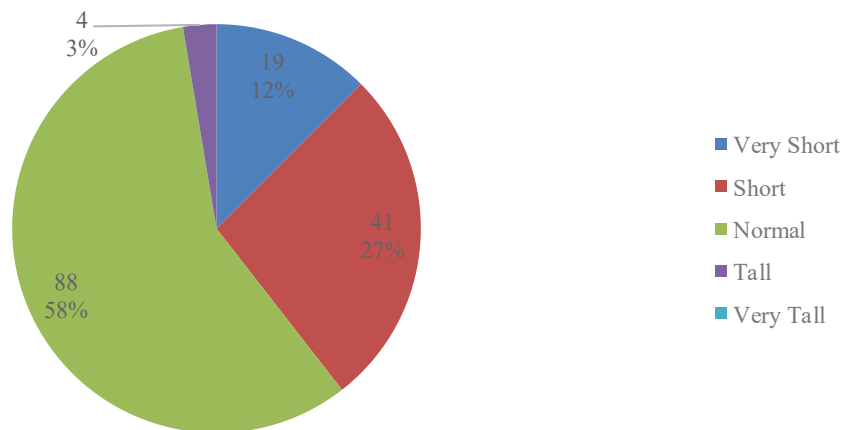


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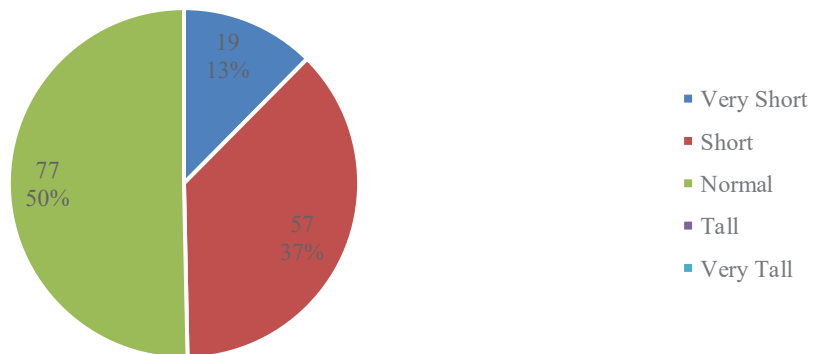


**Table 1.** Demographic profile of the sample

No	Characteristics	Minimal	Average	Maximal
1	Age	15 years	11 17 years 5 months	20 years 6 month months
2	Body Height Percentile	0 <sup>th</sup>	27.8 <sup>th</sup>	93.5 <sup>th</sup>
3	Mid-Parental Height Percentile	0 <sup>th</sup>	20.1 <sup>th</sup>	81.4 <sup>th</sup>
4	Calcium Intake	63 mg/day	755 mg/day	4237 mg/day
5	The intensity of Physical Activity	13 MET/day	1093 MET/day	8817 MET/day



**Figure 1.** Classification of body height growth variable



**Figure 2.** Classification of mid-parental height variable

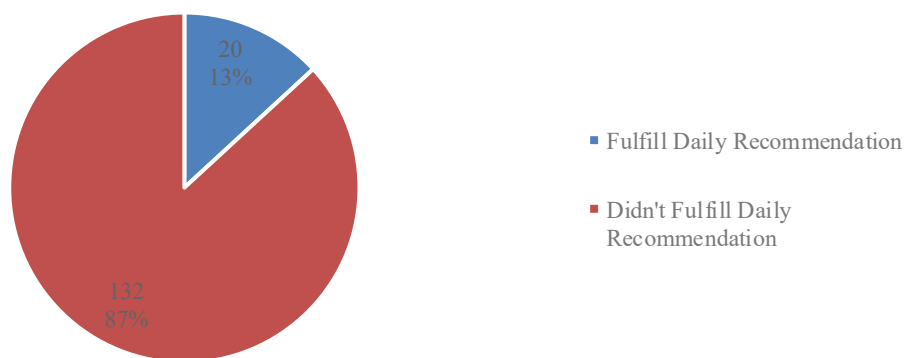


Figure 3. Classification of calcium intake variable

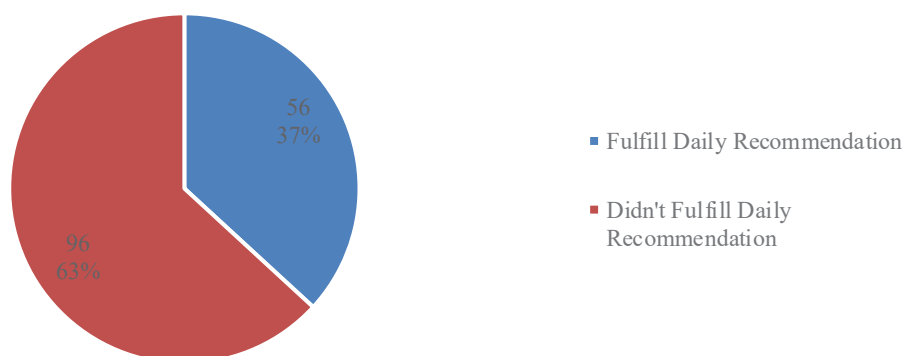


Figure 4. Classification of intensity of physical activity variable

Table 2. Results of statistical analysis between variables

Variable 1	Variable 2	Sig. (P value)	r value
	Mid-Parental Height	0.000	0.356
<b>Body Height</b>	Calcium Intake	0.042	-0.165
	The intensity of Physical Activity	0.278	0.089





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In the “mid-parental height” variable, 19 students or 13% of the total sample, was classified as having “very short” MPH. 57 students or 37% of the students have “short”

In the “calcium intake” variable, 20 students or 13% of the total sample was fulfilled daily requirement of calcium, which is 1200 mg/day. While 132 students or 87% of the total sample was not fulfill daily recommendation of calcium intake. The result was also shown in Figure 3.

In the “intensity of physical activity” variable, 56 students, or 37% of total sample, have fulfilled daily recommendations for daily physical activity, which is 240 MET/day. In comparison, 96 students, or 63% of the total sample, didn’t fulfill the daily recommendation. The result is also shown in Figure 4.

The results of the statistical analysis between variables are shown in table 2. Statistical analysis between the student’s body height and mid-parental height results in P value of 0.000 and an r value of 0.356. This means that the student’s height was significantly related ( $p < 0.05$ ) to mid-parental height with moderate strength. While analysis between calcium intake and student’s body height results in P value of 0.042 and r value of -0.165, this means that calcium intake has significant relation ( $p < 0.05$ ) to the body height, but because the strength is too weak, it was considered to have no correlation. And the analysis of the intensity of physical activity with student’s body height results in a P value of 0.278 with an r-value of 0.089. This means that the intensity of physical activity was not related to the body height of the students.

## DISCUSSION

The result of the statistical analysis means that mid-parental height was positively related to the growth of body height; this result was similar to previous research (Goyal et al., 2020). This relation might happen because parents inherit

genes from their offspring; research has found that no less than 180 genes are related to body height growth (Lango Allen et al., 2010). These genes were also found to regulate biological pathways that have big roles in body height growth such as Hedgehog Signaling Pathway, which regulated by BMP2 and BMP6 (Yang et al., 2015), MAPK signaling pathway, which regulated by FGFR4 and GNA12, TGF $\beta$  signaling pathway, which regulated by GDF5 and ID4 (Guasto & Cormier-Daire, 2021), and Endothelin signaling pathway, which regulated by PRKG2 (Kristianto et al., 2017).

Statistical analysis of calcium intake and body height growth showed no relationship between calcium intake and body height growth. Previous researches have various results regarding this matter; some research found that increased calcium supplementation could support body height growth. One of those researches found that consuming calcium below a specific cutoff value could affect final body height, while increasing calcium intake above the cutoff value didn’t increase final body height but increased the body height’s growth rate. Some researchers also found that calcium intake didn’t correlate with body height (Maharsari, 2018; Winzenberg et al., 2007; Xu et al., 2021). This could happen because calcium has 40-60% absorption rate depending on some factors, like the concentration of calcium ions in the gastrointestinal (GIT) lumen, absorption time of the food in the GIT, and substances that could inhibit calcium absorption, such as phytate and oxalate (Shkempi & Huppertz, 2022).

The result of statistical analysis between body height growth and intensity of physical activity means that there was no relation between the two variables; previous research also found similar results (Jazbinšek & Kotnik, 2020; Kohl et al., 2013; Savitri et al., 2021). This might happen because every person has a difference in responding the physical activity, which



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is the production of hormones and growth factors. The research found that the difference in testosterone concentration in blood before and after the exercise was related to body height, while the intensity of the activity itself was not associated with body height (Kowal et al., 2021).

The result of this research, in general, finds that calcium intake and intensity of physical activity didn't have a correlation with the growth of body height. This might be happened because of the genetic factor that limits the maximum height that could be attained (Perkins et al., 2016). Environmental factors, including calcium intake and intensity of physical activity, support optimum growth.

The limitation of this research was the data collection method, a questionnaire. This method depends on the respondents' memory, which could result in biased data. Another limitation was that this research didn't consider other factors that could affect the calcium absorption rate. To give better understand the relationship of calcium intake and the intensity of physical activity with body height growth, the next research could use cohort method with periodic evaluation from childhood through adolescence, and adulthood to monitor the exact amount of calcium which consumed and the intensity of physical activity of the research samples.

### CONCLUSION

Based on the results of this research, among factors that were analyzed, mid-parental height was the only variable that correlated with the growth of student's body height, while calcium intake and intensity of physical activity was not related to the growth of student's body height. The next research could investigate other growth parameters along with the factors that could affect them.

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## Research Article

# Subchronic exposure to Chlorpyrifos, Carbofuran, and Cypermethrin increase sciatic nerve damage and degeneration in adolescent rats

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## ABSTRACT

Several types of pesticides that are often used are chlorpyrifos (organophosphate), carbofuran (carbamate), and cypermethrin (pyrethroid). Pesticides can kill pests but also can cause toxic effects on humans when exposed. One of the adverse effects of pesticide exposure is a disturbance in the peripheral nervous system. Age is an essential factor in peripheral nerve damage. Nerve injury is one of the most common injuries in children and adolescents and is estimated at 10% to 15% of all exceptional unit cases. However, the outcome of peripheral nerve injury is known better in subjects who sustain the injury at a younger age. This study aims to determine the subchronic exposure effect of chlorpyrifos, carbofuran, and cypermethrin to sciatic nerve histopathology in juvenile rats. This study used 30 male Wistar rats (*Rattus norvegicus*) which were divided into 5 groups, normal group (N), control group (K), chlorpyrifos group (P1), carbofuran group (P2) and cypermethrin group (P3). Subcutaneous injection of pesticides was carried out for 21 days. Rats were sacrificed using the cervical dislocation method, and the right sciatic nerve was taken for histopathological observation. Assessment of the degree of ischiatic nerve histopathological damage is using the Jensen et al., (2018) method. Data were analyzed using the Kruskal-Wallis test and continued with the Mann-Whitney test. This study showed a significantly increased degree of histopathological damage in the chlorpyrifos group, carbofuran group, and cypermethrin group compared to the control group and the normal group ( $p < 0.05$ ). It can be concluded that exposure to chlorpyrifos, carbofuran, and cypermethrin pesticides increased damage and degeneration of the ischiadic nerve in juvenile rats.



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### INTRODUCTION

Pesticides are substances that are often used in the agroindustry to kill pests that have the potential to damage crops. Pesticides can be classified based on their target and chemical composition. Based on their chemical composition, pesticides are divided into several groups, including organophosphates, carbamates, and pyrethroids (Kaur et al., 2019). Several types of pesticides that are often used are chlorpyrifos (organophosphate group), carbofuran (carbamate group), and cypermethrin (pyrethroid group). The use of chlorpyrifos is quite high, reaching 60% in the United States and 53% in China (Foong et al., 2020). Chlorpyrifos is also often used by farmers in Indonesia (Sulaeman et al., 2016). In addition to chlorpyrifos, carbofuran is also often used, especially because organochlorines are prohibited, so carbofuran is an alternative (Indraningsih, 2008). For the pyrethroid group, cypermethrin is often used, such as in Botswana, Africa, where more than 50% of farmers use the pesticide cypermethrin (Sharma et al., 2019).

Pesticides can kill pests but also can cause toxic effects on humans when exposed. Pesticides can enter the human body through various ways, such as inhalation, dermal contact, and ingestion. Dietary exposures are also the main source of nonoccupational exposure to chlorpyrifos (Kadem Majeed et al., 2014; Eaton et al., 2008). Weakness of limbs, muscle tremors, ataxia, convulsions, coma, and even death have been reported as a result of pesticide exposure in humans. Cypermethrin is known to have a toxic dose of 100-1000 mg/KgBW and a potentially lethal dose of 1-10 g/KgWB Exposure to these cypermethrin doses causes symptoms of toxicity and may lead to death (Das & Parajuli, 2007; Yadav, 2018). A study showed that exposure to chlorpyrifos 135 mg/KgBW

had a Case Fatality rate (CFR) of 7.6% in 1376 patients, and carbofuran 8 mg/KgBW had a Case Fatality rate (CFR) of 1% in 479 patients (Dawson et al., 2010)(Dawson et al., 2010).

One of the adverse effects of pesticide exposure is a disturbance in the peripheral nervous system. Chlorpyrifos, carbofuran, and cypermethrin have been shown to cause toxic effects in humans, especially on peripheral nerves. Some of these clinical symptoms in peripheral nerves are numbness, paresthesias, muscle weakness, especially in distal leg muscles, and urinary disturbances (Eaton et al., 2008; Mishra et al., 2020; Yilmaz et al., 2008; Grisold & Carozzi, 2021). In addition to clinical symptoms, the toxicity of pesticides on peripheral nerves can also be assessed from the histopathological features of peripheral nerves. Several studies conducted on rats exposed to chlorpyrifos, carbofuran, and cypermethrin found features of axon degeneration in peripheral nerves. The histopathological picture is vacuolation, digestion chamber, axon swelling, and perineurial edema (Rogers-Cotrone et al., 2010; Sundukov, 2006; Kadem Majeed et al., 2014).

The sciatic nerve is the largest peripheral nerve in the body and has both sensory and motor components. The sciatic nerve has an important role in the body's motor because it is responsible for innervating most of the muscles in the body's lower extremities (Elder, 2007). Pesticides have been known to cause damage to the sciatic nerve (Bostan, 2017). The high use of pesticides increases the risk of sciatic nerve injury in workers in the agroindustry sector due to exposure to pesticides, especially workers who are teenagers. Based on data from the Central Statistics Agency (BPS), the majority of youth aged 16-30 years in rural areas work in agriculture, with a percentage of 39.41%. The data also shows that the highest percentage of rural youth who work in agriculture is in the 16-18 year age group, with a percentage of 32.70%.



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Age is an essential factor in peripheral nerve damage. Nerve injury is one of the most common injuries in children and adolescents and is estimated at 10% to 15% of all cases in specialized units (Costales et al., 2019). However, the clinical outcome of peripheral nerve injury is known to be better in subjects who experienced the damage at a younger age (Chemnitz et al., 2013). Therefore, this study aimed to determine subchronic exposure effect of chlorpyrifos, carbofuran, and cypermethrin to sciatic nerve histopathology in juvenile rats.

### METHODS

Male Wistar rats (*Rattus norvegicus*) aged 30 to 60 days in healthy condition characterized by active movement and good appetite were used in this study. Rats were obtained from the Laboratory of Animal Physiology of UIN Maulana Malik Ibrahim Malang, East Java. Rats were placed in separate cages with each cage containing 2 rats. Rats were fed with pellets and fed with mineral water.

The pesticides chlorpyrifos, carbofuran, and cypermethrin are trademarks of Sigma-Aldrich. The pesticides were then made into stock solutions by dissolving them in dimethyl sulfoxide (DMSO) and sterile distilled water. Chlorpyrifos 20 mg/Kg, carbofuran 0.2 mg/Kg, and cypermethrin 20 mg/Kg were each dissolved in DMSO. The mixture was then dissolved in sterile distilled water until homogeneous. The chlorpyrifos stock solution was stored at low temperature while the carbofuran and cypermethrin stock solutions were stored at room temperature.

In this study, rats were divided into 5 groups, namely groups N, K, P1, P2, and P3. The normal group (N) did not get treatment. The control group was given a subcutaneous injection of 5% DMSO solution. Treatment group 1 (P1) was given a subcutaneous injection of 20 mg/

Kg of chlorpyrifos solution. Treatment group 2 (P2) was given a subcutaneous injection of 0.2 mg/Kg of carbofuran. Treatment group 3 (P3) was given a subcutaneous injection of cypermethrin 20 mg/Kg. The administration of DMSO solution and pesticide injection was once a day and was carried out for 21 days. At the end of the study, the rats were sacrificed using the cervical dislocation method. The rats were then dissected, and the right sciatic nerve was taken for histopathological preparations and observation. This research has received ethical approval from the Ethics Commission of the Faculty of Medicine, University of Jember, number 1.605/H25.1.11/KE/2022.

The sciatic nerve was taken in the right part with a length of 1 cm. Histopathological preparations of the sciatic nerve using longitudinal sections and Hematoxylin-Eosin (H&E) staining. Histopathology was observed by double blinding using an Olympus microscope with a magnification of 400x. Assess the degree of histopathological damage to the sciatic nerve using the Jensen et al., (2018) method. Data were analyzed using the Kruskal-Wallis test and continued with the Mann-Whitney test, with a significance level of 95% ( $\alpha=0.05$ ), with a p-value of  $<0.05$  considered significant.

### RESULTS

The data is the degree of nerve damage based on the criteria of Jensen et al., (2018). The degree of damage to the sciatic nerve can be seen in Table 1. Based on the data on the average degree of damage to the sciatic nerve in each group, it is known that the average degree of damage starts from the highest to the lowest degree, P2 (carbofuran), P1 (chlorpyrifos), P3 (cypermethrin), K (control group) & N (normal group). The highest was in the P2 group (carbofuran) and the lowest was in the normal group. The higher means the damage is



**Table 1.** The sciatic nerve damage degree

Group	Degree of Damage (Average ± SD)
N (Normal)	2.45 ± 0.274
K (Control)	2.50 ± 0.586
P1 (Chlorpyrifos)	3.85 ± 0.821
P2 (Carbofuran)	4.00 ± 0.433
P3 (Cypermethrin)	3.65 ± 0.822

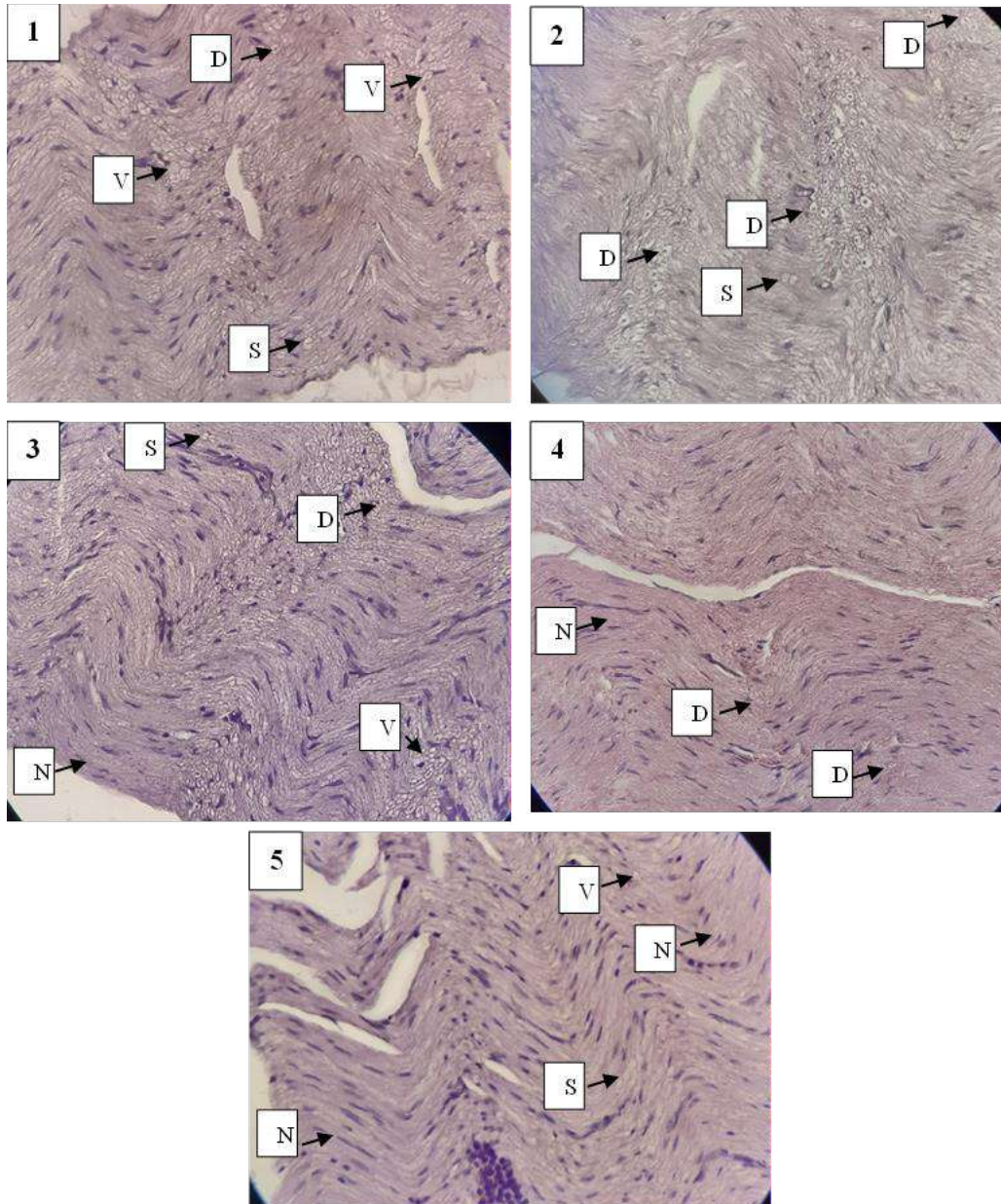
**Table 2.** The Kruskal Wallis test result

	Degree of Damage
Kruskal-Wallis H	16.358
df	4
Asymp. Sig.	.003

**Table 3.** The post hoc Mann-Whitney test result

	N	K	P1	P2	P3
N		0.588	0.008*	0.007*	0.011*
K	0.588		0.015*	0.008*	0.035*
P1	0.008*	0.015*		0.448	0.592
P2	0.007*	0.008*	0.448		0.340
P3	0.011*	0.035	0.592	0.340	





**Figure 1.** The Histopathological picture of the sciatic nerve in the Hematoxylin-Eosin (H&E) staining, 400x magnification; 1. chlorpyrifos administration 20mg/Kg; 2. Carbofuran administration 0.2 mg/Kg; 3. Cypermethrin administration 20 mg/Kg; 4. Control; 5. Normal. (V: vacuolation, D: Digestion chamber, S: swelling of axons and myelin, N: normal axons).



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more severe, and the lower means the damage is lighter.

In the normal and control groups, the histopathological assessment results showed an average degree of slight damage or grade 2. Histopathological appearance at this grade showed that more than 7 axons to less than 25% of axons looked abnormal or degenerated. In the treatment group that was exposed to pesticides, namely groups P1 (chlorpyrifos), P2 (carbofuran), and P3 (cypermethrin) had the same average degree of damage, marked or grade 4. Histopathological appearance at this stage shows that 50-80% of axons appear abnormal or degenerate. Nerve degeneration is indicated by vacuolation and digestion chamber images on axons. The histopathological appearance of the sciatic nerve can be seen in Fig 1.

The data were analyzed using the Kruskal-Wallis non-parametric test. The results of the Kruskal-Wallis test can be seen in Table 2. Based on the results of the Kruskal-Wallis test, the result is 0.003 ( $P < 0.05$ ). These results indicate differences in the degree of damage between groups in the study. The data then continued with the post hoc Mann-Whitney test. The Mann-Whitney test table can be seen in Table 3.

The result showed that the normal group did not show a significant difference in the degree of damage when compared to the control group. The normal group and the control group showed significant differences in the degree of damage when compared to groups P1 (chlorpyrifos), P2 (carbofuran), and P3 (cypermethrin). There was no significant difference in the degree of damage between the P1 (chlorpyrifos), P2 (carbofuran) and P3 (cypermethrin).

## DISCUSSION

Pesticides can increase nerve damage and degeneration through increased production of Reactive Oxygen Species (ROS), resulting in increased oxidative stress on nerves. Increased ROS and oxidative stress can increase nerve damage and degeneration (Fukui, 2016). Pesticides also induce neuronal microtubule damage, interfering with the distribution of the Nicotinamide mononucleotide adenylyl transferase enzyme (Nmnat), which protects neurons from degeneration (Li & Collins, 2019). In this study, adolescent rats were exposed to three pesticides: chlorpyrifos, carbofuran, and cypermethrin. This study showed increased damage and degeneration of the sciatic nerve in juvenile rats exposed to chlorpyrifos, carbofuran, and cypermethrin.

In the normal and control groups, the histopathological assessment results showed an average degree of slight damage or degree 2. In the normal and control groups, histopathological features were found indicating axon degeneration, namely digestion chamber, vacuolation, and axon swelling, although there were slight. The degenerate axon picture can also be found in normal nerves because the axon degeneration process also occurs in normal neurodevelopment. This is in accordance with other studies that the process of axon degeneration can also occur in normal development. Axon degeneration in normal development aims to eliminate unwanted or inappropriate axon branching in its region (Saxena & Caroni, 2007; Luo & O'Leary, 2005).

The treatment group that was exposed to pesticides, namely groups P1 (chlorpyrifos), P2 (carbofuran), and P3 (cypermethrin) had the same average degree of damage, marked or grade 4. The picture of vacuolation, digestion chambers, and axonal swelling on



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the axons showed nerve degeneration. The results of the comparison between the treatment group and the normal group, and the control group showed a significant difference in the degree of damage. The treatment group had a higher degree of injury when compared to the normal group and the control group. These results indicate that the administration of three types of pesticides in the treatment group both increased damage and degeneration of the nerves. Nerve degeneration is shown by vacuolation and digestion chamber images on axons. In the treatment group, there was an increase in the picture of the digestive chamber and vacuolation of the nerves when compared to the normal group and the control group. This is in accordance with several studies conducted by Rogers-Cotrone et al., (2010), Sundukov, (2006), Kadem Majeed et al., (2014) that the three types of pesticides increase nerve damage and degeneration. The increase in axon damage and degeneration in this treatment group may occur because pesticides can increase the production of Reactive Oxygen Species (ROS) and induce microtubule damage resulting in increased nerve damage and degeneration (Karami-mohajeri & Abdollahi, 2011; Gupta et al., 2007). Research conducted on adult rats exposed to organophosphate pesticides showed an increase in vacuolation of the lumbar region of the nerves (Rogers-Cotrone et al., 2010). Another study conducted using adult rats exposed to chlorpyrifos and carbaryl either alone or in combination showed a pathological effect on the sciatic nerve which was observed through histopathological and biochemical observations (Sundukov, 2006). Another study conducted on adult rats with exposure to cypermethrin increased neurodegeneration. The increase in nerve degeneration is indicated by an increase in the vacuolation of the number and size of the spinal and sciatic nerves (Kadem Majeed et al., 2014).

Increased ROS, decreased antioxidants, and microtubule damage can be caused by excessive excitation of nerves due to pesticides (Karami-mohajeri & Abdollahi, 2011; Gupta et al., 2007). The three pesticides in this study, namely chlorpyrifos, carbofuran, and cypermethrin, work by inhibiting the action of acetylcholinesterase (AChE) and modulating sodium and calcium channels and then increasing excitation in the nerves (Eaton et al., 2008; Saquib et al., 2021; Kadem Majeed et al., 2014). Increased excitation of nerves leads to dysfunction of mitochondria. Neurons cannot control ROS production, so ROS production is excessive and results in increased oxidative stress and neurodegeneration (Fukui, 2016; Karami-mohajeri & Abdollahi, 2011). In addition, excess intracellular calcium due to the effects of pesticide exposure induces phosphorylation of Collapsin Response Mediator Protein (CRMP-2) and an increase in HDCA5, which results in microtubule damage. Microtubule damage to neurons disrupts the distribution of Nicotinamide mononucleotide adenylyl transferase enzyme (Nmnat) which protects neurons from damage and degeneration (Li & Collins, 2019). Sub-chronic exposure to chlorpyrifos, carbofuran, and cypermethrin in this study showed an increase in damage and degeneration of the sciatic nerve in adolescent rats. The limitation of this study is that no clinical assessment was carried out to determine the effect of pesticide exposure on the clinical condition of the lower extremities of subjects.

### CONCLUSION

Based on this study, it can be concluded that subchronic exposure to chlorpyrifos, carbofuran, and cypermethrin increase damage and degeneration of the sciatic nerve in adolescent rats.



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## Research Article

# The effectiveness of health education provision of animated video media in improving COVID-19 prevention behavior post-vaccination among students of Muhammadiyah Islamic Boarding School Karangasem Paciran Lamongan

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### ABSTRACT

Vaccination in the context of dealing with COVID-19 has been promoted. The increasing number of cases showed the lack of community compliance in preventing the transmission of COVID-19 after Vaccination. Intrapersonal factors, such as changes in individual behavior, were the main focus of breaking the chain of the spread of COVID-19. This study aimed to determine the effectiveness of providing health education with animated video media on improving COVID-19 prevention behavior after Vaccination among students at the Karangasem Islamic Boarding School Paciran of Lamongan. This study used pre-experimental with one group pre-test and post-test design. The population was Muhammadiyah Islamic boarding school students in Karangasem Paciran Lamongan, which amounted to 460 and took samples of 332 people using a non-probability purposive sampling technique. The research instrument used a questionnaire 30 items. The results of knowledge have increased from pre-test sufficient knowledge (60.84%), and post-test good knowledge (81.02%) using the Wilcoxon signed rank test  $p=0.000 (<0.05)$ . The results of attitudes have increased from pre-test negative attitude (70.78%) and post-test positive attitude (76.81%) using the Chi-square test  $p=0.001 (<0.05)$ . The results of practice have increased from pre-test sufficient practice (62.95%), and post-test good practice (77.71%) using the Wilcoxon signed rank test  $p=0.000 (<0.05)$ . In conclusion, the video animation media of health education was proven to increase post-vaccination COVID-19 prevention behavior among students at the Karangasem Islamic Boarding School Paciran of Lamongan.



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### INTRODUCTION

*Corona Virus Disease* (COVID-19) was first reported in Wuhan, Hubei, China, in December 2019, and in March 2020, the World Health Organization (WHO) declared that COVID-19 had become a worldwide pandemic. (Bedford et al., 2020). Globally, this virus showed a very high transmission rate. At the time of writing this literature, it was estimated that there were 557,917,904 infected with COVID-19 and 6,358,899 deaths (WHO, 2022).

According to the World Health Organization (WHO), COVID-19 can be transmitted through particles that come out of the breath when individuals are within one meter of it. Thus, a person can quickly become infected if using objects or surfaces that have been in contact with an infected person or come into direct contact with that person. Therefore, the WHO recommended using appropriate personal protective equipment, such as face masks, to control the spread of infection (Djalante et al., 2020). In addition, based on the Centers for Disease Control and Prevention (CDC) in controlling COVID-19, it was recommended to maintain social distancing to minimize the possibility of being exposed to the virus. (Han et al., 2020).

Various strategies and development of COVID-19 vaccines were carried out to control the COVID-19 pandemic. Various vaccines have undergone clinical trials with promising results in various countries. Vaccines' effectiveness, safety, and short and long-term side effects were major concerns in clinical trials in these strategies and developments (Setiyo Adi Nugroho, 2021). Based on the previous study, reducing the COVID-19 crisis with a vaccine would significantly positively affect overall risk if a large proportion of people received the vaccine. In addition, if the vaccine was used to complement existing

protective measures such as wearing masks, washing hands, and keeping a distance (Abo & Smith, 2020).

The government was currently implementing a program to break the chain of the spread of COVID-19, such as the COVID-19 vaccination program. According to the Indonesian Ministry of Health (2021), the COVID-19 Vaccine was expected to reduce the transmission or transmission of COVID-19 and morbidity and mortality due to COVID-19. The COVID-19 vaccination program in Indonesia, which began on January 2021, was expected to accelerate the occurrence of herd immunity which will have an impact on reducing the number of infected cases (Nasir et al., 2021). Based on data obtained on March 2022, about 146,577,204 Indonesians have been vaccinated in full doses.

Based on the survey results describing the level of community compliance in implementing the COVID-19 post-vaccination health protocol in Tangerang, it was found that 20% of respondents did not comply with the health protocol, as well as differences in the characteristics of respondents in terms of age, gender, and education. (Mulyawan et al., 2021). The spread of wrong health information caused the public perception of the risk of transmitting the virus low (Eaton & Kalichman, 2020). Public health in dealing with COVID-19 highly depends on social approaches and behavior change as strategies to stop transmission (Eaton & Kalichman, 2020). Intrapersonal factors, namely change in individual behavior a basic in preventing the transmission of COVID-19. Interventions to change individual behavior patterns have an important role in reducing disease spread, including self-isolation and social distancing (Eaton & Kalichman, 2020).

According to *World Health Organization* (WHO) the best way to prevent and slow transmission was to get information about





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SARS-CoV-2, the disease it caused, and how it spreads. (Gray et al., 2020). Prevention activities were very important in breaking the chain of transmission of COVID-19 (Jaga et al., 2020). Prevention of COVID-19 transmission can be delivered through the provision of health education. Education was an effort of persuasion or learning to the community so that they were willing to take actions (practices) to maintain (solve problems) and improve their health (Gray et al., 2020).

Islamic boarding schools have a very high risk of COVID-19 transmission. This is caused by the use of shared public facilities, such as bedrooms, bathrooms, and dining rooms. Implementing health protocols was very important in breaking the chain of transmission. Therefore, this study aimed to examine the effectiveness of providing health education with animated video media on increasing COVID-19 prevention behavior after Vaccination among students at the Karangasem Islamic Boarding School Paciran of Lamongan.

## METHODS

This study used a pre-experimental design with one type of research (one group pre-test-post-test design). This research was conducted by giving a pre-test before doing the intervention.

## RESULTS

**Table 1.** Knowledge Distribution of Post-Vaccination Prevention of COVID-19 Before and After Health Education Provision of Animated Video Media

Knowledge	Pre Test		PostTest	
	N	%	N	%
Well	68	20.48	269	81.02
Enough	202	60.84	63	18.98
Not enough	62	18.68	0	0
Amount	332	100	332	100

$\rho = 0.000 < \alpha = 0,05$   
*Wilcoxon Signed Rank Test*

After that, the intervention was given, then a post-test (final observation) was carried out. This study's population was all female students, about 460 people. The sample of 332 people was obtained using a non-probability purpose sampling technique with the criteria of having been vaccinated at dose 2. The inclusion criteria were 1) female students who provided as respondents, 2) female students who had been vaccinated at dose 2, and 3) female students who were able to communicate well. The exclusion criteria were 1) female students who were not in an Islamic boarding school or having activities, 2) female students who were sick, and 3) female students who were blind and deaf.

The instrument used in this study was a questionnaire to determine the knowledge, attitudes, and practices among students of Karangasem Paciran Lamongan Islamic Boarding School in preventing COVID-19 before and after the intervention. This research was conducted 1 time, providing health education with animated video media for 60 minutes, conducted in July 2022. The data has been analyzed using the Wilcoxon Sign Rank Test and Chi-Square (Pre-Post) statistics in the SPSS 25.00 program. The data is considered to be significant if the results of statistical tests show  $\alpha \leq 0.05$ . This study has been approved by Ethical Committee Universitas Muhammadiyah Surabaya.



**Table 2.** Distribution of COVID-19 Prevention Attitudes Post Vaccination Before and After Health Education Provision of Animated Video Media

Attitude	Pre Test		Post Test	
	N	%	N	%
Positive	97	29.22	255	76.81
Negative	235	70.78	77	23.19
Amount	332	100	332	100

$\rho = 0.001 < \alpha = 0,05$   
*Chi Square*

**Table 3.** Distribution of Post-Vaccination COVID-19 Prevention Practices Before and After Health Education Provision of Animated Video Media

Practice	Pre Test		Post Test	
	N	%	N	%
Well	57	17,17	258	77.71
Enough	209	62.95	74	22.29
Not enough	66	19.88	0	0
Amount	332	100	332	100

$\rho = 0.000 < \alpha = 0,05$   
*Wilcoxon Signed Rank Test*

Table 1 shows a significant increase in knowledge of Post-Vaccination Prevention of COVID-19 after the health education provision using animated video media among students at the Karangasem Islamic Boarding School Paciran Lamongan in 2022.

Table 2 shows a significant increase in COVID-19 prevention attitudes Post-Vaccination after the health education provision using animated video media among students at the Karangasem Islamic Boarding School Paciran Lamongan in 2022.

Table 3 shows a significant increase in COVID-19 prevention practices Post-Vaccination after the health education

provision using animated video media among students at the Karangasem Islamic Boarding School Paciran Lamongan in 2022.

## DISCUSSION

### Knowledge of Post-Vaccination COVID-19 Prevention Before and After Health Education Provision of Animated Video Media Among Students at the Karangasem Islamic Boarding School Paciran Lamongan in 2022

Knowledge is a guide in shaping individual actions (Timmers et al., 2020). Knowledge is the result of knowing, which occurs after people sense particular objects; sensing occurs through the human senses, namely the senses



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of sight, hearing, smell, taste, and touch. Most of the knowledge was obtained from the eyes and ears. Knowledge can be categorized as good, sufficient, and lacking (Jaga et al., 2020). This level of knowledge can be influenced by several factors, including the education level of most respondents and having a secondary education background related to the ability to seek and understand information (Alrasheedy et al., 2021).

The result of this study showed that respondents' knowledge of preventing COVID-19 before being given health education intervention, and animated video media were mostly classified as sufficient knowledge (60.84%) and after being given the intervention, most were classified as good knowledge (81.02%). This knowledge includes general knowledge about the meaning of disease, clinical signs and symptoms, vaccinations, modes of disease transmission, and COVID-19 prevention behavior. The results of this study were in accordance with a previous study that showed there was a difference in knowledge about COVID-19 prevention before and after educational videos for school-age children (Adila & Wijaya, 2021).

Low knowledge can make it difficult for someone to form behavior because knowledge or cognition is a very important domain in shaping a person's actions that are influenced by the learning process. Behavior-based on knowledge will be more lasting than behavior not based on knowledge (Lee et al., 2021). Public knowledge about preventing disease transmission was very important to suppress the transmission of COVID-19. Knowledge is important in forming attitudes and behavior; if a person doesn't have sufficient knowledge, then there will be no real action taken (Law et al., 2020).

Health education interventions were defined as helping patients gain the knowledge, skills, tools, and confidence to be active in their care

so that they can achieve their self-identified health goals (Gray et al., 2020). Learning was influenced by internal and external factors. Internal factors are factors that come from within a person. And external factors were stimulation factors from outside through their senses, one of which was learning media. This study chose animated video as a medium because it can deliver material pleasantly and stimulate many senses in receiving information, especially the eyes. According to a previous study, the eyes were the five senses that channel the most information and knowledge to the brain, which was around 75-87% (Adila & Wijaya, 2021).

Based on the description above, knowledge before being given an intervention was sufficient, and after the intervention was classified as good because one of the factors that influenced the success of health education was the media used to convey messages. If there were no media, the results achieved in health education would be less than optimal. In this study, the media used was animated video media so that when researchers gave explanations about COVID-19, participants could maximize the senses of sight and hearing in receiving health education.

### **Attitudes to Prevent COVID-19 Post Vaccination Before and After Health Education Provision of Animated Video Media Among Students at the Karangasem Islamic Boarding School Paciran Lamongan in 2022**

Attitude was a person's response or reaction to an object. The response then produces a person's behavior in dealing with the object. The formation of attitudes was influenced by several factors, including strong experience, the influence of other people who are considered important, culture, mass media, educational institutions and religious institutions, and the influence of emotional factors (Lee et al., 2021).



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Based on the research conducted, it showed that the results of respondents' attitudes towards preventing COVID-19 before being given health education intervention in animated video media were mostly classified as negative attitudes (70.78%), and after being given the intervention, most were classified as positive attitudes (76.81%). The results of this study were in accordance with the previous research that there was an effect of education about health protocols with audiovisual media on the attitudes of children aged 10-12 years at Brother Bakti Luhur Elementary School. (Sambo et al., 2021).

A person's negative attitude can be influenced by social attitudes because social attitudes are formed from the social interactions experienced by individuals. Social interaction means more than just the existence of social contact and relationships between individuals as members of social groups. In social interaction, there was a mutually influencing relationship between individuals. A reciprocal relationship also affects the behavior patterns of each individual as a member of society (Alrasheedy et al., 2021). This was in accordance with Allport's opinion that attitude was a readiness to react to an object in certain ways. The readiness in question was a potential tendency to react in a certain way when an individual faced a stimulus that required a response. After someone knows the stimulus or object, the next process will be to assess or behave towards the stimulus or health object. A person's negative attitude toward an object is a feeling of being unsupportive or unfavorable to the object (Alrasheedy et al., 2021).

The video media in this study was a supporting factor in the formation of student attitudes toward preventing COVID-19. The use of this media maximizes the reception of information through all the senses so as to allow

information to be better understood. Moving pictures and sound effects can make children interested and pay attention to the given object. This media can significantly influence changes in children's attitudes after going through the learning process (Fitria, 2018). Attitude can be seen in the behavior shown by a person in responding to an object. Attitudes cannot be seen directly. A positive or supportive attitude can be formed from knowledge and experience. Increased knowledge has a positive relationship with changes in attitudes, which will later be applied to behavior

Based on the description above, the attitude before the intervention was classified as negative and after the intervention was classified as positive because one of the influencing factors, namely knowledge, could affect a person's attitude. In addition to knowledge, the methods used in conveying messages or programs also affected a person's attitude change.

### **Post-Vaccination COVID-19 Prevention Practices Before and After Providing Health Education Animated Video Media Among Students at the Karangasem Islamic Boarding School Paciran Lamongan in 2022**

Health practices are all activities of people to maintain health, including practices related to the prevention of infectious diseases (Gray et al., 2020). An attitude was not necessarily manifested in action. To become a real action, a supporting or enabling condition was needed, including facilities or infrastructure. Action (practice) is a person's open response to stimuli from outside the object (Lee et al., 2021). The stimulus in question was the provision of health education. Based on Edgar Dale's theory of experience, the provision of health education media by hearing and seeing will provide 50% memory, so it was expected to influence changes in respondent behavior. The formation of new behavior starts from the formation of cognitive aspects. The new object was a stimulus for



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the individual. The learning process about the stimulus will lead to new knowledge. If the stimulation is increasingly known and realized, it can lead to action in response to the new object.

This study showed that the respondents' practice of preventing COVID-19 before being given health education intervention using animated video media were mostly classified as sufficient practice (62.95%). After the intervention was given, most were classified as good practices (77.71%). This was in accordance with previous research that there was an increase in the number of respondents who have COVID-19 prevention behaviors, namely the behavior of washing hands and wearing masks while traveling (Rahmatina & Erawati, 2020).

Based on the description above, the practice before the intervention was given was quite adequate, and after the intervention was classified as good because there was a relationship between knowledge and attitudes with disease prevention efforts. If knowledge and attitudes were good, it could affect the respondent's actions, and vice versa if knowledge and attitudes were negative, it could affect a person's actions. Limitations of the study, when this research was conducted, the female students were gathered in one large hall, resulting in mass communication which was more at risk of distraction, crowded, and noisy. The female students talk to each other with friends and are less focused on the researcher.

## CONCLUSION

There was an effect of providing health education with animated video media on increasing preventive behavior consisting of knowledge, attitudes, and practices for preventing COVID-19 after Vaccination among students at the Karangasem Islamic Boarding School Paciran Lamongan.

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Research Article

## Effect of ethanol extract of *Hedyotis corymbosa* (L.) Lamk against parasitemia and hepatomegaly in *Plasmodium berghei* ANKA-infected mice

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### ABSTRACT

Malaria is a parasitic infectious disease that remains one of the focuses of world health problems. The ethanol extract of *Hedyotis corymbosa* has biochemical compounds potentially become a new anti-malarial drug. This study aimed to analyze the effect of this extract on parasitemia and hepatomegaly in mice infected with *Plasmodium berghei* ANKA. Twenty five BALB/c mice were infected with *P. berghei* ANKA and grouped into 5 groups. Group 1-3 were treated with 250 mg/Kg BW (HC250), 300 mg/Kg BW (HC300), and 350 mg/Kg BW (HC350) of ethanol extract of *H. corymbosa* (EEHC), respectively. Group 4 was a positive control (POS) which was given dihydroartemisinin-piperquin (DHP) and Group 5 was a negative control (NEG) which was only given CMC Na 1%. Treatments were given orally once a day for four consecutive days. Parasitemia was observed daily on Giemsa-stained tail blood smear. On day 5 the mice were sacrificed, blood were collected by cardiac punctured, the livers were removed and the length, width, and weight were measured. There was no significant difference on parasitemia between Group 1, 2, 3 and NEG. However, the highest inhibition of parasite s growth was found in Group 3 (61.4%. Observation on hepatomegaly, showed that a significant difference on the length of the liver was found between Group 3 and NEG.



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### INTRODUCTION

Malaria is a parasitic infectious disease caused by *Plasmodium spp.* that is spread through the bite of a female *Anopheles* mosquito as a vector. *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium knowlesi* are the five *Plasmodium* species that cause malaria in humans. *P. falciparum* is the species that most frequently causes severe and fatal malaria among the five *Plasmodium* species. Malaria patients might have liver enlargement or hepatomegaly (Kementerian Kesehatan RI, 2019). Hepatomegaly is caused by hepatocyte inflammation, which causes an immunological response (Wilson *et al.*, 2009). Malaria is still a concern to public health across the world, particularly in malaria-endemic areas. According to the World Health Organization, there were at least 229 million malaria infections and an estimated 409,000 malaria deaths in 2019 (Nyunt *et al.*, 2017)(WHO, 2022). In 2020, the total number of malaria cases in Indonesia was 226,364 (Kementerian Kesehatan RI, 2021).

One of the particular targets of the global commitments mentioned in the Sustainable Development Goals (SDGs) is to eradicate malaria by 2030 (Pusat Data dan Informasi Kemenkes RI, 2016). The comprehensive treatment of malaria is one of the eradication efforts in Indonesia. However, the effectiveness of several anti-malarial medications has decreased or even become resistant, such as chloroquine (Kementerian Kesehatan RI, 2019). Parasite resistance to Sulfadoxine-Pyrimethamine, Halofantrine, Quinine, and Mefloquine has also been reported (Bloland & World Health Organization, 2001). Artemisinin resistance has been found in Cambodia, Laos, and Vietnam (WHO, 2019). To counteract the rise of anti-malarial

resistance, new anti-malarial medicines must be provided.

Indonesia has been acknowledged as a country that is rich in natural resources, especially medicinal plants. Some medicinal plants in Indonesia, such as *H. corymbosa*, may be used and developed as novel anti-malarial drugs. The community has used this plant as a traditional treatment, such as fever reducer (antipyretic), anti-inflammatory, antibacterial, diuretic, detoxifying, anticancer, dysentery medicine, a gastric ulcer medicine, blood circulation, postpartum medicine, and medicine for digestion disorders (Soemardji, Anisa, & Damayanti, 2015). The plant *H. corymbosa* has been proven to have significant hepatoprotective effects. This is evidenced by a reduction in the serum level of hepatic enzymes, serum glutamic oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT), as well as serum level of bilirubin, and an essentially normal liver histological image following treatment of *H. corymbosa* extract to wistar rats who had suffered liver injury due to paracetamol overdose (Sadasivan *et al.*, 2006). Bioactive compounds such as alkaloids, flavonoids, tannins, glycosides, terpenoids, and steroids are contained in the ethanol extract of *H. corymbosa* (Selvan, Vellavan, & Sakunthala, 2015), and includes ursolic acid, a hepatoprotective molecule (Sadasivan *et al.*, 2006). The alkaloid has anti-inflammatory and anti-malarial effects by reducing the function of heme polymerase, resulting in heme buildup, which is toxic to parasites and causes parasite death (Louisa, 2016). In addition to alkaloids, flavonoid compounds exert anti-malarial effects by reducing the entrance of L-glutamine and myoinositol into infected erythrocytes and decreasing *Plasmodium* fatty acid biosynthesis (FAS II), hence interrupting *Plasmodium* development and causing *Plasmodium* mortality (Ntie-Kang *et al.*, 2014). This aimed



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to determine the effect of ethanol extract of *H. corymbosa* on parasitemia and hepatomegaly in mice infected with *Plasmodium berghei* ANKA.

## METHODS

### Ethical approval

The study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Airlangga as stated on the certificate number 35/EC/KEPK/FKUA/2022

### Preparation of the ethanol extract of *H. corymbosa* (EEHC)

The EEHC was prepared by maceration of simplicia in 70% ethanol solvent in the Laboratory of Herbal Materia Medika, Batu City, East Java Province, Indonesia. The EEPG was then used to prepare a doses of 250 mg/kgBW, 300 mg/kgBW, and 350 mg/kgBW in 1% CMCNa (Yuliandra, Armenia, Salasa, & Ismed, 2015)

### Research Design

This study was an experimental laboratory study that employed the post-test-only control group design approach. Twenty-five female

BALB/c mice were injected intraperitoneally with 200 µl of *P. berghei*-infected blood from donor mice which was equal with  $1 \times 10^6$  infected erythrocytes. Infected mice were then divided randomly grouped into 5 groups. Group 1-3 were treated with 250 mg/kgBW (HC250), 300 mg/kgBW (HC300) and 350 mg/Kg BW (HC350) of ethanol extract of *H. corymbosa* (EEHC), respectively. Group 4 was a positive control (POS) which was given 187,2 mg/kg body weight dihydroartemisinin-piperquin (DHP) and Group 5 was a negative control (NEG) which was only given sterile water. Treatments were given orally once a day for four consecutive days. Parasitemia was observed daily on Giemsa-stained tail blood smear. On day five all mice were sacrificed, blood was collected by cardiac punctured, and the livers were removed to evaluate the effect of the EEHC administration.

Observation of parasitemia in mice was carried out. The percentage of parasitemia was calculated by counting the infected erythrocytes within 1000 erythrocytes. The percentage inhibition of parasitemia was calculated using the following formula:

$$\% \text{ Inhibition} = \frac{\text{Mean\% parasitemia in NEG} - \text{Mean \% parasitemia in TG}}{\text{Mean \% parasitemia in NEG}} \times 100$$

TG: tested group

NEG: Negative control group

On day five, mice were sacrificed after being anesthetized using chloroform inhalation. Livers were removed to measure the length, width, and weight to assess hepatomegaly. The length and width of livers were measured using a ruler and stated in millimeters (mm) (Arwati *et al.*, 2021). The weight of the liver was measured using an analytical scale (Maslachah, Sugihartuti, & Wahyuni, 2019).

### Data analysis

Parasitemia data were statistically analyzed One Way Anova (analysis of variance), while the weight, length, and width of the liver were analyzed using Mann-Whitney and Kruskal Wallis analysis in SPSS.

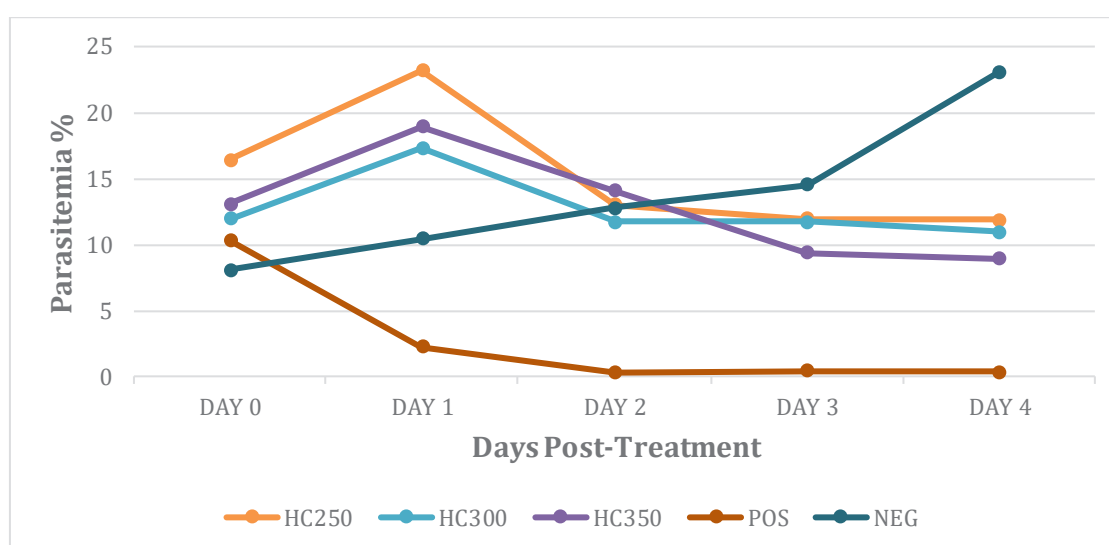
## RESULTS

### Parasitemia and inhibition of parasitemia

Observation of parasitemia resulted in the average percentage of parasitemia, as shown in Figure 1. Parasitemia in the POS

group was completely zero from day 2 to day 4 post-treatment, while in the NEG group, it was increased from day 1 to day 4. The administration of EEHC in the groups caused a decrease of parasitemia since day 2. The percentage inhibition of parasitemia in mice by EEHC 250 mg/Kg BW was the lowest (48.40%). Meanwhile, the highest percentage of parasitemia inhibition was found in the group treated with 350 mg/Kg BW, which was 61.40%.

Statistical analysis of the parasitemia percentage data of mice on day 5 using the OneWay ANOVA test showed a significant difference of parasitemia among EEHC-treated groups ( $p < 0.05$ ). Post hoc Games Howell test showed no significant difference in parasitemia between the treatment groups ( $p > 0.05$ ), and all EEHC-treated groups were significantly different from the POS (DHP) group. The POS group differed significantly from the NEG group ( $p < 0.05$ ).



**Figure 1.** Percentage parasitemia in BALB/c mice infected with *P. berghei* ANKA treated with ethanol extract of *H. corymbosa*



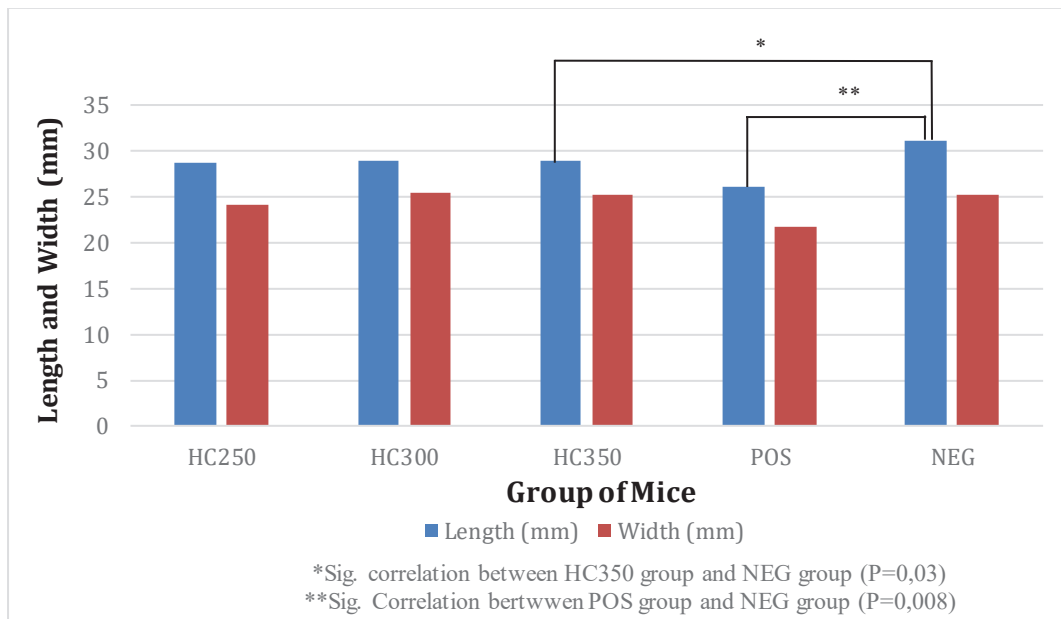
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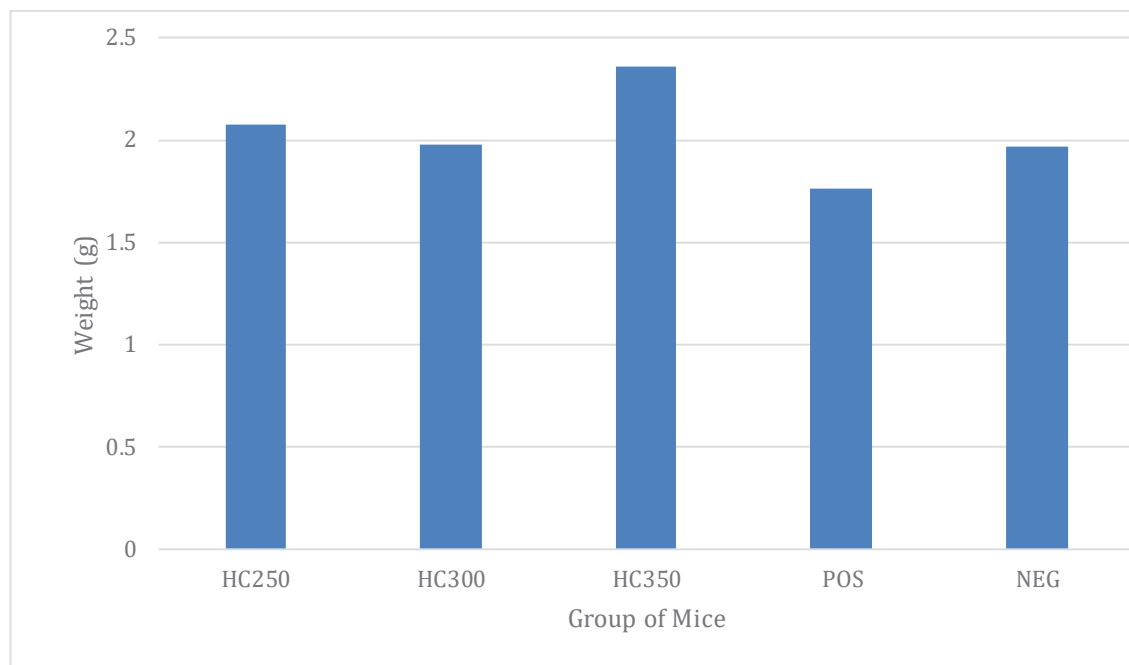
**Table 1.** Parasitemia at day five post treatment with EEHC and inhibition of EEHC on parasitemia

Group	Parasitemia (%)	Inhibition (%)
HC250	11.9	48.40
HC300	10.98	52.39
HC350	8.9	61.40
POS	0.36*	98.44

\*Parasitemia in EEHC treated groups and NEG were different significantly with POS group ( $p < 0.05$ ) by Posthoc Games Howell analysis



**Figure 2.** The mean of liver length and width in mice infected with *P. berghei* ANKA treated with EEHC



**Figure 3.** The mean of liver weight in mice infected with *P. berghei* ANKA treated with EEHC

## DISCUSSION

The novelty of this study is that the antimalaria activity of EEHC and the effect of EEHC on hepatomegaly have not been reported. In this current report, the antimalaria activity of EEHC has been proven against parasitemia in mice infected with *P. berghei* ANKA. Parasitemia is the result of calculating the number of parasites in a thousand erythrocytes and is used to determine the pathology severity of malaria infection. The percentage of parasitemia in the treated mice showed anti-malarial activity of ethanol extract of *H. corymbosa* against *P. berghei* ANKA infection. In this study, the parasitemia percentage of mice in the group given ethanol extract of *H. corymbosa* was lower than NEG but still higher than the treatment group given DHP, although not significant. The percentage of parasitemia between groups of doses of ethanol extract of *H. corymbosa* was also not significantly different. However, on the inhibition percentage, it was found

that the larger the extract dose, the greater the percentage of inhibition of parasitemia. The highest percentage of inhibition was indicated by treatment with ethanol extract of *H. corymbosa* at a dose of 350 mg/Kg BW, which was 61.4%. That showed that the ethanol extract of *H. corymbosa* at a dose of 350 mg/Kg BW has anti-malarial activity inhibiting malaria parasite growth by 61.4%.

The ethanol extract of *H. corymbosa* used in this study contains alkaloids and flavonoids, which have been proven in phytochemical tests. Other study have also proven that the ethanol extract of *H. corymbosa* contains secondary metabolites such as alkaloids, flavonoids, serpentine, terpenoids, quercetin, and other bioactive compounds such as glycosides, steroids, and tannins (Selvan *et al.*, 2015). The alkaloid compound indirectly kill parasites by activating the expression of the transcription factor PPAR $\gamma$  (peroxisome proliferator-activated receptor), which has an impact on suppressing TNF- $\alpha$  (Margono, Suhartono, &



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Arwati, 2016). Furthermore, TNF- $\alpha$  production is related to the parasitic load (Leão *et al.*, 2020). In addition, the alkaloid compound has anti-inflammatory and anti-malarial effects by suppressing heme polymerase activity in *Plasmodium*'s food vacuoles (Louisa, 2016). As a result, *Plasmodium* parasites die due to the accumulation of heme which is toxic to the parasite.

Other phytochemical compounds contained in *H. corymbosa* extract, such as flavonoids, are also known to have anti-malarial activity. A study proved that the flavonoid compounds contained in *Dasymaschalon acuminatum* leaves have antiplasmodial solid activity against *Plasmodium falciparum* (Chokchaisiri, Chaichompoo, Chalermglin, & Suksamrarn, 2015). Another study reported that flavonoid derivatives obtained from the ethanolic extract of *Macaranga gigantea* leaves had potent antiplasmodial activity against *Plasmodium berghei* ANKA (Muhaimin *et al.*, 2019).

As antiplasmodial, flavonoids work through their ability to suppress the biosynthesis of parasitic cell membrane fatty acids, enzymes, proteins, or even DNA that is vital for parasites. Polyphenolic flavonoids have phenolic OH groups capable of causing tissue damage or oxidative damage to parasite cellular components if converted to stable phenoxy anions under cellular oxidative stress *in vivo*. Flavonoids are one of the phytochemical compounds that can modulate strong immunity. Flavonoids induce TNF- $\alpha$  and other anti-inflammatory agents by inhibiting reactive oxygen or nitrogen compounds. In addition, flavonoids can also modify intracellular signaling pathways in immune cells (Afolayan, Adegbolagun, Mwikwabe, Orwa, & Anumudu, 2020). Another research also revealed that the alkaloid and flavonoid compounds contained in the ethanol extract of *Morinda citrifolia* were the

main compounds that acted as antiplasmodials against mice infected with *P. berghei* ANKA (Rahayu, Hernaningsih, & Arwati, 2021).

This study found that the liver of mice in the group treated with the highest ethanol extract of *H. corymbosa*, which was 350 mg/Kg BW (HC350), had a significantly smaller effect on liver length when compared to the negative control group. Meanwhile, at other doses of ethanol extract of *H. corymbosa*, namely 250 mg/KgBW (HC250) and 300 mg/KgBW (HC300), there was no significant difference in liver length against the NEG. On the width and weight of the liver of mice, all treatment groups with ethanol extract of *H. corymbosa* dose had no significant difference with the negative control group. That indicated that the ethanol extract of *H. corymbosa* at a dose of 350 mg/Kg BW had a minor effect on hepatomegaly in *P. berghei* infection due to the shorter liver length.

Previous research reported that the methanol extract of *H. corymbosa* possess hepatoprotective properties due to its ursolic acid content. This is evidenced by the histopathological picture of the liver of wistar rats induced by paracetamol overdose, which is close to normal in the group treated with doses of methanol extract of *H. corymbosa* (Sadasivan *et al.*, 2006). This hepatoprotective property is also due to quercetin compounds in ethanol extract of *H. corymbosa*. Quercetin (2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4-Hchromen-4-one) is a derivative of flavonoid phytochemical compound classified as flavonols (David, Arulmoli, & Parasuraman, 2016). Furthermore, quercetin might be a compound with hepatoprotective properties through their research which revealed the ability of quercetin to treat rat hepatocytes that suffered oxidative damage due to ethanol induction (Liu *et al.*, 2012).



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Besides having hepatoprotective properties, quercetin also has anti-inflammatory properties. In vitro, several studies have shown that quercetin can inhibit the development of lipopolysaccharide (LPS) mediated by TNF- $\alpha$  (Li *et al.*, 2016). Quercetin can also suppress TNF- $\alpha$  and Interleukin (IL)-1 $\alpha$  mRNA levels triggered by LPS and reduce apoptotic neuronal cell death (Bureau, Longpré, & Martinoli, 2008). Another study showed that quercetin could inhibit the emergence of pro-inflammatory inflammatory responses such as IL-1 $\beta$ , IL-6, IFN- $\gamma$ , TNF- $\alpha$ , and IL-12p70 (Michalski *et al.*, 2020). Numerous biological effects of quercetin have been reported; however, the report on side effects of quercetin is very few. Rare cases have been observed in some patients to have headaches and tingling nerve sensation after quercetin consumption. An in vivo study in mice reported the potential toxicity of quercetin is the repression of mitochondrial copy number via decreased POLG expression and excessive TFAM expression in irradiated murine bone marrow.

Hepatomegaly in human malaria infection occurs due to an inflammatory reaction in the liver caused by parasites that develop and replicate in liver cells. One of the solid triggers for the inflammatory response, IL-12p70, is thought to arise as a result from chronic malaria infection that triggers a pro-inflammatory response. The pro-inflammatory response IL-12p70 is known to correlate with the occurrence of hepatomegaly (Wilson *et al.*, 2009). It has been demonstrated that children chronically exposed to malaria have an increased in number and size of Kupffer cells (Walters & McGregor, 1960), and if activated, are a potential source of TNF- $\alpha$ . As levels of TNF- $\alpha$  RII, a neutralizer of TNF- $\alpha$  which releases from human cell lines is triggered by TNF- $\alpha$  itself, were found to

be correlated with Pfs-IgG3, it suggests that the immune system is mounting a reaction to restrict inflammation (Higuchi & Aggarwal, 1994; Van Zee *et al.*, 1992). sTNF-RII levels were likewise related with the presence of hepatomegaly. Control of TNF- $\alpha$  production during malaria infections is partially controlled by IL-10 and levels of circulating IL-10 were substantially linked with Pfs-IgG3 levels and the presence of hepatomegaly (Ho *et al.*, 1998, 1995). The statements above may indicate that the quercetin content in the ethanol extract of *H. corymbosa* may play a role in hepatomegaly in malaria infection by suppressing inflammation in the liver.

The limitation of this study is the lack of information regarding the anti-malarial activity of EEHC, resulting in minimal details on the mechanism of action of EEHC against malaria parasites, changes in host immunity as well as pathological changes. Therefore, further research regarding the EEHC on malaria still needs to be done. Other examinations, such as histopathology of the liver and other organs such as the kidney and spleen, need to be carried out to determine the effect of EEHC on the histopathological changes of these organs in malaria infection microscopically before the antimalaria drug development.

## CONCLUSION

Ethanol extract of *H. corymbosa* did not significantly affect the percentage of parasitemia in mice infected with *P. berghei* ANKA. However, EEHC was able to inhibit the growth of parasites up to 61.4% at a dose of 350 mg/Kg BW. In addition, ethanol extract of *H. corymbosa* at the same dose also affected hepatomegaly, especially the liver length in mice infected with *P. berghei* ANKA.





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## Research Article

# The spiritual and mental health assessment of social workers working for Internally Displaced Persons during Covid-19 in Myanmar

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## ABSTRACT

This study utilizes the spiritual assessment viewpoint to analyze the spirituality of social workers who are working for Internally Displaced Persons (IDPs) in Kachin and Northern Shan State, Myanmar where the working situation is stressful, and security is not guaranteed. The data is collected online during the pandemic and military, in April 2022. It is a quantitative research assessment and the form of Spirituality Assessment of Social Workers Working for IDPs (SASWWIDPs) is designed as three dimensions of SASWWIDPs: Healthy self-awareness (HSA), healthy relationship (HR), and healthy feeling (HF). The accumulated data is interpreted using SPSS 22.0 for statistical analysis. Most of the participants are female (66%) and 34% are male. The results of the three dimensions of the SASWWIDPs are different from their social characteristics: in gender, females' HF in self-care and managing stress is higher than males ( $t=-3.21^{**}$ ). In terms of religion/faith, the group Buddhism's HF is higher than Christianity on the benefits of religion in managing stress ( $t=-2.833^{**}$ ). Regarding working years, people who have been working for 2 years have a more positive mindset on their work than those for 3 years above in HSA ( $t=2.918^{**}$ ); in terms of age, there is no difference among the different age groups. However, both groups agree the role of friends and families is vital to overcoming challenges and stress.



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### INTRODUCTION

The rapid spreading of Covid-19 has been affecting people around the world and its consequences are tremendous since it affects not only the health and economic sectors but also education, transportation, and social problems. With the pandemic, the styles of living, production modes, means of transportation, and learning methods are significantly changed. The changing situation brings forth huge challenges in people's daily life since it is not comfortable and easy to adopt the new normal living style. More or less, people from all levels suffer from the myriad effects of Covid-19 (Haleem et al., 2020). People have to live with fear, uncertainty, and anxiety as they are afraid of their losing their future regarding jobs, families, and financial shortages (Matos et al., 2021). In addition, Covid-19 also hinders social work such as the provision of humanitarian assistance, and health services due to lockdown, quarantine, and insufficient protective pieces of equipment.

However, in Myanmar, the Burmese suffer not only the Pandemic but also a military coup on Feb 1, 2021. To fight against the military, many civilian staffs, especially medical and educational staff join Civil Disobedient Movement (CDM), and, within a short period of time, health and education pillars collapsed. To treat down the rebels, the military uses four cuts and burnt down the villages that causing many people to flee. Besides, transportation is limited, communication is cut in some areas, and permission needs to be applied if field trips want to be made. That causes difficulties for social workers to go to the communities and deliver social services. As evidence, two ICRC staff are killed while providing services for people in need (The Guardian, 2021).

The combination of the pandemic and military coup afflicts the Burmese both in physical and

mental aspects. It is true to say that the daily life of the Burmese is difficult, and social workers who deliver services to communities are also facing challenges due to strict checkpoints. As human beings, social workers are burned out amidst difficulties and hindrances as well as time pressure, they are doing their best to deliver social services. Thus, this study plans to use spiritual assessment to see how social workers working in Kachin and Northern Shan apply spirituality in their daily life and workplace to cope with the challenges.

### LITERATURE REVIEW

#### *Spirituality*

The word spirituality is a Latin word that originates from "Spiritus" which means the breath or breath of life. It is a source of life that gives breath to all creatures to move on. In fact, the word spirituality appears together with Christian tradition though other religions present the word "Spirituality" in their literature. Later, the concept of "spirituality is also used for non-material parts of human beings and regarded as the source of emotions, feelings, psyche, characters, and the connection to divine power which cannot be tested and touched. However, the term "spirituality "is wider than religion since it mentions the non-physical and untouchable human dimension (ten Have and Patrão Neves, 2021). Elkins et al. apply a humanistic approach and categorized spirituality into eight characteristics: the supernatural view, meaning in life, operation in life, the holiness of life, physical tangible values, humanity, being aware of the catastrophe, and benefits of spirituality (Loue, 2017).

Nevertheless, Wolff (2020) points out that the term "spirituality" is generic and there is no exact definition for it. He believes that "spirituality" comes from the Christian society that has a confined definition. He assumes spirituality is



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more than religion and it has multi-dimensional concepts, but religion is easier to define than spirituality. Commonly, spirituality and religion seem the same, but they are different. Snyder and Lopez say that sometimes the two words: religion and spirituality seem to have the same and people get confused about it (Foster & Wall, 2020). Actually, they have different definitions since religion is related to praying, reading the bible, and belief in divine power whereas spirituality is one's strength of mind to expose meaningful life through the practice and the way he/she lives and works. Gisinger et al., add that spirituality is also a way of intellectual self-evaluation to seek a meaningful life (Wolff, 2020). Nonetheless, it is not so sure to include religious thinking. Skrzypinska states that spirituality can be defined as a source of inspiration that motivates us and helps us to build self-confidence to pass through challenges (Wolff, 2020). Though the two words are differentiated, there is no separation in the African American community. Phipps and Benefiel say that spirituality is like a tree and religion is one of the branches (Peltonen, 2017).

To sum up, Hart defines that the clarity of spirituality relies on one's perception since it will be different based on the context one is going to use (Wane et al., 2011). For adults, it will focus on contemplating and religion, but for the workplace, it will be based on the working dynamic. In addition, it would be changed for the children's viewpoint as well.

### ***Spirituality, Religion, and Social work***

Greater attention is now paid to researching the association among spirituality and religion, and their impacts on social work. Furman et al. noted that more consideration is put to spirituality and religion in the 1980 and mid of 1990, then it has been increasing until the Council of Social Work Education has to reinstate to

refer religion and spirituality in the social work program in 1995 (Furness, 2016). Furness and Gilligan declare that legal acknowledgment should be given to study the significance of religion and spirituality in the field of social work and professional development (Furness 2016). Furthermore, consideration should also be put into the assessment, intervention, and practices.

Holloway and Moss identify that some people accept that spirituality has the feature of religion, but it also covers the identification of religion as one of the subdivisions of spirituality (Furness, 2016). The intertwined connection between religion and spirituality is complex. Nevertheless, careful consideration is needed to take religion and spirituality into account since the unawareness of those in social work will cause huge devastating impacts. It is instrumental for social workers to accept clients' religious beliefs and cultural practices because social workers have to deal with clients in their daily life during the time of good and also at the time of suffering. It is easy to proceed with social work at the time of flourishing, but staff would get tired of working at the time of tribulation. Whether the situation is good or bad, social workers have to draw attention to clients' inward strengths in a proper way so that they can help clients to overcome challenges and comprehend their clients' future expectations (Furness, 2016).

Graff (2007:248) conducted research on social work students and found that the majority of the students reported that spirituality is a vital component of human beings, and social workers are necessary to recognize more about the different religions of clients. The knowledge of knowing clients' religion and spirituality is crucial for social workers to deliver competent services as well as it is also a component that highlights the core value of social work. In addition, there is a huge dominance of clients'



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religion in the outcome of social work practice because their beliefs and practices help them to their well-being and construct a sound relationship with others.

### *Spirituality and Mental Health*

The consequences of Covid-19 afflict people who have already had the psychiatric condition and those who did not previously have it. No one is exempted. Notably, the issue is significant among health workers who manage the high risk of Covid-19. The burnout consequences of Covid-19, emotionally and psychologically affect Social (health) workers and unfortunately, it can affect the healthcare system and patient safety (Menon and Bhagat, 2021). However, Jankowski et al. (2022) discovered that there is a reasonable connection between Religion/Spirituality and mental health during the pandemic. Engagement in Religion/Spirituality is one of the protective measures against pandemic-related mental illness. A stronger Religion/Spirituality commitment helps people to pass through adversity and functions well in the healing process.

The working contexts of social workers are different based on the field they choose. More or less, there are challenges and stress. However, social workers working in the context of conflict-affected areas are more challenging than in other contexts since social workers have a high potential and can become victims easily. Furthermore, work must be done under time pressure and the guarantee of security is uncertain. Ozcan et al. (2021) stated that a religion-oriented and spiritual method is a good mechanism since it helps social workers to be calm amidst chaos and helps them to resist direct and secondary trauma. Through this approach, social workers gain motivation, and resilience to fulfill work

demands, and the people they serve as well as their personal needs. Importantly, using this approach to be more effective, the aspects of social connectedness and their mindset toward religion and spirituality are fundamental.

Concurrently, Dhimi et al (2021) also discovered that there is a strong linkage between spiritual intelligence and mental health. Spiritual intelligence works as an agent that causes psychological well-being to enhance the ability and boost motivation to achieve life goal. Owing to this, people possess a life that can resist stress, anxiety, and fear as well as improves spiritual growth that enables them to process their works more effectively and meaningfully.

### *Spirituality and Social Connectedness*

According to Wane et al. (2011, 23), the spiritual connection can be classified into four components: connection to societies, connection to the previous time, connection to bigger frameworks, systems, or ambiguities, and connection to a person's entire life. Dei says that individual grows their spirituality with the connection with social communities, civilization, and nature interaction (Wane et al., 2011). So, it is clear to see that human beings cannot stay outside the community within the framework of relation and social connection. Spirituality is developed by networking, and it has vice-versa effects. Badri et al. (2021) also posit that there is a linkage between depression and social connection by researching adolescents' depression. The factors that cause loneliness and depression include less receiving trust, engagement in social activities with friends, and limited time spent with family. However, those who have regular connections with friends and have more interaction and valuable time with family are less likely to have depression and that increases their well-being.





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## METHOD

### *Research Design and data collection*

This research is a quantitative study of spiritual assessment in social work. A set of questionnaires which is called the Spirituality Assessment of Social Workers Working for IDPs (SASWWIDPs) is designed as three dimensions of SASWWIDPs: Healthy self-awareness (HSA), healthy relationship (HR), and healthy feeling (HF). The 10 questions are designed as a Likert scale, from strongly agree to strongly disagree. The questionnaire is prepared in the Burmese language. Data were collected in April 2022 by using Google Forms.

### *Location and Participants*

This research has been done in Kachin and Northern Shan states. To conduct this research, participants who are from different backgrounds, sex, ethnicities, religions, and positions are selected but specifically those who are working for IDPs in Kachin, and Northern Shan in international and local non-profit organizations. However, Yangon-based staff who are working for IDPs in Kachin and Northern Shan in coordination roles are counted for this research as well. There are 50 participants in this research.

### *Data Analysis*

The collected data are checked and interpreted using Social Science Statistics Software (SPSS) 22.0. The variables are explained using numbers, percentages, mean and standard deviation. The independent sample t-test is used to test the significance of Healthy self-awareness (HAS), healthy relationship (HR), and healthy feeling (HF) in terms of gender, working years, and religion.

### *Ethical Consideration*

In the first part of the questionnaire, there is a declaration related to asking for the consent of the participants. It is clearly explained why data is collected, where they are going to be used and all the information/ data provided will be kept confidential. Participants are given full rights to withdraw participation if they feel uncomfortable. The contact email is also provided to reach the data collector in case they have any questions.

## RESULT

### *Participants' Social Characteristics*

There are 50 participants in this study. The majority are 30 to 39 years old (48%) and the least percentage (2%) are 50 years and above. Most of the workers (52%) have working experience ranging from 5 to 9 years, whereas, working experience under five years follows at second place and above 10 years are at 14%. In this study, females occupy (66%) of the highest number. In terms of location, the social workers from Kachin state stand at 48%, followed by 40% of northern Shan and Yangon at 12%. Then, 84% of the respondents follow Christianity, and Buddhism followers are 16%. With regards to position, 22% of participants hold the position of project coordinator and the lowest 2% are financial controllers. The detail can be seen in the following table 1.

### *Descriptive Statistics of three dimensions of SASWWIDPs*

The three dimensions of the Spirituality Assessment of Social Workers Working for IDPs (SASWWIDPs) are HSA (Healthy Self-Awareness), HR (Healthy Relationship), and HF (healthy Feeling). Their descriptive statistics are the mean value for HAS is 4.13 and SD is 0.56; the mean value for HR is 4.21 and SD is 0.66; and the mean value for HF is 3.48 and SD is 0.67 (see Table 2).



**Table 1.** Participants’ social characteristics

Items	Numbers	(%)	Items	Numbers	(%)
<b>Age</b>			<b>Religion/Faith</b>		
Under 30 y/o	18	(36)	Christianity	42	(84)
30-39 y/o	24	(48)	Buddhism	8	(16)
40-49 y/o	6	(12)	<b>Position</b>		
About 50 y/o	2	(4)	Program Coordinator	5	(10)
<b>Gender</b>			Project Coordinator	11	(22)
Male	17	(34)	Field officer	4	(8)
Female	33	(66)	Area Coordinator	5	(10)
<b>Years of working for IDPs</b>			Community facilitator	6	(12)
Under 5 yrs	17	(34)	Financial controller	1	(2)
5-9 yrs	26	(52)	Accountant	5	(10)
Above 10 yrs	7	(14)	Cashier	4	(8)
<b>Area of working</b>			Monitoring and evaluation coordinator	4	(8)
Kachin	24	(48)	Volunteer	2	(4)
Northern Shan	20	(40)	Other	3	(6)
Yangon	6	(12)			

**Table 2.** The descriptive statistics of three dimensions of SASWWIDPs

Items	Mean	SD
<b>I. Healthy Self-Awareness (HSA)</b>	4.13	0.560
1.1 I satisfy the work I have done for IDP.	4.18	.850
1.2 I am sure that I had the right mindset toward my work.	4.60	.535
1.3 I have one motivational quote/word in my everyday life that makes my day happy.	4.06	.956
1.4 I can control my wrath	3.68	.957
<b>II. Healthy Relationship (HR)</b>	4.21	0.660
2.1 I always try to maintain a good relationship with my family.	4.32	.844
2.2 My friends always encourage me to deal with challenges.	4.04	.856
2.3 The role of friendship is important to enhance spiritual growth.	4.08	.986
2.4 I always keep good relationships with my friends.	4.38	.725
<b>III, Healthy Feeling (HF)</b>	3.48	0.670
3.1 I use a self-care method to deal with my anger.	4.06	.935
*3.2 I have a great fear of any challenges that I am facing and will face in my daily work.	2.90	1.165

Note: \* Item 3.2 is the opposite question



**Table 3.** The participants’ t-test for the dimensions of the SASWWIDPs

Items	HSA			HR			HF		
	mean	SD	t-value	mean	SD	t-test	mean	SD	t-value
Gender			1.647			.568			-3.21**
Male	4.31	.54		4.28	.62		3.12	.52	
Female	4.04	.56		4.17	.68		3.67	.67	
Religion/Faith			-.830			.371			-2.833**
Christianity	4.10	.57		4.22	.64		3.37	.63	
Buddhism	4.28	.49		4.13	.78		4.06	.62	
working years			2.918**			.193			-.217
Below 2 yrs	4.61	.45		4.25	.43		3.43	.67	
Above 3 yrs	4.05	.54		4.20	.69		3.49	.68	

Note: \*p<.05; \*\*p<.01; \*\*\*p<.001

**Participant’s t-test for the Dimensions of SASWWIDPs**

The t-test results of the three dimensions of SASWWIDPs are different from their social characteristics. The types of gender: males and females are significantly different in HF of SASWWIDPs (t=-3.21\*\*), the mean value of females is higher than males. However, in HAS and HR, there is only a slight significance between males and females. In terms of religion/faith, the group “Christianity” is significantly different from the group “Buddhism” in HF (t=-2.833\*\*) and the mean value of Buddhism get higher than Christianity. Nevertheless, there is no significance both in HAS and HR. With regards to working years, people who have been working for 2 years are significantly different from those who have more than 3 years of working experience in HSA (t=2.918\*\*). But there is insignificant in HR and HF (see Table 3.).

**DISCUSSION**

This study discovers that social workers satisfy their work for having done something good for IDPs. Taking pleasure in the works that have been done for needy persons is one of the effective ways to reduce stress encountered in everyday life. However, the right attitude towards work is vital to encourage their selves for what they are doing whenever they suffer challenges. Social workers believe that reciting a quote that strengthens their spirituality is also required to make them feel who they are. Furthermore, the role of friends and family is also important to maintain a good mental status. Social workers believe that supports received from friends and families are valuable to deal with challenges. In addition, maintaining a good association with friends and families is instrumental to enhancing spiritual growth (Badri et al., 2021) However, regarding managing anger, females are better than males. Female social workers possess healthier minds than male social workers. But then, social workers do not fear facing any challenges they are facing and will be facing regardless of gender.



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Social workers believe that religion is one of the factors that helps them to resist the downfall. Religion directs them to have the right mindset on their work and to work more for those who need help since they are good actions. It has been also found that having a good relationship with divine power is a valuable resource to face stress (Dhami et al., 2021). In terms of the finding, Buddhists agree that religion helps them to have more positive feelings than Christianity.

In relation to working experience, those who have below 2 years of working experience have more satisfaction with their work than those who have work experience above 3 years. Regarding the relationship with friends and families, both groups affirm that the role of friends and families play an important role to overcome challenges. However, those who have less than 2 years of work experience take more advice from friends than above 3 years. Likely, the two groups, regardless of working experience, are not afraid to take risks. Nevertheless, constraining anger does not depend on working experience and the self-caring method is crucial to handling stress.

### LIMITATION

This study has been done during Covid-19 and the military coup in Myanmar. Data has been collected using an online google form. However, in some areas, internet connection and transportation are restricted. Therefore, only 50 participants could be recruited and that is a relatively small number. Most of the participants are Christians and more Buddhists are still needed to be included. To be inclusive, other religions and more number should be recruited.

### CONCLUSION

The threat of covid-19 upon people's daily life is huge and significantly changes their lifestyles. This study points out the spiritual need of workers working for IDPs. Difference social characteristics have different mean values of three dimensions of SASWWIDPs. Self-evaluation is very important to know who we are and for whom we are working. This is a radical source to identify yourself and work through challenges. Next, the role of family and friends cannot be ignored. Handling stress requires their support. Finally, religion is one of the effective treatments to deal with stress. In it, people find solace and strengthen themselves.

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Case Report

**The role of common bile duct exploration with biliary drainage in choledocholithiasis during pregnancy**

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**ABSTRACT**

Pregnancy is a risk factor for gallstone disease and may evolve into symptomatic choledocholithiasis/ common bile duct (CBD) stone; however, the treatment of choice is controversial and may not apply to all gestational ages. Standard therapy with endoscopic retrograde cholangiopancreatography (ERCP) exposes the patient and fetus to ionizing radiation; hence other strategies are needed to address this problem. We report a case of 29 years old female presented with biliary pain and jaundice. The patient was pregnant at 14 weeks gestation age. Laboratory data showed biliary obstruction, and abdominal ultrasound showed multiple bile duct stones with significant dilatation in the CBD. CBD exploration with external biliary drainage was performed to treat obstructive jaundice while avoiding ionizing radiation exposure to the fetus and patient. After the procedure, the patient showed clinical improvement. CBD exploration with external biliary drainage avoids ionizing radiation in choledocholithiasis management. This method may be applied as a temporary emergent treatment of obstructive jaundice in pregnant patients with gestational age sensitive to ionizing radiation.



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### INTRODUCTION

Epidemiological studies have shown that women are more likely to have a gallstone, and the risk is higher when taking hormonal drugs and during pregnancy (Everson, 1993). The prevalence of gallstones in pregnant women is 12.2%, with an increase relating to the gravida of patients. Most patients are asymptomatic. However, with the increasing size of the gallstone, the risk of impacting the neck of the gallbladder increases, increasing the risk of biliary colic attack (Valdivieso et al., 1993).

In pregnant women, there is a progressive increase in biliary cholesterol saturation due to increased cholesterol secretion with a decrease in bile acid secretion (Kern et al., 1981). The hepatic effect of estrogen might cause higher cholesterol secretion, while lower bile acid secretion might be due to an impairment of motility by progesterone (Everson et al., 1991; Shaffer et al., 1984; Everson, 1993). Other risk factors of gallstone disease include family history, genetic predilection, ethnic background, age, obesity, metabolic syndrome, drugs, diet, and chronic liver disease (Stinton & Shaffer, 2012).

Gallstones may cause complications such as cholangitis and choledocholithiasis. The management is challenging since standard therapy with endoscopic retrograde cholangiopancreatography (ERCP) exposes the fetus and the patient to ionizing radiation (Chamberlain & Croagh, 2020). This case report will focus on obstructive jaundice in pregnancy bile duct exploration and T-tube drainage for the treatment.

### CASE REPORT

A 29-year-old female came to the emergency room with a chief complaint of nausea,

vomiting every meal, and upper right abdominal pain that had been going on for two weeks. The patient said she had been admitted with a similar complaint with brief improvement. The patient also said the symptoms have worsened for the last two days, and she developed yellowish skin. The patient was pregnant at 14 weeks gestation with a history of hepatitis B infection. The patient had direct bilirubin of 8.09 mg/dL and total bilirubin of 12.50 mg/dL. The patient also had an increase in the liver enzyme (AST of 208 U/L and ALT of 128 U/L) with mild electrolyte imbalance (sodium 133 mmol/L and potassium 3.3 mmol/L). Two days prior, the patient underwent an abdominal ultrasound, and three 1.1 cm common bile duct (CBD) stones were found with significant dilatation in CBD, CHD (common hepatic duct), and IHBD (intrahepatic bile duct).

The common practice to treat the condition of this patient is using ERCP. Nevertheless, this procedure exposes the patient to ionizing radiation. Considering the gestational age, the patient refused to use any ionizing radiation during the treatment. Common bile duct exploration with external biliary drainage was chosen for the emergent treatment to resolve obstructive jaundice.

During surgery, it was found that the CBD was dilated about 2 cm, and a choledocholithotomy was performed to remove the gallstones. Normal saline was pushed in CBD with no resistance found, and T-tube drainage was placed in CBD. Post-op revealed the jaundice was reduced with minimal pain in the surgery site. Eight weeks of follow-up showed significant clinical improvement in the mother. Both the fetus and the mother were healthy during the follow-up period. T-tube drainage was planned to be removed after the delivery, along with ERCP to evaluate the patient.





**Figure 1.** An ultrasonographic exam showed the dilatation of CBD with a non-mobile 1.1 cm CBD stone

## DISCUSSION

Pregnancy predisposes to gallbladder diseases through increasing cholesterol secretion by estrogen and decreasing bile acid secretion by progesterone. Progesterone also causes a reduction in gallbladder contraction, hence increasing biliary stasis (Kern et al., 1981). Gallstones occur in 7% of nulliparous women, 12% in pregnant women, and 19% in women with two or more pregnancies. The symptoms are similar to gallstone disease in non-pregnant patients (Valdivieso et al., 1993; Parangi et al., 2007). The obstruction of the cystic duct causes symptoms of gallstones during bile expulsion from the gallbladder. The smooth muscle of the gallbladder contracts and activates visceral nerve fibers, causing referred pain in the associated dermatome in the epigastrium and

back. It is often poorly localized and coincides with vomiting/nausea. This condition may evolve into cholecystitis, choledocholithiasis, or cholangitis. (Beckingham, 2020) These complications only occur in 10% of symptomatic patients, making biliary obstruction due to choledocholithiasis quite rare (Chan & Enns, 2012).

Generally, either openly or laparoscopically, choledocholithiasis is approached by ERCP or bile stone exploration. (Beckingham, 2020) The main concern of ERCP in pregnancy is that it exposes the patient and fetus to ionizing radiation during fluoroscopy. Ionizing radiation directly acts on the tissue's biochemical structure, including DNA, protein, and other molecules. Ionizing radiation also causes the formation of free radicals that can indirectly



break the structure of the cell’s critical part. Radiation increases the risk of teratogenicity to childhood cancer. The severity is dose-dependent yet also stochastic. The fetus is most susceptible to ionizing radiation during organogenesis [2-7 post-conception] and in the early fetal period [8-15 post-conception]. Radiation exposure in fetal development also increases the risk of the number of non-malignant problems, including failure to implantation during blastogenesis [0-2 weeks post-conception]; major malformation and growth restriction during organogenesis [2-7 weeks post-conception]; and growth restriction, IQ reduction, mental retardation, malformations, also miscarriage during fetogenesis [8-38 weeks post-conception] (Williams & Fletcher, 2010; Jackson et al., 2008).

Despite the radiation risk, several studies report that ERCP can be performed if indicated. The only meta-analysis about ERCP in pregnancy that we can find has been done by Azab et al., showing that ERCP is a relatively safe bile duct decompression procedure to prevent life-threatening complications both to the mother and fetus. Maternal adverse

events of ERCP include pancreatitis, bleeding, and cholecystitis, which are higher than usual ERCP outcomes. ERCP is associated with preeclampsia, preterm labor, and intrauterine growth retardation. Regarding the fetal adverse event, there is no report of malformation due to ERCP; however, radiation exposure before 16 weeks of gestational age increases the risk of intellectual disability (Azab, et al., 2019).

The estimated radiation dose absorbed during ERCP in pregnancy varies from 0.4 – 3.1 mSv (Kalaleh et al., 2014; Tham et al., 2003). However, radiation exposure is recommended not to exceed 1 mSv in the first trimester and 5 mSv in the whole pregnancy. Furthermore, there is a concern that these estimations underestimate scattered radiation (Chan & Enns, 2012). Due to the sensitivity to radiation regarding the patient’s gestation age, open cholecystectomy and CBD exploration with external drainage was chosen.

Surgical management is considered safe whenever cholelithiasis in pregnancy becomes symptomatic. A study by Otheman et al. (2012) shows that conservative management of cholelithiasis in pregnancy is associated with recurrent biliary symptoms, increased visits to the

**Table 1.** Comparison of CBD exploration with external drainage to ERCP in the treatment of CBD stone

	CBD exploration with external drainage	ERCP
<b>Benefits</b>	<ul style="list-style-type: none"> <li>Does not exposes the patient and fetus to ionizing radiation.</li> </ul>	<ul style="list-style-type: none"> <li>Standard treatment for CBD stone.</li> <li>Well studied; however, studies of ERCP in pregnant patients are limited.</li> </ul>
<b>Harms</b>	<ul style="list-style-type: none"> <li>Limited study, to the general population and pregnant patients.</li> <li>External drain is left, causing discomfort to the patient.</li> </ul>	<ul style="list-style-type: none"> <li>Exposes the patient to ionizing radiation.</li> </ul>



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emergency department, higher hospitalization, and more likely to undergo cesarean section (compared to operative and endoscopic groups). This fact is further confirmed by a multicentre study of 78 pregnant women reveals that out of patients managed medically, 34% had relapses requiring hospitalization prior to delivery, 28% developed preterm contractions needed tocolytic drugs, 22% required labor induction to decrease the severity of their biliary disease, 17% had a preterm delivery, and 9% had an emergency cesarean for fetal distress. In contrast, 31% of patients treated with open or laparoscopic cholecystectomy had a premature contraction that responded to tocolysis. No report of preterm delivery, relapse of disease after surgery, maternal ICU admission, or maternal/fetal death was reported in the surgery group (Lu et al., 2004).

External drainage after open common bile duct exploration in pregnancy is not well studied. Biliary drainage is traditionally inserted to prevent the build-up of bile in CBD because of temporary swelling. Bile leak into the peritoneal cavity also can be life-threatening. Moreover, the dye can be injected into the tube to look for the residual stone. However, the use of drainage is controversial. Biliary drain correlates with longer operation time and extended hospital stays; there is no significant difference in mortality and morbidity (Gurusamy et al., 2013). Further study to determine its applicability is required.

### CONCLUSION

Pregnancy is a risk factor for biliary stone disease. While ERCP is generally accepted in pregnant patients who develop symptomatic choledocholithiasis, management approaches require consideration of gestational age since certain periods have high sensitivity to ionizing radiation. This case report demonstrates successful management of biliary obstruction

due to cholelithiasis with the treatment of CBD stone exploration with external biliary drain. The patient and the fetus are healthy during our eight weeks follow-up. This study may be applicable to a pregnant patient with biliary obstruction that is gestational age sensitive to ionizing radiation while considering the harm versus the benefit to the patient. The clinical benefit of this technique compared to traditional ERCP is unclear due to limited studies.

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### Case Report

## Intraocular foreign body (IOFB)

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### ABSTRACT

Intraocular foreign bodies (IOFBs) were 16-40% of open globe trauma and could cause severe visual loss. Therefore, they require immediate diagnosis and treatment. This is a case of an 18-year-old man who came to the hospital complaining of a metal piercing in his left eye while cutting some metal about 2 hours before entering the hospital. On ophthalmologic examination, visual acuity of the left eye was 3/60, and a full-thickness laceration of the cornea with an IOFB was seen at the anterior chamber base. Immediate IOFB evacuation was carried out on the same day as the incident happened. During the operation, a metal intraocular foreign body with a sharp tip, 4x2x1 mm in size, was successfully removed in intact condition. Next, the laceration and the corneal limbus incision were sutured using 10.0 nylon. The stitches are tight, and the anterior chamber depth is maintained. Evaluation on the fourth week after IOFB evacuation showed that visual acuity in the left eye was 6/20 with lens correction C-1.50 x 150° become 6/7.5. Appropriate and prompt diagnosis and management of open eye injury can contribute to preserving a good anatomical and functional result.



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### INTRODUCTION

Intraocular foreign bodies (IOFBs) are characterized as intraocularly retained, accidental projectiles that require immediate diagnosis and treatment to prevent blindness or eye loss (Erakgun & Egrilmez, 2008; Liu et al., 2017; Patel et al., 2012; Yeh et al., 2008). The intraocular foreign body can consist of almost any substance, most of which are metal, as most patients are injured when holding a hammer. Patients' visual prognosis can be affected by physical and chemical damage from the pathogens of IOFBs (Virgana & Widyanatha, 2021).

Sixteen to forty percent of open globe trauma are IOFBs and often can cause severe visual loss. Younger men constitute 92-100% of the patients with IOFBs. The usual age of the affected person with an IOFB is twenty-nine to thirty-eight years old, with most of them (66%) between twenty-one and forty. After the workplace (54-72%), the home is the second most common place for injury (30%) Wulan et al., 2018).

Laceration or bleeding from IOFBs can lead to ocular damage and visual loss directly after the injury; otherwise, retinal detachment or endophthalmitis also causes visual loss due to the consequent development. Visual results in patients with IOFBs are related to various factors. Those factors consist of the preliminary visual acuity, size and location of the IOFB entry wound, length and location of the IOFB, presence of relative afferent pupillary defect (RAPD), intraocular bleeding, detachment of the retina, and endophthalmitis (Jung et al., 2021).

Effective therapeutic plans, intraoperative guidance, prognosis, and counseling can be achieved by promptly evaluating patients with possible IOFBs based on prior signs and symptoms. The preoperative preparations

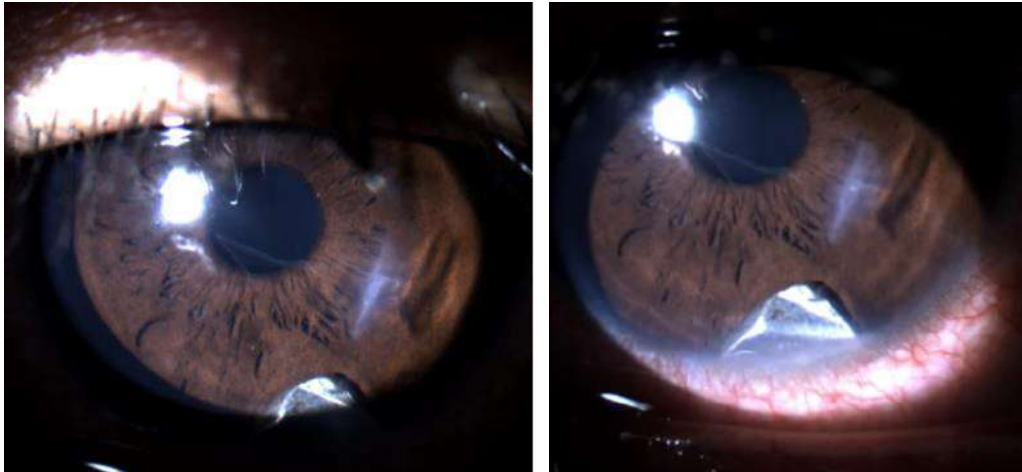
include obtaining a clinical history and ophthalmic evaluation, characteristics of IOFBs found by neuroimaging, and consideration of antibiotics medication. Besides clinical exams on the slit-lamp and indirect funduscopy, diverse imaging methods are treasured for the recognition and localization of IOFBs (Wulan et al., 2018).

The main goal of the treatment is to eliminate the IOFBs, clear up complications that already took place, restore the anatomy of the eye, and decrease feasible complications in the future (Jung et al., 2021). This case report describes the clinical findings, diagnosis, management, results, and follow-up plan in patients with IOFBs.

### CASE REPORT

An 18-year-old man came to the eye clinic of PKU Muhammadiyah Gamping Hospital with a complaint that his left eye was pierced by metal while he was cutting some metal about 2 hours ago. The patient felt pain in the left eye and blurred vision. On examination, visual acuity of the left eye was 3/60, and there is conjunctival hyperemia and corneal edema with a total thickness laceration on the cornea about 4 mm. A piece of metal foreign body was seen at the anterior chamber base that penetrated the patient's eye. The anterior chamber was deep, and there was no leakage from the corneal laceration. Iris was within normal limits, with no laceration and prolapse of the iris tissue, and the pupil looked round. The lens looks clear, and there is no tear in the lens capsule. The posterior segment was within normal limits. The patient was diagnosed with perforating left eye injury with intraocular foreign body (IOFB).

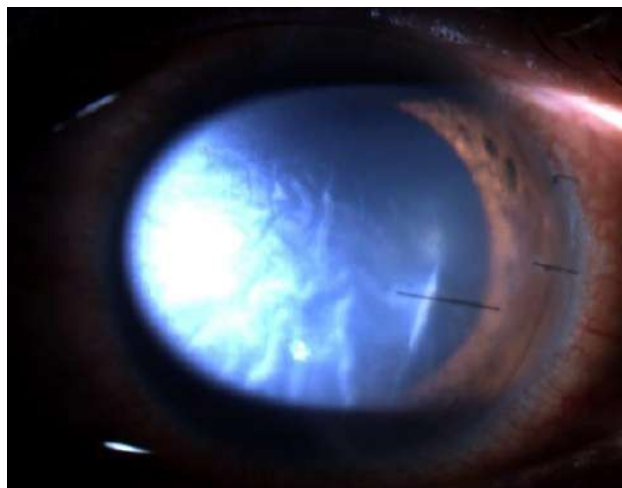
The general examination found that the general condition was good, with adequate nutrition and good awareness. The blood pressure was 110/70 mmHg, pulse 72x/minute, respiration rate 20x/



**Figure 1.** The results of the slit-lamp biomicroscopic examination on the patient's first day showed a corneal laceration.



**Figure 2.** The metal foreign body (4x2x1 mm) that was successfully evacuated



**Figure 3.** Day 5 after IOFB evacuation

minute, body weight 58 kg, and temperature 36.2°C. The heart and lungs are within normal limits, liver and spleen are not palpable.

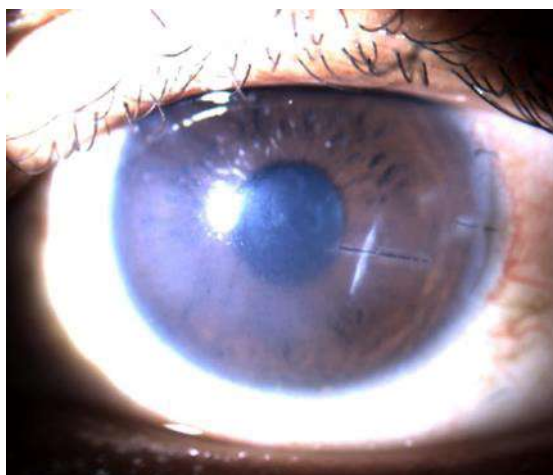
Blood examination revealed leukocytes  $14.4 \times 10^3/\text{ml}$ , hemoglobin 16 g/dl, platelets  $333 \times 10^3/\text{mL}$ , hematocrit 46.5%, PPT 14 seconds, APTT 38.7 seconds, random blood glucose 81 mg/dl, non-reactive HBsAg, and negative SARS CoV-2 antigen. The thorax x-ray examination shows a normal broncho vascular pattern, both sinuses are taper, both diaphragms are smooth, and cor within normal limit.

The patient underwent an intraocular foreign body evacuation on the same day as the incident happened. Premedication was an injection of 1 gram of Ceftriaxone and Levofloxacin eyedrops every 2 hours. The operation was performed under general anesthesia. During the operation, a metal intraocular foreign body with a sharp tip, 4x2x1 mm in size, was successfully removed using Keelman tweezers in the intact condition through a 6 mm incision at the temporal side of the corneal limbus. Next, the laceration and the corneal limbus incision were sutured using 10.0 nylon thread. The stitches are tight, and the eye's anterior chamber can be maintained in depth.

The medication given after surgery were Levofloxacin tablet once daily, Mefenamic Acid tablet three times daily, Methyl Prednisolone tablet 16 mg 2-1-0, Levofloxacin eye drops every 3 hours, Polymyxin-Neomycin-Dexamethasone eye drops every 3 hours, and Atropine sulfate 1% eye drops two times a day.

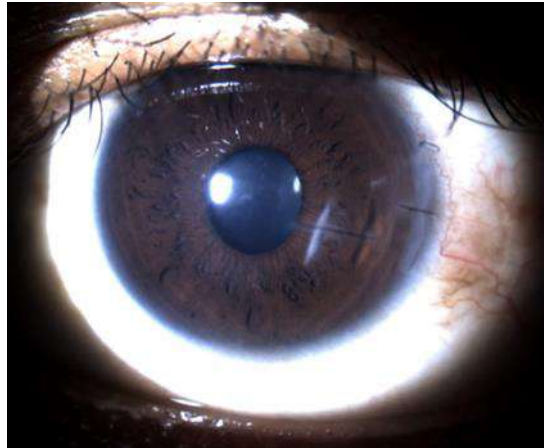
On the fifth day after IOFB evacuation, the visual acuity of the left eye was 1/300, the cornea looked edematous, corneal Descemet's folds were found, corneal and limbus sutures were tight, and conjunctival hyperemia was found (Figure 3). The anterior chamber was deep, the iris was within normal limits, the pupil was dilated by 8 mm due to the effects of atropine sulfate eye drops, the lens was clear, and the posterior segment was difficult to visualize. Postoperative therapy of Methyl Prednisolone tablet 16 mg twice daily, Levofloxacin eyedrops every 3 hours, and Polymyxin-Neomycin-Dexamethasone eye drops every 3 hours was given.

Two weeks after IOFB evacuation, visual acuity of the left eye was 6/60, corneal edema was reduced, corneal Descemet's fold disappeared, corneal and limbus sutures were tight, and conjunctival hyperemia was reduced. The anterior chamber was deep, the iris was



**Figure 4.** Two weeks after the IOFB evacuation





**Figure 5.** Four weeks after the IOFB evacuation.

within normal limits, the pupillary diameter had returned to normal (3 mm), the lens was clear, and the posterior segment was within normal limits (Figure 4). The therapy given was Methylprednisolone 8 mg 2 – 1 – 0 tab for a week, then 1 – 1 – 0 tab for the following week, and Polymyxin-Neomycin-Dexamethasone eye drops four times a day.

On the fourth week after IOFB evacuation, visual acuity of the left eye was 6/20 with lens correction C-1.50 x 150° become 6/7.5. The cornea was clear, the corneal and limbal sutures were within normal limits, and conjunctival hyperemia was minimal. The anterior chamber was deep, the iris and pupil were within normal limits, the lens was clear, and the posterior segment was within normal limits (Figure 5). The patient was given Methylprednisolone 4 mg 1 – 1 – 0 tab for five days, and artificial tears eye drops four times a day.

## DISCUSSION

IOFBs have been formerly categorized in line with their location (anterior chamber, posterior chamber), material characteristics (metal, magnet, wood), length, mechanism of trauma, setting (workplace, battlefield), and period (acute, chronic). The Ocular Trauma Classification organization subdivided open

globe injuries into: (1) penetrating injuries if there is an entry wound; (2) perforating injuries if there is an entry also an exit wound; and (3) lacerations and blunt ruptures, and as being either with or without a retained IOFB. The wound's most posterior extent is a marker to categorize the entry site: zone 1 for cornea; zone 2 for sclera until 5 mm behind the corneoscleral limbus; and zone 3 for sclera more than 5 mm behind the limbus (Parke et al., 2013).

The patient, in this case, had penetrating trauma to the left eye, which resulted in a corneal laceration, and the foreign body remains in the anterior chamber. The patient complained of pain and blurry vision in the traumatized eye, the visual acuity at baseline was 3/60. Pain and decreased vision caused by corneal lacerations. The cornea is the front wall of the eyeball, in the form of transparent and avascular tissue, with a shape like a watch glass. The cornea is sensitive to pain because it is innervated by the ciliary nerve (branch of the trigeminal nerve). The cornea functions as a refraction tool (the greatest refractive power). It is also very sensitive because of its clarity and curvature, which results in minimal structure and shape changes and can cause visual disturbances (Suhardjo & Agni, 2017).



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On examination, there was a foreign/metal body 3 mm in size at the base of the anterior chamber, iris and pupil round, central, pupil diameter 3 mm, direct and indirect light reflexes (+), clear lens, clear vitreous, well-defined papillae and optic discs, CD 0,3 mm, retina within normal limits, IOP 14 mmHg. This examination shows that the IOFB only reached the anterior segment, while the posterior segment appeared within normal limits, and there was no vitreous leak. Thus, according to the literature mentioned above, the IOFB, in this case, belongs to zone 1 in the anterior segment. According to Parke et al., the anterior chamber is the most common place for IOFBs to be found about 21% to 38% of the time. Slit-lamp examination alone can diagnose IOFBs in the anterior chamber, iris surface, or intravitreal. When anterior segment IOFBs are suspected, a gonioscopy examination is required to achieve complete visualization of the angle (Parke et al., 2013).

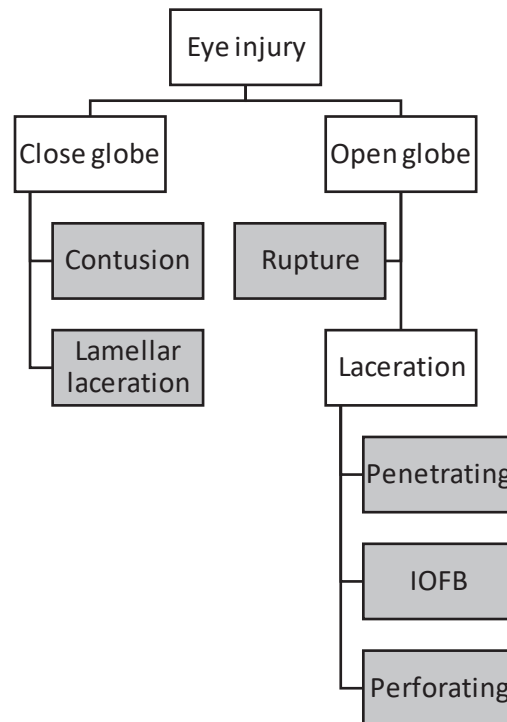
The clinician should execute signs and symptoms of endophthalmitis by doing a complete exam of the ocular structure, such as visual acuity, pupils response, IOP, slit-lamp biomicroscopy, evaluation of media clarity, wounds size, iris color, lens position, signs of retinal tears and detachments (Wulan et al., 2018). Ocular imaging such as ultrasonography, B-scan, X-ray imaging, CT scan, and MRI have been used to detect IOFBs. The appropriate diagnostic devices for visualization and localization rely on the suspected composition and vicinity of the IOFBs. Metal and non-metal material can be detected by CT scan with one millimeter section and no contrast. Although the plain film may be failed to recognize up to sixty percent of the time metallic foreign bodies; however, it is still a cheap and effortlessly obtainable examination the physicians could ever get. Ultrasonography may be up to

ninety-eight percent sensitive in detecting IOFBs. Detachment of retinal and intraocular bleeding, signs of endophthalmitis, and scleral wound entry also can be detected by the USG. MRI can be used after the existence of metallic IOFB is excluded (Wulan et al., 2018).

This patient was diagnosed IOFB based on Birmingham Eye Trauma Terminology (BETT) mentioned in Figure 6. Khun et al. recommended the BETT for precise definitions of all ocular trauma types. Open globe injury is defined as a complete-thickness wound within the corneoscleral wall. Closed globe injuries are subdivided into lamellar lacerations and contusions relying on the presence of a partial-thickness wound. Open globe injuries are subdivided into lacerations and ruptures. Laceration and rupture are both full-thickness wounds of the eye wall, and the difference is that a blunt object causes that rupture; meanwhile, the laceration is caused by a pointy object. In the case of open globe injury with rupture, because the eye is full of incompressible liquid, the effect consequence is a momentary increase in IOP. The eyewall budge at its weakest point at the affected site or somewhere else, such as the actual wound and an old cataract wound, is produced by an inside-out mechanism. An outside-in mechanism can cause a wound at the affected site in open globe trauma with laceration (Jung et al., 2021).

After the diagnosis, this patient immediately planned for an IOFB evacuation operation under general anesthesia. The intravenous and topical antibiotic was given preoperative. Oral antibiotics, analgetic, and steroid; topical antibiotic steroid; and cycloplegic were given after surgery.

Dexamethasone is a product that contains a combination of a fixed-dose corticosteroid and one or more anti-infective drugs. Ophthalmologists use it primarily to treat



**Figure 6.** Overview of BETT (Birmingham Eye Trauma Terminology). The shaded boxes represent the actual diagnoses that are used clinically (*Source: Kuhn et al., 2004*)

conditions requiring both, e.g., marginal keratitis due to a combination of staphylococci infection and allergic reactions, blepharoconjunctivitis, and phletenular keratoconjunctivitis. This mixture of drugs is also used postoperatively (Flach & Fraunfelder, 2019). Ophthalmic corticosteroids are more effective in suppressing inflammatory mediators that cause pain than ophthalmic NSAIDs. Corticosteroids can speed up the healing response and prevent tissue scarring by reducing inflammation. This is important because corneal scarring can cause permanent vision loss. Levofloxacin is an anti-microbial agent inhibiting gram-positive and gram-negative bacteria (Katzung & Trevor, 2015). Systemic ceftriaxone is given as an antibiotic premedication to prevent endophthalmitis (Parke et al., 2013).

Prophylactic antibacterial is extensively given in many forms with some evidence-based

for effect on endophthalmitis rate. Systemic penicillin, vancomycin, cephalosporin, or fluoroquinolone are generally given before or during the IOFBs extraction. After systemic administration, fluoroquinolones in intravenous or oral forms have been proven to have better intraocular penetration. In some centres with low reported postoperative endophthalmitis rates, intraocular ceftazidime and vancomycin are used at the time of the surgical procedure as prophylactic properties (Parke et al., 2013).

Atropine sulfate 1% is an antimuscarinic drug that has capabilities as a pupil dilator and relaxes the eye muscles. Patients with ocular injury could experience a deep, painful sensation, intense photophobia from the ciliary body, and iris muscle irritation. One percent of atropine sulfate or one percent of homatropine hydrobromide inhibits muscarinic receptors in the ciliary body and iris sphincter. Therefore,



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cycloplegics dilate the pupil and prevent the lenses' ability to accommodate for 1 to 12 days. Cycloplegics offered a larger amount of pain relief by rendering the involved muscles inactive and fixing the pupil. Cycloplegics are also beneficial because they inhibit the leakage of additional inflammatory proteins through blood-aqueous barrier stabilization. Thus, it also prevents synechia, whether it is anterior or posterior (Dinardo & Boncher, 2012).

The patient's health status, the character of the injury, the composition of the IOFBs, and the availability of the ophthalmologist and the equipment are several factors that determine the operating time. Yeh et al. proposed the potential benefits of immediate IOFB extraction, such as decreased proliferative vitreoretinopathy (PVR), decreased risk of endophthalmitis, and a patient's single procedure. The risk of PVR is likely to be accelerated by the presence of an IOFB and post-traumatic infection (Wulan et al., 2018).

Different techniques need to be employed within the extraction of IOFBs, relying on the material, location, and size of the IOFBs. The removal approach for IOFBs is primarily based on their size and material. Small (<1 mm), metallic, and ferromagnetic IOFBs may be eliminated with an intraocular magnet, whereas small, nonferrous materials can be removed with the vitreous cutter alone. Intraocular or basket forceps can be used to eliminate intermediate-sized (1-3 mm) IOFBs, regardless of the material. Diamond-coated forceps are required to remove larger (3-5 mm) and glass materials IOFBs to prevent slippage of the IOFBs during removal. Regarding the vicinity of the IOFBs, IOFBs from the anterior chamber, including the cornea, anterior chamber, and intralenticular IOFBs, are typically extracted together with cataract removal (Jung et al., 2021).

Metallic IOFBs are also related to non-infectious toxicity. Metal is stated in 60-88% of IOFBs, up to 90% of which may be magnetic. Copper, lead, zinc, iron, and nickel can trigger ocular toxicity, with the most harm caused by copper and iron. Iron creates heterochromia, degeneration of retinal pigment, cataracts, and alternation of retinal vascular, and further causes Siderosis bulbi. Diffused siderosis may be best identified by an electroretinogram with a decreased B wave. Chalcosis bulbi secondary to copper depends on the copper ion concentration. If the IOFBs are more than 85%, it could produce tremendous inflammation with hypopyon, rapid progression to phthisis, and sterile endophthalmitis. Kayser-Fleisher rings, sunflower cataracts, or refractile retinal and anterior chamber crystals can be produced by chronic mild chalcosis (Lit & Young, 2002; Yan et al., 2016).

Primary surgical intervention must be performed immediately. It is critical to reduce the risk of endophthalmitis and limit the extrusion of ocular contents by suturing the entry sites. The presence of endophthalmitis upon presentation likewise mandates urgent surgical closure, culture, and antibiotic administration (Parke et al., 2013). Surgical priorities consist of closure of the entry access, elimination of the intraocular foreign body, and prevention or treatment of endophthalmitis (Cosar et al., 1999).

## CONCLUSION

Many factors affect the presentation, results, and prognosis of IOFBs. The clinician should conduct a comprehensive history taking, ocular examination, and imaging to evaluate the patient with suspected IOFBs. The benefits and downsides of the deliberate surgical procedure should be considered carefully as a determination of the surgical timing. The approach of IOFB extraction should be selected cautiously based on numerous concerns.



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Preventing and treating feasible complications is crucial after the procedure. Early treatment and complete evaluation of patients are critical to achieving a good prognosis.

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## Case Report

# A successfully treated Basal Cell Carcinoma using elliptical excision surgery

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## ABSTRACT

Basal cell carcinoma (BCC) is a non-keratinization cell-derived neoplasm. Surgical excision is the most common way to remove a tumor. The excision depends on the tumor type, size, and location. This paper reported a 44- years-old woman presented with the chief complaint of a single bump that bleeds easily in the facial region that began one year ago. Dermatology examination revealed hyperpigmented plaque with an ulcer in central, solitary, oval, 2 cm x 1 cm in size, covered with blackish crust on top. A Dermoscopy examination showed blue dots and globules, arborizing vessels, and ulceration. Histopathology examination findings were in concordance with BCC. The patient was treated with elliptical surgical excision. The lesion was successfully removed and showed good results with minimal scarring. BCC occurs in 75% of all skin cancers. Elliptical surgical excision on the left cheek was performed after considering the location anatomy, defect size, age, and general condition patient and postoperative cosmetic estimates. The minimal scar that occurs is planned to be performed with a fractional laser. The prognosis is generally good. There is no recurrence until one year later. In conclusion, elliptical surgical excision is an effective standard treatment if performed with a safe margin. In this case, we used 5 mm safe outer margin.



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### INTRODUCTION

As the most general carcinoma category, Basal cell carcinoma (BCC) consists of melanoma and non-melanoma skin cancer (NMSC) (Leiter, Ulrike, Thomas Eigentler, 2014). BCC is the most common human skin cancer, increasing incidence rates worldwide. Men generally have higher rates of BCC than women (Al Wohaib *et al.*, 2018).

High BCC predilection occurs in the head or neck (52%), trunk (27%), upper arm or leg (13%), and arm or lower leg (8%) (Carucci and Leffell, 2012). If by area calculated body surface, the highest number was found in both men and women, namely on the face, especially the eyelids, lips, and nasolabial folds, followed by the ears, nose, and cheeks. BCC can also appear on the neck, back, shoulders, and arm parts outside the Australian population (Sundoro *et al.*, 2021).

Exposure to the sun becomes the primary source of threat for a patient with BCC (Apalla *et al.*, 2017). However, it is believed that more factors present to worsen this condition, including multiple modifiable and nonmodifiable risk factors (Dai *et al.*, 2018). Although it rarely spreads and develops rapidly, mortality can be the crucial result of BCC, which can occur with the deterioration of local tissues permeable into the vital underlying organs (De Giorgi *et al.*, 2020).

BCC has several subtypes different and can appear in other anatomic locations also. Early clinical BCC generally is small, translucent, or pearly and appears in areas with dilated blood vessels (telangiectasia). The presence of lesions that do not heal should be considered in the direction of skin cancer. BCC is often diagnosed in patients with easy lesions bleeding, who recover completely, and then relapse return (Sumaira and Brent, 2012).

BCC therapy is carried out based on the location and histologic picture. BCC therapy can be performed surgically and non-surgically. It is essential to differentiate between primary and recurrent tumors, which may lead to differences in therapeutic modalities and possible cure rates (Carucci and Leffell, 2012). Surgical techniques include curettage and cautery, cryosurgery (with liquid nitrogen), excision, and 'Mohs' micrographic surgery. The best chance to heal is with therapy adequate primary BCC because recurrent tumors are more likely to relapse and cause local destruction further (Sumaira and Brent, 2012). However, the options for multiple treatments for BCC are available these days. This report describes a case of a patient suffering from BCC treated with elliptical excision surgery. Elliptical excision is indicated to remove benign or malignant neoplasms of small to medium size (Jiang *et al.*, 2007). Excision surgery is effective because the healing time is relatively short, the cure rate is around 90%, and the results are cosmetically satisfactory (Verkouteren *et al.*, 2017). This paper reported a 44-year-old Basal Cell Carcinoma patient who successfully treated using elliptical excision surgery

### CASE REPORT

A 44-year-old female patient visited the Dermatology and Venereology Outpatient Unit on February 24, 2021, complaining of a lump that had been bleeding easily since 1 year ago. The lesion begins as a small, reddish lump that grows in size. The longer it lasts, the wider and becomes blackish, accompanied by itching. She's felt that the lump is bleeding more frequently and is quite a pain. The patient said she was often exposed to the sun when drying clothes. She rarely used sunscreen and never wore a hat or shield when exposed to the sun. There is no history of keloid or family members having cancer. No family members suffered from the same disease.

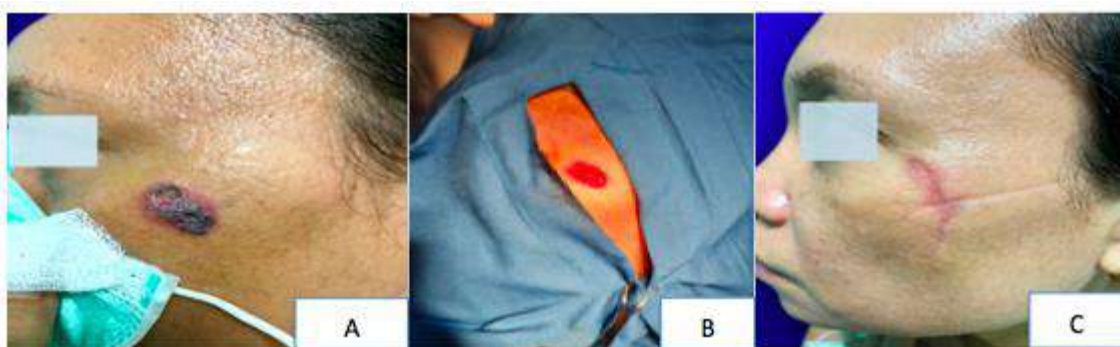


A good general condition was concluded as the result of a physical examination recording 140/90 mmHg for blood pressure, 80 beats per minute for pulse rate, 18 times per minute for respiratory rate, and 36.0 degree Celsius for body temperature. Head and neck examination showed no anemia, icterus, cyanosis, or dyspnea. Physical examination revealed no cardiac, pulmonary, liver, or spleen abnormalities. Lymph node enlargement on the neck, axillae, and groins was not palpable. Dermatologic examination showed hyperpigmented plaque et erythematous, clearly defined size 2 cm x 1 cm, covered with blackish crust on top and accompanied by an ulcer in the middle on regio facialis (Figure 1). Supporting examination included dermoscopy examination; there were asymmetrical lesions, irregular borders, and then blue dots and globules (orange arrows), and arborizing vessels in black star, namely telangiectasia with an unregulated pattern, and there was ulceration. Histopathology result was achieved two weeks after. It showed tumor growth arranged in solid nests, consisting of a

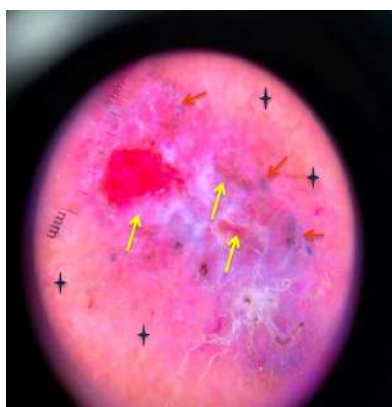
proliferation of anaplastic basal epithelial cells with round-oval nuclei, mild pleomorphic, hyperchromatic, narrow cytoplasm. Tumors were arranged in palisade on the edges, partly arranged to form hair follicles. The conclusion was a pigmented basal cell carcinoma with adnexa tissue differential. Based, and border tissues were free from tumor cells. The final diagnosis was basal cell carcinoma.

Diagnosis of BCC was made for the patient according to the results of physical and supporting examination along with the historical background check related to BCC. When the lesion is relatively small, it could be removed by simple elliptical excision. The patient comes back on March 9 for elliptical excision.

Regularly performed control examinations found no complications 2 months after the operation. The patient considers the functional and cosmetic results of the procedure as excellent.



**Figure 1.** A. Hyperpigmented plaque et erythematous, clearly defined size 2cm x 1cm covered with blackish crust on top and accompanied by an ulcer in the middle on region facialis. B. The tumor is excised with 5 mm safe outer margin to achieve free tumor. C. Postoperative day 28, tissue was seen minimal scarring.



**Figure 2.** Asymmetrical lesions, irregular borders, and then blue dots and globules (orange arrows), and arborizing vessels, in black star, namely telangiectasia with unregulated pattern and also shows ulceration (yellow arrows).

## DISCUSSION

BCC is the most prevalent category of human cancer. Incidence is growing rapidly by 3 to 10% per year (Tang, Epstein and Oro, 2019). At a minimum, patients are much more likely to increase a second BCC in the event that they have a BCC records as compared to sufferers without a records of non-melanoma skin cancer (Skoda *et al.*, 2018). UV light is the top etiological within the improvement of BCC, especially the UVB wavelengths. However, UVA wavelengths also can be expected. A detailed review of the literature with meta-analysis and sensitivity analysis shows a significantly higher risk for outdoor workers, with an inverse courting among occupational UV publicity and BCC chance with latitude. The Fitzpatrick skin is a superb predictor of the relative opportunity of BCC amongst white race individuals (Kamath *et al.*, 2018); (Martens *et al.*, 2018).

Most BCC causes are the UVR exposure to the skin, particularly the ultraviolet (UV) B spectrum, which is able to induce tumor suppressor genetic mutations, deteriorate DNA contributing to the genetic alterations

and neoplasms, and also p53 tumor suppressor genetic mutations (50% cases) (Wozniak-Rito, Zalaudek and Rudnicka, 2018). The increased environmental degradation, especially related to ozone depletion, skin bleaching cultures, and the use of tanning beds, are among the increased risk factors for BCC. Other risk factors are commonly associated in organ transplant recipients with exposures to therapeutic ionizing radiation and immunosuppression (Litaie *et al.*, 2020).

Diagnosis of BCC can be supported with histopathology and dermoscopy (Litaie *et al.*, 2020). A skin biopsy is essential for clinical confirmation of BCC. A shave, punch, or excisional biopsy are all options, taking care to consist of a few part of the epidermis withinside the specimen to distinguish among superficial and different invasive histologic subtypes of BCC. Punch and shave biopsy can also be done for histopathology examination (Weber *et al.*, 2018). Dermoscopy may be helpful to the clinician, helping the analysis of non-pigmented and pigmented BCCs. The hallmark of BCC on dermoscopy is the presence of well-targeted arborizing vessels. Additional findings encompass a couple of blue-grey globules, leaf-



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like structures, massive blue-grey ovoid nests, and spoke-wheel areas (Cameron *et al.*, 2019). The application of dermoscopy can enhance the precision of the diagnostic and provide variants of BCC's certain subtypes (Litaïem *et al.*, 2020). Meanwhile, the final and determining diagnosis is crucially concluded by using histopathology (Marzuka and Book, 2015).

Therapy depends on the patient's age and gender in addition to the size, site, and form of the lesion. No single treatment technique is right for all lesions or all sufferers. A biopsy has to be finished in all sufferers with suspected BCC to affirm the prognosis and determine the histologic subtype. Treatment of BCC is typically surgical; however, a few sorts of BCC are amenable to clinical or radiation. The numerous kinds of therapy consist of Mohs micrographic surgery (MMS), surgical excision, EDC, radiation, photodynamic therapy, cryosurgery, topical therapies, and systemic medications such as Vismodegib (Hughley and Schmalbach, 2018).

The principal goals of treatment for BCC are (1) to excise the tumor completely so that there is no recurrence of the tumor at a later time, (2) to avoid any functional impairment resulting from the excision of the tumor, and (3) to provide the best possible cosmetic outcome, especially for the lesions that are on the face (Drucker *et al.*, 2018).

Management of this patient used elliptical excision surgery (Litaïem *et al.*, 2020). Elliptical excision is indicated to remove benign or malignant neoplasms small to medium in size (Robinson, 2008). Excision ellipse provides good cosmetics with minimized tissue lift, movement of skin, and incision length (Goldberg and Alam, 2004). For cosmetic results, optimal elliptical excision should be oriented along the RSTL, which is generally perpendicular to muscle pull in the area (Aasi and Pennington, 2008). We usually make 3-5mm safe outer margin before excision to ensure tumor-free on the preserved tissue.

**Table 1.** Several factors independently affect the likelihood of cure.

Factors	Description
Anatomical site	The 'H zone' (face, nose and ear) on the face is often referred to as a site where tumours are most difficult to eradicate.
Size	The European Dermatology Forum (EDF) guidelines on surgical excision margins of BCC recommends 3 to 4 mm peripheral margins for low-risk BCC, and 5 to 10 mm peripheral margins for high-risk BCC
BCC sub-type	BCCs with a morphoeic growth pattern often have indistinct margins with a large extent of sub-clinical tumour invasion.

Source: Kappelin *et al.*, (2020)



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**Table 2.** Data from the studies with the title of BCC and conclusion

Author and year	Country	Purpose of the study	Result
Ito <i>et al.</i> , (2015)	Japan	A narrow excision margin is a reliable method for the excision of well-demarcated, primary-pigmented BCC	Surgical removal with a 2-3mm excision margin is an adequate treatment for well-defined, primary-pigmented BCC, with a 99% complete removal rate
Lin <i>et al.</i> , (2016)	Taiwan	Treatment of pigmented BCC with 3mm surgical margin in Asians	The study suggests that a 3mm margin is reliable for the excision of pigmented BCC. Nonpigmented BCC had a higher risk for recurrence and thus needs careful follow up
Ünverdi, Yücel and Berk, (2020)	Turkey	Recommended surgical margins for BCC is 3 mm safe enough?	A 3-mm surgical margin is sufficient for BCC excision

Source: Sohail J, (2020)

The prognosis of BCC patients is generally good (Verkouteren *et al.*, 2017). BCC rarely becomes a deadly outcome. One study reported a 5-year survival rate for primary BCC treated with surgical excision of 95.2%. However, all treatments that have been carried out must be continuously monitored, considering that about 20% of recurrences usually occur between 6-10 years postoperatively, and it is estimated that 40%-50% of patients with primary carcinoma will develop at least one or more BCC within five years (Low, Alexander and Lomas, 2015) with appropriate treatment, the prognosis for most BCC patients is excellent (Carucci and Leffell, 2012). The risk of recurrence depends

on the BCC area and histopathological features (Newlands *et al.*, 2016). Patients should follow up after therapeutic procedures to see any signs of recurrence, and generally, follow-up is done in the third and fifth year (Kasumagic-Halilovic, Hasic and Ovcina-Kurtovic, 2019). It is recommended that patients with a history of BCC conduct full-body skin examinations and sun protection counseling periodically (Kasumagic-Halilovic, Hasic and Ovcina-Kurtovic, 2019). It is because the increased threat of melanoma occurs in patients with a history of BCC. In addition, protecting the skin from UV exposure during childhood and adolescence can be the main strategy for decreasing the risk of getting BCC (Sreekantaswamy *et al.*, 2019).



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### CONCLUSION

This report describes a successful treatment of elliptical excision surgery in a BCC case. The patient's history, along with both physical and supporting examinations, e.g. dermoscopy and histopathology, were implemented for deriving a diagnosis. Elliptical excision surgery is the effective standard treatment for BCC as long as it is performed with a safe margin.

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Case Report

## Mid-term functional outcome after distal Achilles tendon rupture anchoring screw repair in elderly osteopenia as a reliable technique: A case report

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### ABSTRACT

The management of distal Achilles tendon rupture is still controversial, especially in elderly patients, due to poor bone quality and tendon stump integrity. One of the proposed repair techniques is by using an anchoring screw. Here we report the mid-term follow-up of two patients with distal Achilles tendon rupture treated with an anchoring screw. Two elderly males in their sixties came to the outpatient clinic with similar complaints of intermittent pain, reddening, and ankle swelling after falling. Both patients were diagnosed with distal Achilles tendon rupture and were treated with open repair using a Krakow suture and anchoring screws. Functional outcome evaluation postoperatively found a good outcome. Previous studies have shown that repair with the anchoring technique is better biomechanically than with ordinary sutures. Repairs with this technique can withstand greater forces and loads before they fail. An anchoring screw repair technique for total distal Achilles tendon rupture repair provides good results in elderly with osteopenia.



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### INTRODUCTION

The largest and strongest tendon in a human, the Achilles, connects the gastrocnemius and soleus muscles to the calcaneal bone. The incidence of Achilles tendon rupture has increased from year to year. Most cases occur during sporting activities. Other factors, such as gender, medications, and intrinsic structural variations, increase the risk of rupture. Rupture in the elderly is challenging since biomechanical tendon changes are associated with aging, and bone quality may determine the treatment and outcome (Benjamin, Toumi, Ralphs, *et al.*, 2006).

The main objectives of treating an Achilles Tendon Rupture are to guarantee a speedy recovery and avoid complications. Surgeons more often perform operative action because nonoperative management often causes more complications. The complications of nonoperative management include stiffness due to prolonged immobilization, a greater possibility of re-rupture, and the addition of tendon length, which results in reduced tendon strength, especially in the elderly (Zurita Uroz, Paniagua, Kelly, *et al.*, 2022). The treatment becomes more challenging in distal tendon rupture since such a rupture will prevent an end-to-end direct repair. Previous studies have shown that repair with anchoring screws is better biomechanically than repair with ordinary sutures in a distal rupture in which bone quality at the site of tendon insertion is essential. Repairs with anchoring screws can withstand greater forces and loads than standard suture techniques before they fail (Boin, Dorweiler, McMellen, *et al.*, 2017).

Various scoring methods can measure the functional outcome; the most popular is the Foot & Ankle Outcome Score (FAOS). This method has been used universally and has a high validity rate to assess the return of

function on therapeutic management. That has been carried out by evaluating certain subscales (Nilsson-Helander, Thomee, Silbernager, *et al.*, 2007).

Considering the poor bone quality and the integrity of the tendon stumps in the elderly, distal Achilles tendon rupture treatment is challenging but feasible using anchoring screws. This report describes the functional outcome of distal Achilles tendon rupture treated with anchoring screw in elderly with osteopenia.

### CASE REPORT

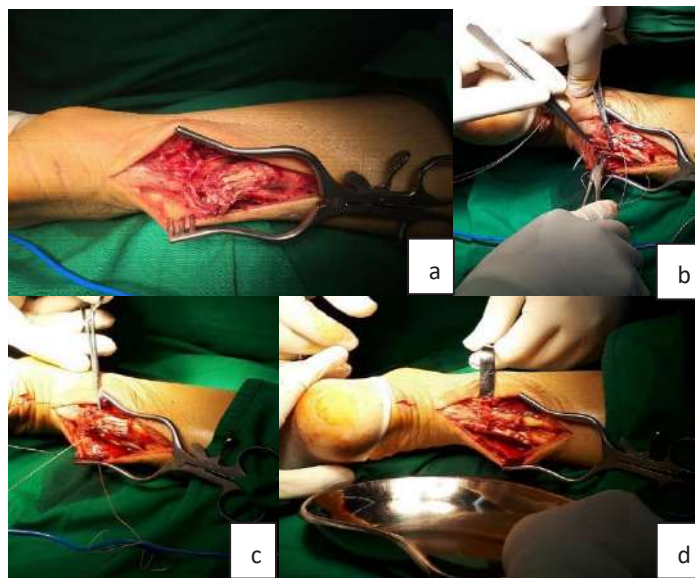
For the first case, a sixty-eight-year-old male came to the outpatient clinic after having their ankle intermittently reddens and swells. The patient had a history of sudden huge pain and swelling on his left ankle 2 years ago when playing badminton. Afterward, the patient went to a physiotherapist and underwent alternative therapy because the pain was tolerable, and the patient could still walk. One month after the incident, the patient went to an outpatient clinic and was diagnosed with Achilles tendon rupture and underwent surgery. The previous history of diabetes, cardiac conditions, hypertension, stroke, and other significant disease is denied. Previous surgery is also denied. On FAOS Score, the lowest score was obtained on the 'Sports and Recreational Activities' subscale, with a score of 15 indicating the category that had the most problems in patient 1. The highest score was obtained on the subscale 'Pain' with a score of 55, indicating the category that had the least problem in patient 1. We performed BMD on the patient, and it was found that the patient had a T-Score below -2.5 SD.

For the second case, a 60-year-old Male came to the outpatient clinic after slipping when walking down a stair. After the fall, the patient could not stand and complained of swelling and pain in the left ankle. The patient was

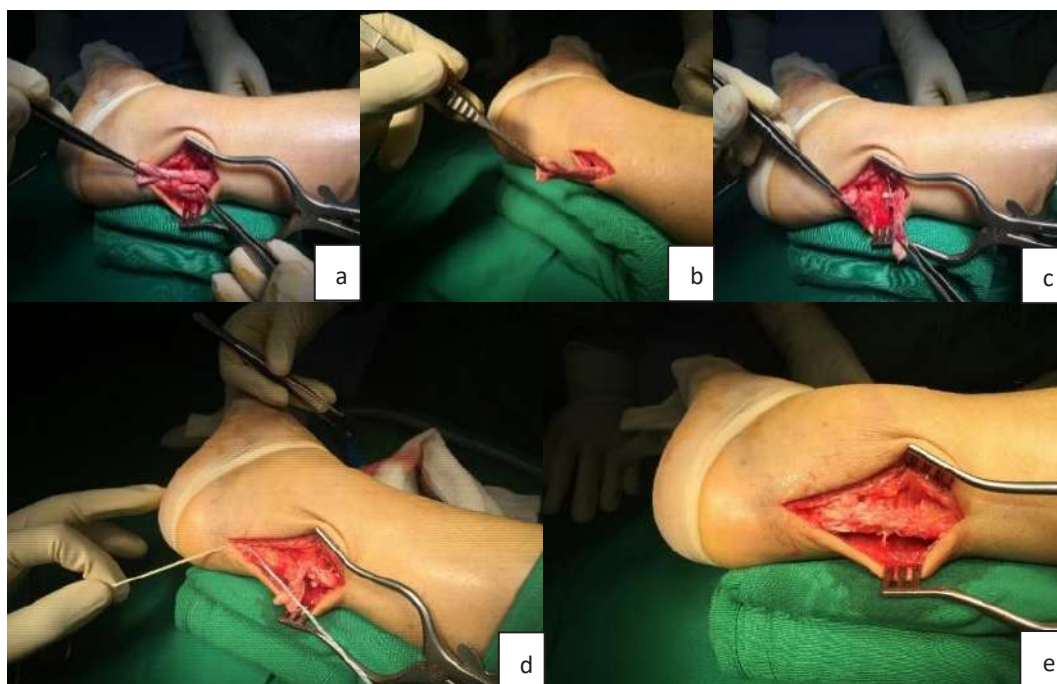
taken to the orthopedic outpatient clinic and diagnosed with Achilles tendon rupture. The patient then underwent surgery for repair. The previous history of diabetes, cardiac conditions, hypertension, stroke, and other significant disease is denied. Prior surgery is also denied. On FAOS Score, the lowest score was obtained on the 'Sports and Recreational Activities' subscale with a score of 27, indicating the category that had the most problems in patient 1. The highest score was obtained on the subscale 'Other symptoms' with a score of 64, indicating the category that had the least problem in patient 1. The patient also had a T-Score below  $-2.5$  SD. Preoperative evaluation of bone density showed osteopenia in both patients. Both patients have similar physical examination results, treatment, and postoperative care. Upon physical examination, no abnormalities were found on other parts of the body. On the left ankle, a postoperative scar of  $\pm 10$ cm

was observed on the posterior ankle. Pain on palpation is not found, and the range of motion is within normal limits. The patients were diagnosed with tendon Achilles rupture. They were treated with open repair using Krakow suture and anchoring screws, as documented in picture 1 for the first case and picture 2 for the second case.

After 2-year of follow-up, the first patient said he could do the activity as usual. Pain is felt after prolonged and heavy activities and subsides when resting. Evaluation using FAOS is described in table 1. The highest score was obtained on the 'Activities of Daily Life' subscale with a score of 97.1, indicating the category with the least problems in patient 1. The lowest score was obtained on the subscale 'Sports and Recreational Activities' with a score of 65, indicating the category with the biggest problem in patient 1.



**Figure 2.** Clinical Photo during the operation on the 2<sup>nd</sup> patient. (a & b) complete rupture of Achilles tendon is clearly visible, (c & d) tendon repair with Krakow suture technique and anchoring screw, (e) appearance of Achilles tendon after repair



**Figure 1.** Clinical Photo During the Operation of 1<sup>st</sup> patient (a) Achilles tendon rupture is clearly visible during the operation, (b & c) repair of the tendon with Krackow suture technique and anchoring screw, (d) Presentation of Achilles tendon after repair.

**Table 1.** FAOS evaluation upon presentation and on 2 year follow up on both patient

	Patient 1			Patient 2		
	Initial	On 2 year follow up	Difference	Initial	On 2 year follow up	Difference
<b>Pain</b>	55	94.4	39.4	54	94.4	40.4
<b>Other symptoms</b>	53	96.4	43.4	64	100	36
<b>Activities of Daily Living</b>	46	97.1	51,1	51	98.5	47.5
<b>Sports and Recreational Activity</b>	15	65	50	27	85	58
<b>Quality of Life</b>	31	75	44	45	95.2	50.2



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The second patient was followed up three years later and stated that the patient felt no more pain and could return to daily activities as before the rupture. The evaluation of the second patient using FAOS is detailed in table 1. The highest score was obtained on the 'Other symptoms' subscale with a score of 100, indicating no problem in patient 2. The lowest score was obtained on the subscale 'Sports and Recreational Activities' with a score of 85, indicating the category with the biggest problem in patient 2.

### DISCUSSION

The three mechanisms that can cause Achilles tendon rupture are propulsion of the weight-bearing foot with knee extension, sudden ankle dorsoflexion, and excessive dorsiflexion of plantar flexion of the ankle. Maffulli et al. reported that 53% of patients experienced an Achilles tendon rupture with a push-off mechanism, as many as 17% with sudden ankle dorsiflexion, and 10% with excessive dorsiflexion of the ankle plantar flexion. Three to six centimeters proximal to the insertion of the calcaneal Achilles tendon is the most common site of rupture due to several factors: hypovascularity, a limited cross-sectional area, and a high eccentric load.

The first patient in the case reported experiencing pain and swelling after playing badminton two years ago, while the second patient had a history of slipping down the stairs. Sports activities such as jogging, running, jumping, and agility activities that involve explosive plyometric contractions in the first patient are the initial mechanism for rupture; a person experiencing this mechanism will experience a popping event which can be described as "kicked from behind" or like crackling in the calf. One of three frequent mechanisms of Achilles tendon rupture will be triggered by highly rapid aberrant loading or intense plyometric-based

exercise. Additionally, as was the situation with the second patient in this case report, severe loading of the Achilles tendon with subtalar joint inversion and eversion enhances the risk of damage. One of three frequent mechanisms of Achilles tendon rupture will be triggered by highly rapid aberrant loading or intense plyometric-based exercise. Additionally, as was the situation with the second patient in this case report, severe loading of the Achilles tendon with subtalar joint inversion and eversion enhances the risk of damage.

Following surgery, proper therapy will hasten recovery. According to a meta-analysis of studies conducted by Suchak et al., recurrence rates were lower in patients treated with a functional postoperative brace (2.5 percent) compared to plaster in a comparison of various rehabilitation programs following surgical and nonoperative care (3.8 percent). It is unclear exactly how these research differ from one another. Nevertheless, other ideas contend that they only affect a small number of patients or are caused by variations in surgical technique or the postoperative functional brace protocol. The literature on nonoperative management reveals three randomized controlled trials comparing casts for immobilization with accelerated rehabilitation performed by Jones et al. in 2012. Compared to eight of seventy patients (11.4%) in the cast for immobilization group, the recurrence rupture has happened in two of sixty patients (3.3%) in the fast rehabilitation group. According to the recommendations Jones et al. made to the AAOS, they "cannot recommend for or against immediate functional bracing in individuals with acute Achilles tendon rupture.

Previous studies have shown that repair with the anchoring technique is better biomechanically than with ordinary sutures. Repairs with this technique can withstand greater forces and loads before they fail. We



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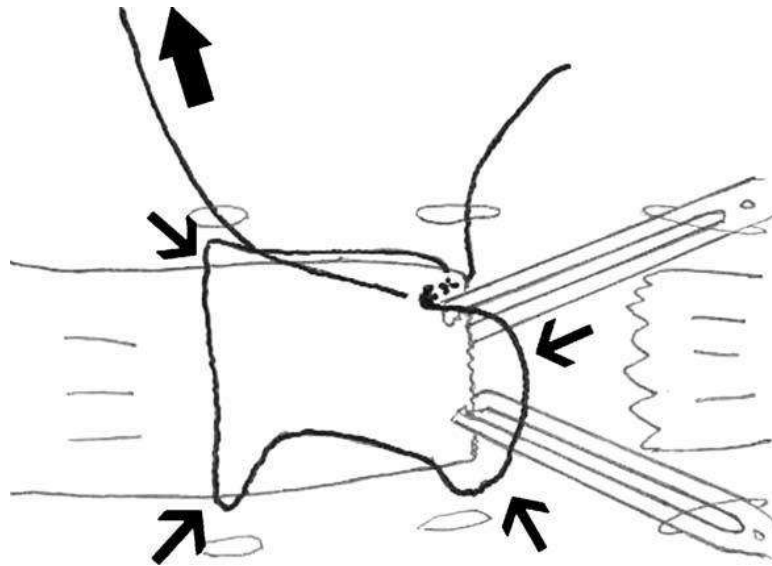
believe that this technique is biomechanically stronger for several reasons. First, this repair bypasses the tissue tear's short end and has primary fixation via an anchor attached to the calcaneus. It is even more useful in patients with Achilles tendinosis because the short end of the tissue tear is often degenerative and less suture-resistant than a healthy Achilles tendon. A study by Kim et al. investigated the biomechanical significance of accessible tendons in flexor tendon repair. They found an increase in repair strength with increasing reachable tendon length. Due to the short tearing end of the tissue, there is a limitation of the tendon that the suture can pass. Therefore the length of the tendon that can be reached is shorter, so the construction is weaker. Using a lag screw as fixation is also effective for cases with calcaneal avulsion due to its compression technique. Still, it requires a large fragment to attach to the Achilles tendon so that at least two screws are inserted with a washer.

Krackow sutures and anchoring were employed during the open method procedure on both patients. The key conclusion of the previous study was that an endoscopic approach might be used to apply a Krackow-type locking suture. However, a substantial percentage of the time (33%) no Krackow lock suture was established, only the end of the tendon that the suture "grasped". Grasping the end of the torn tendon with two Allis tissue forceps (Medicon, Tuttlingen, Germany) before passing the superficial suture to the forceps is a preventative measure for one suturing difficulty. Allis forceps are used to grasp the ruptured proximal stump tendon at its distal end through the medial and lateral portals of the wounds, and the suture is then passed through the proximal stump. Similar to this, a suture is inserted through the tip of the stump after forceps are used to grasp the distal

stump and terminate tendon rupture through the proximal medial and lateral portal wounds (Işık and Tahta, 2017).

Rest, elevation, pain management, and functional bracing are the first lines of treatment for Achilles tendon rupture. The possible advantages and disadvantages of surgical intervention are still up for debate. Studies have shown positive functional outcomes and patient satisfaction with both operational and nonoperative techniques. With a reported risk difference in a re-rupture rate ranging from 5% to 7%, several meta-analyses of randomized controlled trials (RCTs) have demonstrated that surgical treatment considerably lowers the risk of tendon re-rupture compared with nonoperative treatment (Ochen, Beks, Van Heijl, *et al.*, 2019).

We found out that both patients had a T-Score below -2.5 SD on BMD. This osteopenic condition may lead to failure of tendon reattachment. Studies suggest that the low bone density in some regions is consistent with the reports that suture anchors may be difficult to anchor securely within that region because of variable bone quality. (Meyer, Fucentense, Koller, *et al.*, 2004)(Barber, Feder, Burkhart, *et al.*, 1997) So, we emphasized the need for stronger, more gap-resistant repairs as more of the Achilles insertion becomes separated since the degenerative tendon tissue may not be able to withstand the stresses of regular everyday activities and may be susceptible to re-ruptures Tendon gap creation causes increased granulation tissue, slow healing, decreased strength at the site of repair, and may eventually have a negative impact on the clinical outcome. So, we proposed the importance of site gapping of less than 5 mm, because as little as 5mm of gapping might be considered an essential parameter for clinical failure, as reported by Lee et al (Lee, Goldsmith, Nicholas, *et al.*, 2008).



**Figure 3.** The ruptured tip of the proximal stump tendon is captured by Allis tissue forceps through the distal medial and lateral portal wounds before passing the suture through the superficial proximal stump to the forceps. This can prevent the suture from falling onto the end of the tendon rupture (Işık and Tahta, 2017)

The two patients in this case report showed that the FAOS score results on the assessment of five subscales, namely Pain, Other Symptoms, Daily Activities, Sports and Recreational Activities, and Quality of Life, with a score ranging from 0 to 100 with a score of 0 indicating the worst possible foot/ankle symptom and 100 indicates no foot/ankle symptoms. The first patient got the highest score on the 'Activities of Daily Life' subscale with a score of 97.1, indicating the category that had the least problems in the patient, while the lowest score on the 'Sports and Recreational Activities' subscale with a score of 65 indicated the category that had the biggest problems in the first patient. The second patient got the highest score on the 'Other Symptoms' subscale with a score of 100, indicating a category that had no problems in the second patient, while the lowest score on the 'Sports and Recreational Activities' subscale with a score of 85 indicated the category that had the most problems in patient 2. From the two

samples with the same background, gender, and age, it can be said that this technique is successful in degenerative Achilles tendon conditions considering that the age of both samples is elderly patients, and it is likely to be much better in more advanced tendon conditions (Callahan, Cleveland, Allen, *et al.*, 2021).

The first patient's sports and recreational activities are more impaired than the second patient's. We hypothesized that the factors contributing to these results are the difference in the time of the patient receiving the proper medication, as in the first patient, he sought medication one month after the incident, and in the second patient, he immediately sought medication after the injury. The first patient is immobilized for a longer time compared with the second patient. This may be critical for the different outcomes between these patients, as the onset of physical therapy is essential for the functional outcome of patients with Achilles



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tendon rupture. Also, the harmful effect of prolonged immobilization is widely known (Vargas-Mena, Burgos-Elías and Pérez-González, 2013).

Roos et al., in 2001, stated that the FAOS score met the established validity and reliability criteria. FAOS is also helpful for the evaluation of patient-relevant outcomes concerning ankle reconstruction. However, to fully validate FAOS for foot and ankle problems, additional studies are needed over time in different populations (Roos, Brandsson and Karlsson, 2001).

### CONCLUSION

Achilles tendon rupture incidence increases from year to year. Osteopenia is the most common risk factor of Achilles tendon rupture. This case's management needs to be concerned; surgical management is still promising in outcomes and minimal complication. Treatment with open Krakow suture and anchoring screws shows good outcomes measured with the FAOS scoring system.

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