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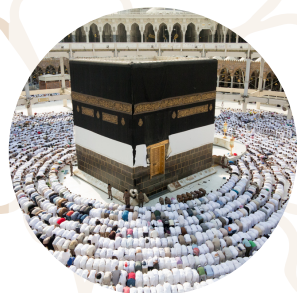
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## Ethical Principles as Student Motivation Continuing Education at Medical Faculty, Nahdlatul Ulama University, Surabaya

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### ABSTRACT

**Background :** Ethics is an important component in human life to distinguish good and bad behavior. Motivation is very important when an individual wants to do something and decides something. Ethics supports a person's motivation to do things they think are good, including determining education at medical school.

**Objective :** The research aims to find out students' thinking principles based on the science of ethics so that by knowing these thinking principles researchers can find out students' motivations in choosing and continuing their studies at medical faculty.

**Methods :** This research is a quantitative study with a descriptive approach on all students of the Class of 2022 FK UNUSA. The survey used secondary data from student interviews from the new student admissions committee, data analysis using descriptive analytics and data validity using correlation tests.

**Result :** The results of this research show that 81% of students have the principle of virtue ethic thinking, supported by Personal Characteristics Test data showing that 72% of students are advised to be accepted as students at the medical faculty.

**Conclusion :** So, it can be concluded that virtue ethics is a motivation to continue education at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya.

### Introduction

Ethics is one of the important components in human life to distinguish good and bad behavior (Bertens,2013). If we study ethics more deeply we will find various principles of ethical thinking, where based on these principles it can be seen that indicators of good and correct behavior according to the results of actions from the human point of view (Bertens,2013). It is hoped that the principles in the science of ethics can help in the Medical Education

System at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya by finding out through the motivation of new students who choose their field of study interest at the medical faculty because it is based on the lecturer's report.

Lecturers at the Faculty of Medicine and clinical teaching doctors at Jemursari Islamic Hospital, Surabaya, the ability of students at the pre-clinical and professional stages, when viewed from the length of the study period, is experiencing delays.

Motivation is a very important thing when an individual wants to do something and decides something (Anizio et al, 2021). So it is necessary to carry out research that links the principles of ethical thinking with the motivation of students to choose and continue their education at the medical faculty, especially at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya (Damian, 2021)

The research aims to find out students' thinking principles based on the science of ethics so that by knowing these thinking principles researchers can find out students' motivations in choosing and continuing their studies at medical faculty. So it is hoped that the research results obtained will provide information to the faculty to be better prepared to face the consequences of each student's ethical thinking principles (Jacob, 2020). This provides positive feedback to the medical faculty to maintain and even always improve the quality of education in the academic and non-academic fields so that the indicators for achieving the strategic plan can be met in accordance with the vision and mission of the University and the Faculty of Medicine, Nahdlatul Ulama University, Surabaya.

This innovation has been carried out by lecturers at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya, but researchers want to specify it further by investigating in the realm of ethics towards

student motivation. This research has innovations including the formation of a newer education system that still adapts to the National Standards for Indonesian Medical Education and has an Islamic Aswaja culture, effective learning methods for students and lecturers and the formation of a policy when accepting new students and during the teaching and learning process.

## **Methods**

This is a quantitative study with descriptive analysis

### ***Study population***

The population in this study is secondary data. The secondary data used are the results of interviews with prospective new students and personal characteristics tests. The total number of prospective new students accepted at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya was 110 people.

### ***Study Data***

The data used in this research are the results of student interview tests from personality aspects. Personality aspects consist of 4 indicators

1. motivation
2. desire to learn
3. hope
4. point of view

Then the personal characteristics test data, this data contains recommended or not

recommended based on the scores produced during the test. The two test results above are used to determine the ethical principles possessed by students as motivation to continue their education at medical faculty.

## Results and Discussion

The two test results above are used to determine the ethical principles possessed by students as motivation to continue their education at medical faculty. The research was carried out later than the planned schedule, which was originally in mid-May 2023 and then postponed until it was carried out on August 8-9 2023.

The research took place during 2 days of research data collection without any problems. Required research data collection includes secondary data from interviews from prospective new students at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya in 2022 face to face (offline), Scholastic Potential Test and Personal Characteristics Test with a test model using a Computer Based Test.

The interview test for prospective new students in 2022 explores three aspects, namely personality, social and family. The personality aspect of the medical faculty student interview test has 4 indicators, namely:

1. Motivation
2. Desire to learn
3. Hope

## 4. View of life

The assessment categories are:

4 = very good

3 = good

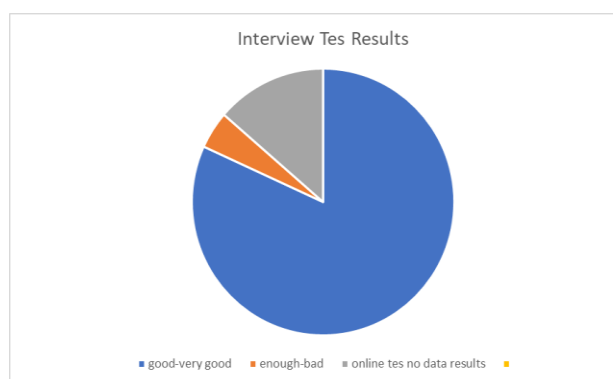
2 = sufficient

1 = less

These four indicators can be the basis for researchers to understand the principles of ethical thinking as motivation to continue their education at the Faculty of Medicine.

The maximum score that can be obtained by prospective new students is 16 in the very good category to be accepted as a medical faculty student, then the next score is 12 in the good category to be accepted as a medical faculty student, then a score < 12 is in the moderate or poor category to be accepted as a faculty student. medical.

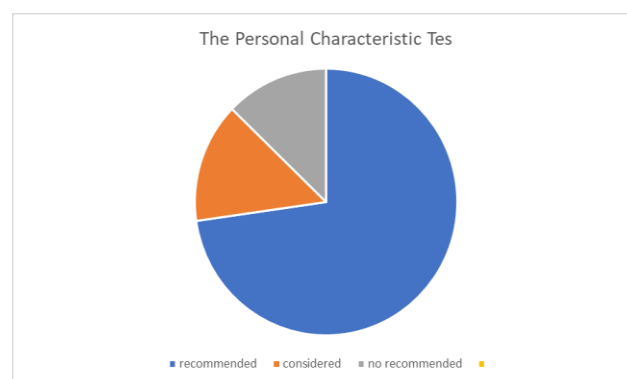
The number of students from the Faculty of Medicine, Nahdlatul Ulama University Surabaya accepted in 2022 is 110 students. There were 90 students with interview test results in categories ranging from good to very good. 5 students with interview test results in the adequate to poor category. 15 students carried out an online interview test and assessed it using a separate formula. The results of interview tests for prospective medical faculty students can be displayed via a pie chart as below.



**Figure 1.** Interview Test Results

Apart from using interview test results for prospective new students, researchers used additional secondary data from the Personal Characteristics Test as another medium besides psychological tests. The Personal Characteristics Test is a test used to measure the daily character of test takers related to the culture of the work environment.

The results show that among prospective new students at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya, there are 80 people who are recommended to be accepted, 16 people who are considered to be accepted and 14 people who are not recommended to be accepted as medical faculty students. The results of the Personal Characteristics Test can be displayed in the form of a pie chart as follows:



**Figure 2.** The Personal Characteristic Test

The results of research conducted by the research team show that the principle of ethical thinking that motivates students to continue their studies at the Faculty of Medicine, Nahdlatul Ulama University, Surabaya is virtue ethics or in Indonesian it means Virtue Ethics. Virtue ethics has the meaning of ethics based on characteristics.

In the research results, there were 90 students who had good to excellent personality status, which was obtained from motivation, desire to learn to become a doctor, hope and outlook on life. Then, the research team obtained data from the Personality Characteristics Test which showed that 80 people were recommended to be accepted as medical faculty students. These two test results prove that Virtue Ethics is a motivation for students to continue their education at the Faculty of Medicine, Nahdlatul University, Surabaya.

## Conclusion

Based on the results of the interview test using personality aspects which consist of 4

indicators, namely motivation, desire to learn, hope and outlook on life as well as the results of the personal characteristics test, it shows the principle of ethical thinking as motivation for students to continue their education at the Faculty of Medicine, Nahdlatul Ulama University Surabaya is virtue ethics.

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## The Relationship Of Anti-Inflammation Non Steroid Use Patterns With Side Effects In Patients Post Appendectomy At Jemursari Islamic Hospital

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### ABSTRACT

**Background:** Appendicitis is a condition where there is acute inflammation of the vermiform appendix which causes patients to undergo surgery frequently. NSAIDs are given to patients after appendectomy surgery to relieve pain. Inappropriate pattern of NSAID use can cause drug side effects.

**Objective:** This study aims to analyze the relationship between the pattern of use of non steroidal anti-inflammatory analgesics and drug side effects in post-appendectomy patients at Jemursari Hospital Surabaya in 2019-2020.

**Methods:** This type of research is descriptive analytic with a cross sectional design. This study used 62 samples medical record of post-appendectomy patients in 2019-2020 who were given NSAID therapy. Chi-Square Test and Fisher's Exact Test ( $p < 0.05$ ) was used to analyze the relationship between NSAID use patterns and side effects.

**Results:** There was a relationship between the type of drug Mafenamic Acid 500mg with nausea, Ketorolac 30mg with hypotension, Ketorolac 90mg with dizziness, and Santagesic 500mg with dyspepsia ( $p < 0.05$ ). Administration of therapy with less dose was associated with hypotension ( $p < 0.05$ ). The duration of therapy for 4 days was associated with nausea, vomiting and duration of therapy for 5 days was associated with constipation and dyspepsia.

**Conclusion:** The use of drugs (type of drug, accuracy of dose and duration of therapy) of NSAIDs in post-appendectomy patients is associated with drug side effects.

### Introduction

Appendicitis is a condition where there is acute inflammation of the vermiform appendix caused by bacterial infection, tumors of the appendix, and worms which can cause blockages to form in the lumen (Diantari *et al.*, 2018). The presence of these blockages can cause more mucus production and a decrease in the elasticity

of the appendix wall and a feeling of pain occurs (Flum, 2015).

In Indonesia, appendicitis patients account for around 27% of the population (Kemenkes, 2018). In 2017 in East Java, there were 5,980 cases of appendicitis and 177 of them died (Dinkes Jatim, 2017). Appendicitis can cause complications if left unchecked and can lead to perforation of the

appendix if not treated immediately. The most appropriate action to treat appendicitis is an appendectomy (Sjamsuhidajat, 2016). Appendectomy is a surgical procedure or surgical removal of the appendix by opening the abdomen. Almost all patients feel pain after surgery (Zulfikar *et al.*, 2015).

The analgesic used in post appendectomy patients is to use non-steroidal anti-inflammatory drugs (NSAIDs) (Baumann and Strickland, 2014). Inadequate pain management in post-appendectomy patients can have side effects (drug related problems) in patients (Handayani *et al.*, 2019).

Drug Related Problems (DRP) are unwanted events experienced by the patient concerned that are related to drug therapy, this can disturb achievement of therapeutic goals. According to Michele's research (2015) DRP is a case that can cause patient mortality and morbidity.

## Methods

This type of research is descriptive analytic with cross-sectional design. The population of this study were all post-appendectomy patients who received post operative analgesic therapy in 2019-2020 as many as 143 and the sample used was 62 research subjects. The sampling technique uses the technique non-random sampling by taking samples purposive sampling.

Univariate data analysis used a frequency distribution with a percentage size for categorical data and numerical data used the mean or average value. Bivariate data analysis using Chi-Square or Fisher's exact test with a significance level of 5% ( $P < 0.05$ ).

## Results and Discussion

### *Pattern of use of NSAID group analgesics in post-appendectomy patients*

#### *a. Drug type*

**Table 1.** Characteristics of NSAID drug types

No	Drug Type & dose (mg)	Frequency	Percentage
1	Mefenamic Acid 500 mg	4	6,40
2	Ketorolac 30 mg	36	58,06
3	Ketorolac 90 mg	6	9,67
4	Antrain 500 mg	6	9,67
5	Santagasic 500 mg	2	3,22
6	Santagesic 1000 mg	4	6,40
7	Ibuprofen 30 mg	3	4,83
8	Ibuprofen 90 mg	1	1,61
Total		62	100,00

Based on Table 1, it can be obtained that most of the respondents (58.06) used the type of drug Ketorolac 30 mg. The choice of the type of drug Ketorolac 30mg is widely used because it is similar to the drug morphine, but Ketorolac does not cause side effects on the central nervous system. This study is in accordance with Darajatun *et al.*, (2017) that Ketorolac is effective as a



substitute for morphine in post surgical patients.

*b. Drug dose*

**Table 2.** Accuracy of NSAID Dosage

No	Accuracy of Doses	Frequency	Percentage
1	Less doses	6	9,67
2	Therapeutic doses	51	82,25
3	More doses	5	8,06
	Total	62	100,00

Based on Table 2, information can be obtained that in general (82.25%) of respondents received NSAID doses according to the therapeutic doses. This research agrees with the research conducted by Ramadani *et al.*, (2011) that the administration of NSAID therapy according to the therapeutic doses effects to recovery of post operative patients.

*c. Length of therapy*

**Table 3.** Duration of NSAID Therapy

No	Long Therapy	Frequency	Percentage
1	1 day	2	3,22
2	2 days	6	9,67
3	3 days	45	72,58
4	4 days	7	11,29
5	5 days	2	3,22
	Total	62	100,00

Based on Table 3, information was obtained that most of the respondents (72.58%) received NSAID therapy for 3 days.

Administering a therapeutic dose for 3 days is the minimum duration of therapy that can relieve pain in postoperative patients. Using drugs for a long time or too fast can interfere with the mechanism of

action of the drug so that it can cause side effects (Tejovathin et al., 2017).

*Side effects of using NSAIDs in the patients post appendectomy*

**Table 4.** Number of Respondents

Experiencing of NSAIDs's Side Effects

No	Side Effects	Frequency	Percentage
1	Yes	44	71,00
2	No	18	29,00
	Total	62	100,00

Based on Table 4 most (71.00%) respondents experienced side effects of NSAID.

**Table 5.** Description of the side effects of NSAIDs

No	Side Effects	Frequency	Percentage
1	Itchy	2	3,33
2	Headache	9	15,00
3	Nausea	21	35,00
4	Vomiting	3	5,00
5	Diarrhea	0	0,00
6	Constipation	2	3,33
7	Hypotension	6	10,00
8	Hypertension	13	21,66
9	Dyspepsia	4	6,66
	Total	60	100,00

Based on Table 5, almost half (35.00%) of the respondents who received NSAIDs experienced the side effect of nausea. Most patients experience side effects after NSAID therapy because the drug works by inhibiting prostaglandins (Kumar et al., 2018).

**The relationship between NSAID use patterns and drug side effects (drug related problems) in the patients post appendectomy**

**Table 6.** The relationship of NSAID Drug Types with Drug Side Effects (Drug Related Problems)

<i>Chi-Square Test, Fisher's Exact Test (p&lt;0.05)</i>									
Drug Type	Itchy	Head ache	Nausea	Vomiting	Diarrhea	Constipation	Hypotension	Hypertension	Dyspepsia
Mefenamic Acid 500 mg	0,87	0,52	<b>0,01</b>	0,18	0,00	0,87	0,65	0,38	0,76
Ketorolac 30 mg	0,35	0,12	0,57	0,07	0,00	0,18	<b>0,005</b>	0,12	0,21
Ketorolac 90 mg	0,81	<b>0,003</b>	0,67	0,73	0,00	0,81	0,52	0,10	0,65
Antrain 500 mg	0,81	0,62	0,67	0,73	0,00	0,18	0,09	0,22	0,34
Santagesic 500 mg	0,93	0,72	0,43	0,90	0,00	0,06	0,18	0,62	<b>0,03</b>
Santagesic 1000 mg	0,84	0,55	0,44	0,22	0,00	0,84	0,06	0,28	0,70
Ibuprofen 30 mg	0,90	0,61	0,28	0,14	0,00	0,90	0,73	0,10	0,81
Ibuprofen 90 mg	0,96	0,85	0,66	0,95	0,00	0,96	0,90	0,21	0,93

\*Description: Numbers with bold is significant (p<0.05)

**Table 7.** The relationship of NSAID Drug Doses with Drug Side Effects (Drug Related Problems)

<i>Chi-Square Test, Fisher's Exact Test (p&lt;0.05)</i>									
Drug Doses	Itchy	Head ache	Nausea	Vomiting	Diarrhea	Constipation	Hypotension	Hypertension	Dyspepsia
Less doses	0,81	0,62	0,32	0,73	0,00	0,18	<b>0,009</b>	0,22	0,34
Therapeutic doses	0,67	0,19	0,19	0,55	0,00	0,32	0,06	0,58	0,55
More doses	0,84	0,14	0,44	0,77	0,00	0,84	0,59	0,28	0,70

\*Description: Numbers with bold is significant (p<0.05)

**Table 8** The relationship between NSAID therapy duration and drug side effects

<i>Chi-Square Test, Fisher's Exact Test (p&lt;0.05)</i>									
Long Therapy	Itchy	Head ache	Nausea	Vomiting	Diarrhea	Constipation	Hypotension	Hypertension	Dyspepsia
1 day	0,93	0,27	0,56	0,90	0,00	0,93	0,81	0,37	0,87
2 days	0,81	0,37	0,07	0,73	0,00	0,81	0,52	0,10	0,65
3 days	0,52	0,22	0,32	0,18	0,00	0,07	0,13	0,25	0,30
4 days	0,78	0,31	<b>0,03</b>	<b>0,03</b>	0,00	0,78	0,47	0,17	0,61
5 days	0,93	0,72	0,56	0,90	0,00	<b>0,002</b>	0,81	0,62	<b>0,03</b>

\*Description: Numbers with bold is significant (p<0.05)

Based on Table 6, it is informed that the types of drugs associated with side effects is:

- a. Mafenamic Acid 500mg related with side effects of nausea ( $p < 0.05$ ) and has a weak correlation value of 0.343 or  $< 0.5$  in the *Cramer's V test*.
- b. Ketorolac 30 mg is associated with side effects of hypotension ( $p < 0.05$ ) and has a weak correlation value of 0.389 or  $< 0.5$  in the *Cramer's V test*.
- c. Ketorolac 90 mg is associated with side effects of headache ( $p < 0.05$ ) and has a weak correlation value of 0.429 or  $< 0.5$  in the *Cramer's V test*.
- d. Santagesic 500 mg is associated with side effects of dyspepsia ( $p < 0.05$ ) and has a weak correlation value of 0.400 or  $< 0.5$  in the *Cramer's V test*.

Based on Table 7, it is informed that the use of NSAIDs at less doses is associated with side effects of hypotension ( $p < 0.05$ ) and the value of strong relationship is 0.598 or  $> 0.5$  on the *Cramer's V test*.

Based on Table 8, it is informed that the types of drugs associated with side effects are:

- a. The duration of 4 days of therapy is associated with side effects of nausea ( $p < 0.05$ ) and has a weak correlation value of 0.325 or  $< 0.5$  in the *Cramer's V test*.

- b. The duration of 4 days of therapy is associated with side effects of vomiting ( $p < 0.05$ ) and has a weak correlation value of 0.395 or  $< 0.5$  in the *Cramer's V test*.
- c. The duration of 5 days of therapy is associated with side effects of constipation ( $p < 0.05$ ) and has a strong correlation value of 0.701 or  $> 0.5$  in the *Cramer's V test*.
- d. The duration of therapy of 5 days is associated with side effects of dyspepsia ( $p < 0.05$ ) and has a strong correlation value of 0.558 or  $> 0.5$  in the *Cramer's V test*.

Non-opioid analgesics widely used in post-appendectomy patients are non-steroidal anti-inflammatory drugs (NSAIDs) and can cause side effects in their use. Drug side effects are unwanted events that occur in patients related to drug therapy (Luke *et al.*, 2017). Using analgesics non-opioid (NSAIDs) that are widely used in post-appendectomy patients are NSAIDs which work to prevent the formation of prostaglandins in response to impulses thereby reducing the number of pain impulses received by the CNS. NSAIDs are lipophilic and acidic, so they can cause damage topically, while the systemic effects of NSAIDs are caused by mucosal damage that occurs due to decreased prostaglandin production. Decreased production of prostaglandins can also cause damage to the

stomach and duodenum (Baumann & Strickland, 2014).

In this study the types of drugs associated with side effects were the use of Mefenamic Acid 500 mg with side effects of nausea, Ketorolac 30 mg with side effects of hypotension, Ketorolac 90 mg with side effects of headache, Santagesic 500 mg with side effects of dyspepsia and had a weak relationship strength ( $<0.5$ ). The administration of Mefenamic Acid 500 mg, Ketorolac 30 mg, Ketorolac 90 mg and Santagesic 500 mg therapy causes side effects with weak relationship because basically every administration of therapy will always cause unexpected side effects. All drugs in this class is NSAID drugs that work by inhibiting prostaglandins and COX inhibitors.

Mefenamic acid is a class of NSAID drugs that are COX non-selectively that works to inhibit pain stimuli in organs that secrete cyclooxygenase enzymes (Kresnadi & Mulyo, 2016). The dosage for using Mefenamic Acid is 250 mg – 500 mg with a maximum dose of 1500 mg per day (Catamara, 2016). This drug has side effects on the gastrointestinal tract such as nausea, vomiting, dyspepsia, diarrhea to bloody diarrhea, and other symptoms of irritation to the gastric mucosa (Gunawan, 2016). This study agrees with research conducted by Amrullah and Utami (2016), and Idacahyatiet al., (2019) that the use of

Mefenamic Acid at a dose of 250mg-500mg causes the most side effects, namely nausea. Nausea caused by Mefenamic Acid works as COX inhibitors which can inhibit prostaglandin synthesis, if prostaglandin production decreases it will cause clinical symptoms such as nausea, vomiting and even stomach damage (Kang, 2011).

Ketorolac is a carboxylic acid pyrrolizine class of drugs which has a moderate anti-inflammatory effect and is a potent analgesic for pain relief. Ketorolac exerts an anti-inflammatory effect by inhibiting COX-1 and inhibiting granulocyte attachment to damaged blood vessels, stabilizing lysosomal membranes and inhibiting migration leukocytes to the site of inflammation (Kumar et al., 2018). In this study Ketorolac at a dose of 30 mg was associated with hypotension, whereas a dose of 90 mg was associated with headache. Ketorolac often causes disturbances in lowering blood pressure and headache, but the exact mechanism is not known (Kang, 2011). Decreased production of prostaglandins (PGE1 and PGE2) is believed to be one of the mechanisms by which these side effects occur (Landefeld et al., 2016).

Santagesic is one of the anti-inflammatory drugs inflammation non-steroids (NSAIDs) they contain metamizole, this drug works by inhibiting the synthesis of prostaglandins in the

peripheral and central nervous systems (Gunawan, 2016). This study agrees with previous research by Ida cahyati *et al.*, (2019) that the use of NSAIDs such as Santagesic often causes dyspeptic side effects. The mechanism of dyspepsia occurs due to inhibition of prostaglandin synthesis which causes reduced resistance of the gastric mucosa (Amrulloh & Utami, 2016).

In this study, the use of NSAIDs at low doses was associated with side effects of hypotension and had a strong relationship ( $>0.5$ ). NSAIDs that use less doses are Antrain 500 mg (5 respondents) and Santagesic 500 mg (1 respondent) which are given to respondents aged 12-15 years. These side effects arise due to the inappropriate use of NSAIDs in the selection of doses. Selection of the less dose will be cause unexpected drug reactions, especially in children, because the body's response to drugs is not as good as that of adults.

The results of this study stated that the administration of NSAIDs with a duration of therapy of 4 days was associated with side effects of nausea and vomiting. While the duration of therapy of 5 days is associated with side effects of constipation and dyspepsia and has a strong relationship ( $>0.5$ ). NSAIDs are prostaglandin inhibitors and COX inhibitors, so the longer the therapy is given, the stronger it will cause digestive tract disorders. This

research agrees with previous research conducted by Amrulloh & Utami, (2016) and Idacahyatiet al., (2019) that the longer the administration of NSAID therapy increases the incidence of nausea, vomiting, constipation and even dyspepsia.

## Conclusion

1. The pattern of use of non-steroidal anti inflammatory analgesics in post appendectomy patients at Jemursari Surabaya Hospital in 2019-2020 is:
  - a. Most of the NSAIDs used were ketorolac 30 mg (58.1%).
  - b. The most widely used doses of NSAIDs are generally the dose according to therapy (82%).
  - c. The duration of administration of NSAIDs to most of the respondents was 3 days (72.58%).
2. The side effects of using non-steroidal anti inflammatory group analgesics in post appendectomy patients at RSI Jemursari Surabaya in 2019-2020 which caused almost half of them were nausea (33.9%).
3. Statistically, there is a relationship between patterns of NSAID use and side effects based on:
  - a. Types of NSAID drugs: Mafenamic acid 500 mg for nausea, Ketorolac 30 mg for hypotension, Ketorolac 90 mg for headache, and Santagesic

500 mg for dyspepsia and have a weak correlation value ( $<0.5$ ).

- b. Dosage accuracy: The use of NSAIDs is less associated with hypotension and has a strong correlation value ( $>0.5$ )
- c. Length of therapy: 4 days associated with nausea and vomiting and has a weak correlation value ( $>0.5$ ).

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## Case Study : Prognosis of Recurrent Depressive Disorder with Somatic Symptoms

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### ABSTRACT

**Introduction:** Depression is a common disease worldwide, with more than 264 million people affected. Especially if it lasts a long time and is of moderate or severe intensity, depression can be a serious health condition. Depression can cause affected people to suffer greatly and function poorly at work, at school, and in the family. At its worst, depression can lead to suicide. In general, the good prognosis of depressive episodes can be achieved as well as good response to treatment and early interventions, but with the absence of any other complication such as psychotic symptoms and somatic complaints. This paper discusses the prognosis of recurrent depressive disorders with somatic complaints through a case study.

**Case:** Male 23 years old complained of headaches that did not improve with pain medication and often recurred for two weeks, feels tingling and heavy in the back, worsening at night, interfere with the patient's daily activities and sleep in the night. These depressive symptoms have recurred since the patient was 19 years old. The patient experienced repeated stress due to arguments between his parents who were often involved in verbal abuse. The patient's prognosis is analyzed using several aspects according to Maramis prognosis analysis, including age, premorbid personality, type of disorder, course of treatment, hereditary factors, and the presence/absence of precipitating factors.

**Discussion:** According to the course of the disease, the patient experienced recurrent depression since the age of less than 20 years, with somatic symptoms currently accompanying his depressive disorder. The patient experienced repeated recurrences even though he was stated to have improved by the treating doctor, which indicates that the patient's stress management was inadequate. The patient is currently experiencing a skin disorder that worsens his pessimistic feelings and is receiving SSRI antidepressants to improve his depressive symptoms. Based on the analysis of the course of the disease, the prognosis for depressive disorders in patients is poor, or *dubia ad bonam*.

**Conclusions:** Recurrent depressive disorders involving younger ages, complications such as somatic symptoms, suboptimal social support, inadequate coping mechanisms, will worsen the prognosis of depression even after receiving adequate treatment.

### Introduction

Depression is a common disease worldwide, with more than 264 million people affected. Especially if it lasts a long time and is of moderate or severe intensity,

depression can be a serious health condition (J.C. *et al.*, 2013). Depression can cause affected people to suffer greatly and function poorly at work, at school, and in the family (Chang, Hong and Cho, 2012).

At its worst, depression can lead to suicide. Nearly 800,000 people die by suicide every year. Suicide is the second leading cause of death among 15 – 29-year-olds (Bilsen, 2018).

A person suffering from depression may exhibit a range of behaviors, such as being extremely sensitive and irritated, sobbing uncontrollably, not wanting to socialize with others, or displaying a lack of excitement at school (Gomez et al, 2018). Research has shown that a multitude of physical complaints, a depressed mood or anhedonia, or behavioral changes including bullying, violence, or social disengagement are among the symptoms that can occur (James et al. 2018). Because the behavior shown does not have certain characteristics, often these symptoms of depression are not detected by those around teenagers. Parents, family, or friends are often insensitive to the changes shown by depressed teens (Juwita et al. 2015).

Surely the depression is treatable, and the prognosis of depressive episodes is good, based on the recurrence of the episodes, the absence of complications such as psychotic symptoms and somatic complaints, early intervention planning and the treatment responses (Krauz et al, 2019). The prognosis of depressive episodes is evaluated by several factors, including premorbid personality, disease course (acute or chronic), the type of disorders and

complications, disorders occurrence either in young or old age, and heredity. This paper discusses those prognostic factors of recurrent depressive episodes with somatic complaint based on a cases study.

## **Case**

### ***Present disorders***

Male 23 years old complained of headaches that did not improve with pain medication and often recurred for two weeks, feels tingling and heavy in the back, worsening at night, interfere with the patient's daily activities and sleep in the night. The patient had also felt intermittent chest palpitations for the past few days. He also complained itching in the forearm, felt pain and pus appeared and had been taken to a dermatologist and given medication so that the complaint improves. After all, the patient felt hopeless about his general condition. He then came to the psychiatry outpatient clinic and received the antidepressant treatment Sertraline.

### ***History of past disorders***

The patient had suicidal ideation and self-harm in 2017, because felt betrayed by his own friends. He became difficult to trust others and became less confident. During his initial visit in 2017 to 2019, the patient had administered combined therapy such as maprotiline 50 mg, risperidone 2 mg, trihexyphenidyl 2 mg, and lorazepam 2

mg. In 2019 patient had recovered from depression and agreed to tapering the medication off by the psychiatrist at that moment.

In 2020, he was studying in a private university majoring in oceanography. This major was a choice from his parents, due to his indecisive act about his future. The patient felt angry and was not enthusiastic about studying and has been truant for a month. He felt sensitive and very uncomfortable with all the regulations in his major and admitted that he had been on leave for a year before finally drop out from his university in 2022. The patient has a view that his future is gloomy because he couldn't finish college according to his parents' expectations. The patient also felt a dilemma because basically he didn't like the major. The patient in 2021-2022 had been treated again in a psychiatric outpatient clinic with a diagnosis of depression, had received treatment with the same medication as before, and felt better and was in remission in 2022.

### ***Family history***

The patient is the eldest of the two siblings, has a good relationship with his brother, poor relationship with father since childhood but closes to his mother. His last education was high school, when in high school the patient was active in the organization as a student council.

Since teenager, the patient stressed due

to patient's parents' marriage was not well. They have frequent quarrels and verbal abuses, so that it interfered with patient's attention on his work. The patient felt pessimistic and confused about his future. The patient did not want this bad influence to be experienced by his younger sibling, so the patient tried to be a good older sibling by accompanying his younger sibling in the room when his parents were quarreling. Patients feel that self-esteem and confidence are reduced as he couldn't perform well at work.

The patient diverted his stress by getting involved in playing games, wanted to take part in tournaments, but on the one hand, patient often refuse friends' invitations to take part in matches and felt unsure about winning in the game tournament.

### ***Physical and mental examinations***

Currently in 2023, the patient decided to work as a freelancer at an animation company. The patient uses his animation talents to find a job that suits his interests. As time goes by, patients experience stress at work because deadlines pile up. The patient had experienced skin allergies for several months, an illness he had never experienced before. His skin was itchy and festering, so he received treatment from a dermatologist. The patient feels under pressure due to his physical condition.

Physical examination was obtained after

the patient calmed down in the treatment ward. During the interview, the general condition of the patient was *compos mentis*, the appearance was appropriate for age, the patient sat quietly and could answer all questions well and made good eye contact with the examiner. The patient was cooperative during the interview. Spontaneous speech with clear articulation. The patient had a sad mood, depressive affect, but harmonious. The patient did not find a history of hallucinations and delusions. Thinking processes were realistic, the flow of conversation was good, and the content of thought was adequate. The patient did not have any delusion or hallucination. Movement and psychomotor within normal limits and the intellectuality there seem to be no problem. The patient has a good insight of his condition.

At the current psychiatric outpatient clinic, the patient is receiving therapy with sertraline 50 mg and clobazam 10 mg as well as psychotherapy for the patient and the patient's family in the form of education about the disease and the treatment given to the patient.

## Discussion

In this instance, the patient's antidepressant of choice was sertraline when it was discovered that he had signs of depression. The antidepressant medication

sertraline is a member of the SSRI (Selective Serotonin Reuptake Inhibitor) class. The first class of antidepressant medications is sertraline. SSRIs are generally safe since they have little adverse effects (which improve drug adherence), are broad spectrum antidepressants, cause very little withdrawal symptoms, and have high lethal dosages. The working principle of anti-depressant drugs is to inhibit aminergic transport, causing desensitization of serotonin receptors, resulting in desensitization of serotonin receptors. serotonergic pathways normalize. Hopefully the state of the patient's depressive phase can be resolved. And given Clobazam 10 mg as a benzodiazepine augmentation. Clobazam as a benzodiazepine augmentation is convincing evidence that antidepressants are useful in the treatment of depression in rational patients (Kraus et al. 2019).

Administration of a combination of antidepressants and benzodiazepines is recommended, where benzodiazepines do have maximum efficacy quickly, but the effect diminishes after 4 weeks (Gomez et al. 2018), in contrast to antidepressants which gain maximum efficacy after 4-8 weeks. From this the authors see that the combination of these two drugs can relieve the side effects of dependence on benzodiazepines (Maslim, 2013).

Non-pharmacotherapeutic therapy is



given with interpersonal psychotherapy, which focuses on the social context of depression and the patient's relationship with others, and cognitive psychotherapy, namely behavioral therapy focuses on correcting negative thoughts, feelings of guilt, and pessimism of the patient. Patient education in the form of education about the condition and explaining the patient's illness, the therapy used will take a long time and the side effects of treatment that can occur, educate the patient about his condition so that he can accept his condition, and the family that the patient's condition requires support from the family in, especially in terms of motivating patients to achieve their recovery.

The prognosis is dependent on several elements, such as the nature of the issue, how long it has persisted, the patient's strengths and limitations, and the presence of a support network. The projected result of any kind of medical therapy, including mental health, is referred to as a prognosis. It basically forecasts the course of a person's potential recovery and the degree of that recovery (Maslim, 2013).

Different factors can affect the prognosis in everyone. The basis for making prognostic decisions of moderate recurrent depressive disorder with somatic symptoms is influenced by several factors, namely: premorbid personality, disease course (acute or chronic), type of disorder, young

age or oldage, and heredity (Maramis and Maramis, 2009)

#### **a. Premorbid Personality**

The prognosis in depressive individuals with premorbid personality traits is *ad bonam* and personality disorder is *adnight*. Psychiatric comorbidities have been shown to influence outcomes in both treated and untreated patients. In a meta- analysis study it was stated that comorbid personality disorders increase the likelihood of a worse outcome (Patton *et al.*, 2014)).

#### **b. Acute or Chronic**

When a depressive episode occurs acutely, the prognosis is better than if the illness starts slowly (Maramis, 2009).

#### **c. Type of depression**

The prognosis of mild depressive episodes is better than other types because they have a good response to treatment moderate depressive types with somatic symptoms are a complex problem which can lead to the prognosis of *dubia ad malam* (Maramis and Maramis, 2009)

#### **d. Age**

Age is an important factor in the onset of a depressive episode in a person. The prognosis for adult-onset age is better than that of early-onset age. This is because at the early age of onset symptoms usually appear slowly, tend to be chronic, show large deficits in almost all cognitive measurements, so that most of the prognosis is poor and sometimes can be

exacerbated by environmental factors (Wulandari, 2013).

#### ***e. Early/late intervention***

The sooner treatment is given, the better the prognosis (Maramis and Maramis, 2009). Social support is associated with a prognosis that is independent of treatment but has a better prognostic direction by adjusting for depressive symptoms and duration of depression (Buckman et al. 2021). Early intervention in the form of drugs and psychosocial is very important because the longer the person is not treated, the more likely it is to relapse and the resistance to therapy increases strong (Syarif, 2020).

#### ***f. Heredity Factor***

The prognosis becomes more severe if in the family there are one or more people who also suffer from depression (Shadrina, Bondarenko and Slominsky, 2018). Even though his parents often quarreled and were involved in verbal abuse, there was no history of depression from the patient's parents or the two generations above them.

#### ***g. Etiology Factor***

Prognosis of depressed patients will be better if the patient has precipitating factors such as physical illness or psychological stress. This is because a depressive episode whose main identification is stress will respond faster than without a clear cause (Maramis and

Maramis, 2009).

**Table. 1 Prognosis Evaluation Items**

<b>Evaluati on Items</b>	<b>Ad Bonam</b>	<b>Ad Malam</b>
Premorbid personality	Active, Sociable	-
Acute or chronic	-	Chronic, recurring, breaking up treatment
Type of depression	-	moderate depression with somatic symptoms
Age	-	<20 years old
Early/late intervention	-	Late intervention
Etiology factor	-	Yes
Heredity factor	No	-

From the evaluation table above, it can be concluded that the prognosis of the patient in this case is *Dubia Ad Malam*.

## **Conclusion**

The conclusion offers the most important findings from the case without references. This section should highlight current

understanding of the scientific problems in the case report/study.

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## Case Report: Ischaemic Stroke Presented with Hemichorea-Hemiballism

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### ABSTRACT

**Introduction:** Movement disorders can be separated into hypokinetic disorders, which cause paucity or slowness (bradykinesia), and hyperkinetic disorders, which cause excessive, aberrant involuntary motions. Less than 5% of individuals with cerebrovascular diseases presented with involuntary movement. It might be difficult to identify and diagnose hyperkinetic disorders.

**Case:** We describe a 56-year-old man who arrived at the hospital with 5 hours of abrupt, uncontrollable movement in his right upper and lower limbs. A complete neurological evaluation revealed an uncontrolled, nonrhythmic, non-patterned, aimless, and frequently jerky movement of the right upper and lower limbs with a ballistic component that varies in amplitude and frequency. Higher psychic function and cranial nerves were normal. Chest radiography, electrocardiography were normal. Hemorrhage was ruled out by a brain non-contrast CT scan at admission. The patient was diagnosed with hemichorea-hemiballism caused by an ischemic stroke based on clinical evidence of a sudden neurological deficit of aberrant involuntary movement. After receiving medical treatment for five days, the involuntary motions stopped occurring without causing any more neurological abnormalities or weakening.

**Discussion:** Ischemic stroke diagnosis relied on skilled clinical assessment without explicit neuroimaging. While hemiballismus is characterized by violent irregular flinging movements of the limbs brought on by contractions of the proximal muscles, hemichorea consists of continuous random, anarchic, and jerking movements involving both the distal and proximal muscles (though it is occasionally localized more distally).

**Conclusion :** Hyperkinetic movement disorders are a rare presentation of stroke. The pathophysiology of these abnormal movements remains uncertain. Even though they are uncommon, following a stroke, aberrant motions can occur suddenly or develop gradually. Hemichorea-hemiballismus with abrupt onset should be treated as an acute stroke unless proven other causes.

### Introduction

Movement disorders can be separated into hypokinetic disorders, which cause

paucity or slowness (bradykinesia), and hyperkinetic disorders, which cause excessive, aberrant involuntary motions

(Tater & Sanjay, 2021). Less than 5% of individuals with cerebrovascular illnesses have hyperkinetic and hypokinetic movement abnormalities (Caproni & Colosimo, 2017). It might be difficult to identify and diagnose hyperkinetic disorders (Alonso et al., 2015). Less than 4% of all strokes result in post-stroke movement problems (Caproni & Colosimo, 2017; Tater & Sanjay, 2021). The incidence peak occurs in the sixth and seventh decades of life, and there are no appreciable variations between males and females (Caproni & Colosimo, 2017). Between 0.4% to 0.54% of acute ischemic stroke patients had hemichorea-hemiballismus, with a frequency of 1% (Chen & Xu, 2020).

A stroke can cause a variety of movement abnormalities, each with a unique natural history, prognosis, and course of therapy from its idiopathic counterpart (Tater & Sanjay, 2021). One of the most striking diseases in neurology is hemichorea-hemiballismus. In the emergency room, it is not usually observed (Alonso et al., 2015; Carbayo et al., 2020). Because it is clinically uncommon, post-stroke hyperkinetic movement disorder can sometimes develop gradually over time rather than immediately after an acute stroke, which makes diagnosis more challenging and prone to mistake (Chen & Xu, 2020). This is an uncommon case of an

ischemic stroke patient who had an abrupt involuntary movement.

### **Case**

A 56-year-old man presented to the emergency room with sudden involuntary movement in the right upper and lower limbs for 5 hours before he came to hospital. This movement disappeared only during sleep, and it was impairing his basic activities of daily living. There was no headache, language difficulty, visual disturbance, paraesthesia, or sign of infection. He had no family history of such disorders. There was no history of diabetes mellitus, hypertension, epilepsy, trauma and no prior exposure to neuroleptics. Patient is an active smoker.

On initial exam, patient is obese the blood pressure was 119/81 mmHg, the temperature was 36,5°C, the pulse was 98 beats per minute, the respiratory rate was 22 breaths per minute, and the oxygen saturation was 99% while breathing room air. He was alert and cooperative. The patient had no carotid bruits and no significant jugular venous distention. Cardiovascular exam revealed a regular rate and rhythm with no murmurs. A complete neurological evaluation revealed an uncontrolled, nonrhythmic, nonpatterned, aimless, and frequently jerky movement of the right upper and lower limbs with a ballistic component that varies in amplitude



and frequency. Higher psychic function and cranial nerves were normal. Sensations in all limbs were intact. Other systemic evaluations were unremarkable. There was no postural instability, ataxia, myoclonus, abnormalities on visual field evaluation, facial deviation, dysarthria, tremor or rigidity. Muscle power and reflexes were normal, and there was no clonus or positive Babinski sign.

Blood count and chemistries were found to be in normal limit as follows; Hb 15,2 g/dl, Hct 47%, WBC 12.700/ $\mu$ l, Plt 237.000/ $\mu$ l, AST 20,5 U/L, ALT 29,7 U/L, BUN 22,4 mg/dl, Cr 1,24 mg/dl, T-Chol 149 mg/dl, LDL-Chol 115 mg/dl, Glu 113 mg/dl, uric acid 6,3 mg/dL, Na 144 mEq/L, K 3,6 mEq/L, Cl 107 mEq/L. Chest radiography, electrocardiography were normal. Brain non-contrast CT scan on admission excluded hemorrhage (Figure 1.).



Figure 1. Non contrast brain CT scan examination did not shown any abnormality

Based on clinical clinical of sudden neurological deficit of abnormal involuntary movement and radiological findings with limited perfusion CT or MRI

facilities for further evaluation the patients was diagnosed with hemichorea-hemiballism due to ischaemic stroke. Unfortunately, the patient did not get thrombolytic therapy due to excessive time since symptom onset upon arrival. The patient was treated with long term low dose aspirin, piracetam as a neuroprotectant and patient's involuntary movement was treated symptomatically with haloperidol. After 5 days of treatment in hospital, the involuntary movements disappeared without any further weakness or neurological abnormality.

## Discussion

Movement disorders are characterized by a slowness or paucity of movement (bradykinesia and hypokinesia), or at the other hand of the spectrum, excessive movement caused by abnormal involuntary movements, such as tremor, dystonia, chorea, ballism, athetosis, and myoclonus (hyperkinetic movement disorders) (Caproni & Colosimo, 2017). Sudden cease of movements and appearance of new focal neurological signs require clinical reassessment and possibly neuroimaging studies to look for ischaemic or haemorrhagic insults (Carrion & Carrion, 2013). Hyperkinetic movement disorders are a rare presentation of stroke. The pathophysiology of these abnormal movements remains uncertain (Carbayo et

al., 2020). The prevalence of hyperkinetic diseases tends to exceed that of hypokinetic syndromes (Caproni & Colosimo, 2017). A range of hyperkinetic movement disorders called hemichorea-hemiballismus include choreic and/or ballistic motions of variable intensity (Alonso et al., 2015; Wei & Zhang, 2021). Hemichorea describes motions that impact both the proximal and distal limbs and are similar in nature but less in amplitude. Early in the presentation, there is a pronounced hemiballismus, and as the condition resolves, a lesser amplitude hemichorea emerges (Alonso et al., 2015). Movement disorders share common etiologies, prognoses, and treatments, hence there is probably little pathophysiologic variation between them. In actuality, they frequently coexist in the same patient (Alonso et al., 2015; Tater & Sanjay, 2021).

A hyperkinetic movement disease called hemichorea-hemiballismus causes unintentional, large-amplitude limb excursions that primarily affect distal body regions. Choreic motions are not frequently observed in emergency situations. Acquired hemichorea-hemiballismus syndrome can result from a number of disorders polycythemia rubra, chorea gravidarum, oestrogen or levodopa replacement therapy, infectious, autoimmune, structural damage to deep brain structures (cerebrovascular disease, infection, trauma, neoplasia), or neurodegenerative conditions (Chen & Xu,

2020; Guida et al., 2013; Ueta et al., 2021). Focused brain lesions have been linked to hemichorea, hemiballismus, dystonia, tremor, myoclonus, parkinsonism, and asterixis, among other abnormal involuntary movements (AIMs) (Defebvre & Krystkowiak, 2016). These disorders can be classified by their genesis as primary (caused by one of several neurodegenerative diseases) or secondary (caused by a specific cause). Cerebrovascular diseases cause roughly 22% of secondary movement abnormalities, but aberrant movements may be seen as a result of an acute stroke in 1 – 4% of patients (Alonso et al., 2015; Caproni & Colosimo, 2017; Tater & Sanjay, 2021).

Cerebral small artery disease with tiny deep infarcts in the contralateral subthalamic nucleus or nearby structures is the most prevalent subtype of stroke that causes hemichorea-hemiballismus. The most common cause of vascular hemichorea, also known as hemiballismus, is an ischemic or hemorrhagic lesion of the basal ganglia and surrounding white matter in the region of the middle or posterior cerebral artery (Alonso et al., 2015; Caproni & Colosimo, 2017). However, reports of big vessel atherothrombotic stroke with cortical or watershed zone infarcts as well as cardiac cerebral embolism have also been made. A rare vasculopathy called isolated middle cerebral artery (MCA) dissection

can cause an ischemic stroke by mechanisms such as thromboembolism, hypoperfusion, or, very rarely, local branch blockage (Chen & Xu, 2020). Hemichorea, an uncommon manifestation of acute ischemic stroke, involves sudden, hyperkinetic movements and typically involves malfunctioning of the subthalamic nucleus and other basal ganglia structures. Either in the chronic phase of stroke involving the contralateral basal ganglia, particularly the subthalamic and lentiform nuclei, or in the acute phase of predominantly thalamic infarction as a result of deafferentation. Recently, areas causing chorea in strokes have included cortical ischemia lesions (Carbayo et al., 2020). A pertinent prevalence of hypertension, high cholesterol, obesity, diabetes, and smoking was noted in subjects without a history of vascular illness. Lower motor function and cognitive impairment were linked to the patient with two vascular risks (Caproni & Colosimo, 2017). Hemiballismus and hemichorea resulting from acute basal ganglia dysfunction are also frequently caused by poorly controlled diabetes because it raises the risk of cerebrovascular ischaemia and lowers cerebral blood flow (Cincotta & Walker, 2022).

The original theory that hemiballism results from involvement of the subthalamic nucleus has been challenged by the

discovery of various different localizations, including the caudate nucleus, putamen, and thalamus. Most frequently, chorea is caused by vascular damage to the striatum, globus pallidus, or thalamus. Hemichorea is caused by regions in the thalamus and basal ganglia (Hao et al., 2015). A clinical-radiological correlation study revealed that the areas most frequently linked to hemichorea were the subthalamic nucleus, caudate, putamen, and cortical lesions on the side opposite the affected one. This localization is similar to that of hemiballism, which is expected given the close phenomenological relationship between the two disorders. Ballism and chorea brought on by vascular insults are often self-limited and gradually become better over time (Alonso et al., 2015). High-level motor control is mediated by a complex network involving the basal ganglia and subthalamic nucleus, which has reciprocal connections to a number of other brain areas. It is hypothesized that disruption of this functional link results in the recognizable hemichorea-hemiballismus movements (Chen & Xu, 2020). Lenticulo-striatal arteries carry the majority of the blood to the basal ganglia. These penetrating arteries have a modest diameter and branch out at a right angle from the middle cerebral artery's M1 segment. The basal ganglia are particularly susceptible to hypoxia or ischemia since

their distribution zone lacks a collateral blood supply and is functionally characterized as "terminal" (Guida et al., 2013). The regular basal ganglia circuitry transmission pattern would be interrupted by increased dopamine release brought on by ischemia. Acute circuitry dysfunction would cause excessive motor facilitation and a lack of thalamic movement control (Guida et al., 2013; Laganier et al., 2016). Less frequently, the cortex in the superficial area of the middle cerebral artery may also be affected by the stroke lesion (parietal, insular and temporal cortex) (Laganier et al., 2016).

Gamma-aminobutyric acid (GABA) transmission disruption from the striatum to the external globus pallidus (GPE) may be the pathogenesis of hemichorea caused by contralateral lesions of the striatal neurons of the indirect striato-thalamocortical pathways, which can then increase GPE neuronal activity and inhibit the subthalamic nucleus (Cincotta & Walker, 2022; Defebvre & Krystkowiak, 2016). Such inhibition would cause the internal globus pallidus (GPI) neurons to lose control, which could ultimately result in the motor thalamus's ability to inhibit movement. The same dysfunction, with a lack of motor thalamic inhibition, may be brought on by lesions of the subthalamic nucleus. An excitatory neural circuit from a portion of the frontal or parietal cortex (the

somatosensory cortex projecting into the caudate nucleus and putamen) must be disrupted in order to create AIMs in cases of hemichorea-hemiballism brought on by a cortical injury. Patients with cortical strokes have a functional prognosis that is significantly better than patients with subthalamic lesions; in the former group of patients, AIMs are likely brought on by transient hypoperfusion or a functional "disconnection" rather than by the breakdown of basal ganglia circuitry (Defebvre & Krystkowiak, 2016).

There have been numerous theories put forth: Although the indirect pathway only accounts for one-third of the overall population of motor striatal neurons, specific disruption of the indirect pathway is required to cause AIM. The striatal infarct is very large and also involves the pyramidal tract, which causes a motor deficit. Alternatively, the transient nature of these AIMs may be caused by regulation of the accessory striato- nigro-striatal, cortico-striato-nigro-thalamocortical, and cortical pathways, which are thought to regulate the indirect pathway (compensatory mechanisms) (Defebvre & Krystkowiak, 2016). Recent studies has been published detailing instances of ischemic strokes solely affecting the cerebral cortex and not the basal ganglia, leading to aberrant movements like chorea or ballism (Carbayo et al., 2020).

Post-stroke movement disorders can manifest with lesions affecting any segment of the motor circuitry; be it cortical which includes the primary motor, supplementary motor, and premotor cortical areas; or subcortical affecting the basal ganglia, thalamus, internal capsule, diencephalon, and mesencephalon; or cerebellar circuitry. The motor circuitry transmits information from the brain to the thalamus and back through its primary subcortical component, the basal ganglia. Two circuits make up the cerebellar circuitry: the GMT (Guillain-Mollaret triangle), also known as the dentate-rubro-olivary pathway, and the cortico-cerebello-cortical, also known as the dentate-rubro-thalamic pathway. Strokes that impact the subcortical regions are known to be more likely than cortical strokes to cause aberrant motions (Tater & Sanjay, 2021). Movement abnormalities are three times more common after subcortical strokes than after cortical strokes, with the basal ganglia (44%) and thalamus (33%) being most frequently affected. Movement difficulties following a stroke are uncommonly associated with cerebellar abnormalities that affect it alone (Hao et al., 2015; Tater & Sanjay, 2021).

Ischemic stroke diagnosis relied on skilled clinical assessment without explicit neuroimaging (Chen & Xu, 2020). While hemiballismus is characterized by violent irregular flinging movements of the limbs

brought on by contractions of the proximal muscles, hemichorea consists of continuous random, anarchic, and jerking movements involving both the distal and proximal muscles (though it is occasionally localized more distally) (Defebvre & Krystkowiak, 2016). Chorea is a symptom that is distinguished by sudden, uncontrollable movements brought on by an ongoing stream of erratically contracted muscles (Ueta et al., 2021). Ballism is a type of high-amplitude flinging chorea, which is characterized by short, arrhythmic movements that seem to flow from one muscle to the next (Caproni & Colosimo, 2017). While chorea frequently affects the entire body and is widespread, it can also be noticeably asymmetrical or even unilateral in a considerable number of circumstances. While stroke is the most prevalent cause of unilateral involvement and is traditionally associated with a contralateral anatomical lesion, such as one of the putamen or the subthalamic nucleus, systemic disease can also result in unilateral or noticeably asymmetric presentations (Chen & Xu, 2020).

The involvement of several extra-striatal cortical areas and subcortical regions in movement disorders has been demonstrated by a number of functional neuroimaging studies based on positron emission tomography and resting state functional magnetic resonance imaging, emphasizing

a role of network dysfunction and abnormal functional connectivity in these conditions (Caproni & Colosimo, 2017). The mean age of onset was lower (35 years) in cases of other major causes of hemichorea-hemiballism (abscesses, metastatic lesions, AIDS, levodopa medication, Sydenham's chorea, neonatal anoxic brain injury, multiple sclerosis, and central nervous system lupus) than in the stroke subgroup (61 years) (Defebvre & Krystkowiak, 2016). This type of AIM should be treated as a neurological emergency and treated as soon as feasible in a stroke center because any delay in diagnosis may have detrimental effects on the patient's clinical and therapeutic management. Patients with ischemic or hemorrhagic stroke, as well as those with cerebrovascular abnormalities and dural arteriovenous fistulas, can exhibit AIMs (Defebvre & Krystkowiak, 2016). Any anatomo clinical correlations will be easier to make if the vascular lesion is confined and has clearly defined limits. Numerous reports of clinicopathological correlations based on both single instances and short series of patients with lesions in the aforementioned structures have been generated by computed tomography (CT) and magnetic resonance imaging (MRI) examinations (Defebvre & Krystkowiak, 2016).

In 85% of cases, AIM started immediately the day of the stroke, but they

can sometimes deteriorate progressively over many weeks or come back after a latent period of several months. They are noticed on the side opposite the stroke; only when bilateral basal ganglia lesions are seen on brain MRI do bilateral symptoms become apparent. Usually, both the upper and lower limbs are affected, but occasionally, only one body portion is (neck, arm or leg) (Defebvre & Krystkowiak, 2016). Hemichorea typically appears within a few hours of the start of the stroke (as in our patient's case), although delays of up to five days have also been documented. The idea of pathogenesis mediated by restorative neuroplasticity has been brought forward as a result of this delay (Guida et al., 2013; Ueta et al., 2021). Hemichorea appears to happen a few days after stroke, whereas hemiballism is typically seen to happen promptly with the onset of stroke. However, there have been cases where a delay of up to five months was reported (Tater & Sanjay, 2021).

Some treatment options are shared by vascular movement disorders and idiopathic variants of these illnesses (Caproni & Colosimo, 2017; Carbayo et al., 2020). All patients with acute ischemic stroke who meet the requirements for this treatment within 4.5 hours of stroke start are advised to receive thrombolytic therapy (Bembenek et al., 2015). In rats with ischemic stroke, piracetam has been shown to improve brain



penetration and drastically reduce infarct volume (Paliwal et al., 2018). Animal experiments showed that piracetam could help humans who are suffering from an acute stroke (Tortiglione et al., 2002). A meta-analysis of research using rat models of cerebral ischemia and stroke provided more evidence for piracetam's potential value (Wheble et al., 2008).

Hemichorea/hemiballism following a stroke frequently goes away on its own, thus a wait-and-see approach is recommended. The majority of instances resolve on their own, but when movement is significant and harmful enough to cause injury, pharmaceutical therapy is required (Tater & Sanjay, 2021). A symptomatic approach may be helpful for some individuals with hemichorea/ hemiballism whose involuntary movements have a major impact on their quality of life, increase their risk of falling, and reduce their independence in daily tasks (Caproni & Colosimo, 2017; Tater & Sanjay, 2021). The most popular treatment option is typical and atypical neuroleptics, which block dopamine receptors using typical and atypical neuroleptics and catecholamine-depleting drugs (Caproni & Colosimo, 2017; Tater & Sanjay, 2021).

Haloperidol, pimozide, perphenazine, and fluphenazine are examples of common neuroleptic medications that function by inhibiting dopamine receptors (D1 and D2)

(Tater & Sanjay, 2021). Because they inhibit the D3 and D4 dopamine receptors, the atypical neuroleptic medications olanzapine, quetiapine, and sulpiride are less likely to result in tardive dyskinesia and parkinsonism. Clozapine has been used in refractory instances, however it produces agranulocytosis. Tetrabenazine depletes presynaptic dopamine by blocking postsynaptic dopamine receptors and inhibits brain synaptic vesicular monoamine transporter type 2 (VMAT2). Reserpine has a presynaptic impact as well, but it also has negative side effects such as severe depression, suicidal thoughts, hypotension, and parkinsonism. Clonazepam and sodium valproate are two more GABAergic medications that have been tried (Caproni & Colosimo, 2017; Chen & Xu, 2020; Tater & Sanjay, 2021). There have been reports of antiepileptic medications including clonazepam, sodium valproate, and topiramate being successful in tiny uncontrolled numbers of patients (Caproni & Colosimo, 2017). Surgery may be an alternate form of treatment for rare, severe, and persistent instances when pharmaceutical medicines are ineffective or when a patient is unable to tolerate medical therapy (Caproni & Colosimo, 2017; Tater & Sanjay, 2021). Surgery such as stereotactic ventral intermediate thalamotomy and continuous thalamic stimulation can be used to effectively treat

refractory hemichorea and hemiballism (Caproni & Colosimo, 2017; Tater & Sanjay, 2021).

Immediately after a stroke, abnormal involuntary motions start to appear and may eventually go away on their own. This usually happens within a few hours or days (Siniscalchi et al., 2012). In six months, up to 90% of these movement abnormalities with abrupt onset may go away (Caproni & Colosimo, 2017). Minimal functional impairment may linger in post-ischemic hemichorea-hemiballismus. The prognosis for syndromes connected to cortical ischemia localizations is believed to be better (Guida et al., 2013).

## Conclusion

Even though they are uncommon, following a stroke, abnormal involuntary movement can occur suddenly or develop gradually. It can be either hypokinetic or hyperkinetic (most frequently hemichorea-hemiballismus) (most commonly vascular parkinsonism). Strokes can happen anywhere throughout the motor circuit, although the majority are brought on by lesions in the basal ganglia or thalamus. Although many are self-limiting, symptom management may necessitate therapy. The growing accessibility of sophisticated structural and functional neuroimaging methods may be crucial in advancing knowledge of vascular movement

disorders. Hemichorea-hemiballismus with abrupt onset should be treated as an acute stroke unless proven differently.

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## Case Report : Diagnosis and Management of Peripartum Cardiomyopathy

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### ABSTRACT

**Introduction:** Peripartum cardiomyopathy (PPCM) is generally viewed as a diagnosis of exclusion in women presenting with heart failure and systolic dysfunction of unclear identifiable etiology. Etiology of PPCM is not fully understood and multifactorial. The purpose of this case is to review the diagnosis and management of PPCM based on our experience in managing a 31 years old woman with PPCM.

**Case:** A 31 year old woman presented with dyspnea persisting for two days, exacerbated over the last 24 hours. She gave birth to her third child seven months ago. Patient had been experiencing dyspnea for 4 months earlier but sought no medical help. Upon physical examination, hemodynamic was stable, wet rales were noted in two thirds of the lung fields. Echocardiography revealed dilated left ventricle with eccentric hypertrophy and reduced ejection fraction (18%). Treatment was initiated with furosemide IV to resolve dyspnea, then Ramipril, bisoprolol, forxiga and spironolactone was given as heart failure therapy.

**Discussion:** PPCM should be suspected in any peripartum women presenting with symptoms and signs of heart failure. Careful history taking and diagnostic testing especially echocardiography is important to help physicians determine the diagnosis.

**Conclusion:** Treatment with medication adjusted for pregnancy and lactation may prevent adverse outcome, improve clinical symptoms and improve the overall cardiac functions. Long term follow up is important for patients with PPCM, since the optimal duration of medications after recovery is still unknown.

### Introduction

Peripartum cardiomyopathy (PPCM) is a rare, idiopathic, life threatening cardiomyopathy, characterized by acute or slowly progressing left ventricular dysfunction late in pregnancy, during

delivery, or in the first postpartum months in women with no previously known cardiac disease.(Davis et al., 2020; Honigberg & Givertz, 2019; Sliwa et al., 2021) PPCM is generally viewed as diagnosis of exclusion in women presenting

with heart failure and systolic dysfunction of unclear identifiable etiology. (Honigberg & Givertz, 2019; Sliwa et al., 2021)

Global estimates of the incidence of PPCM vary by regions, as high as 1 in 10 deliveries in Nigeria, 1 in 300 deliveries in Haiti, to as low as 1 in 20.000 deliveries in Japan. In the US the reported incidence ranges from one in 1000 to one in 4000. (Davis et al., 2020) A recent study using the US Nationwide Inpatient Sample found that its incidence increased from one in 1181 live births in 2004 to one in 849 live births in 2011. Proposed reasons for this increase are rising rates of advanced maternal age, pre-eclampsia, and multiple gestation, increasing prevalence of cardiovascular risk factors such as hypertension, diabetes, and obesity among women of reproductive age; and increased recognition of PPCM. (Honigberg & Givertz, 2019) Risk factor associated with PPCM are African ancestry, preeclampsia and hypertension, multiparity, multigestational pregnancy, older maternal age >30 years, obesity, prolonged use of tocolytics. (Davis et al., 2020; Ziccardi & Siddique, 2023) Genetics also plays role in the development of PPCM. The most notable example is mutation in the sarcomeric gene titin (TTN). Reports also suggest that a number of PPCM patients have a positive degree family history for

heart failure and cardiomyopathy. (Davis et al., 2020; Ziccardi & Siddique, 2023)

Etiology of PPCM is not fully understood and multifactorial. Suggested mechanism for PPCM are nutritional deficiencies, viral myocarditis, autoimmune process, hemodynamic stress of pregnancy, and the role of 16-kDa prolactin fragment as a vasculotoxic and pro-apoptotic agents. (Davis et al., 2020) The “two hit” model is considered as PPCM pathogenesis, where a vascular insult caused by antivasular or hormonal effects of late pregnancy and the early postpartum period induces cardiomyopathy in women with an underlying predisposition. (Honigberg & Givertz, 2019)

Clinical progression varies, where end-stage heart failure may occur within days and spontaneous recovery may also be seen. (Iorgoveanu et al., 2021) Women often present with non-specific symptoms of heart failure late in pregnancy, during delivery or in the postpartum months. Distinguishing signs and symptoms of PPCM from the spectrum of normal pregnancy or common fatigue post-delivery is challenging. A substantial proportion of women that present postpartum have few physical signs despite substantial cardiac dysfunction. (Davis et al., 2020) Therefore it is important to recognize signs and symptoms of PPCM, provide early diagnosis and treatment to prevent further

deterioration and to preserve heart function in women suspected with PPCM. The purpose of this case is to review the diagnosis and management PPCM based on our experience in managing 31 years old woman with PPCM.

### Case

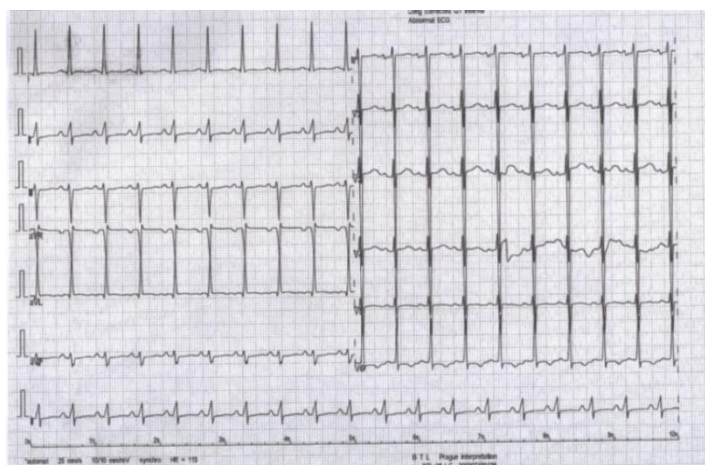
A 31-year-old female patient referred to our Emergency Department with a chief complaint of dyspnea persisting for two days, exacerbated over the last 24 hours. Dyspnea present with sudden onset and worsened with physical activities. Patient

had experienced dyspnea over the past four months during activities and resolved at rest but seek no medical help. She gave birth to her third child seven months ago. She had no pre-existing cardiac disease, exposure to cardio toxic agents nor family history of pregnancy related heart disease. Hypertension was identified as a risk factor for heart disease.

Upon physical examination, the patient appeared dyspneic with stable hemodynamic with blood pressure of 135/80 mmHg and heart rate of 92 beats per minute, respiratory rate of 24 breaths per



**Figure 1.** Chest X-ray showing



**Figure 2.** ECG showing sinus tachycardia with 100 beats per minute, T wave inversion at V6.

minute, temperature of 36.8 degrees celsius, and oxygen saturation of 98% on room air. Physical examination revealed wet rales in two thirds of the lung fields with no wheezing. The abdomen was supple, and there was no edema in the extremities. Echocardiography revealed dilated left ventricle with eccentric hypertrophy and severe left ventricular (LV) dysfunction with 18% Ejection Fraction. The LV end systolic diameter and diastolic diameters were pathologically enlarged of 53 mm (35-52 mm) and 58 mm (<30 mm) respectively. Further investigations included Troponin I HS level of 37.3, and Potassium level of 3.3 mmol/L. Electrocardiogram (ECG) shows tachycardia 100 beats per minute with inverted T in V6. Chest X-ray showed cardiomegaly (**Figure 1.** and **Figure 2.**)

Patient was diagnosed with Acute Decompensated Heart Failure with Dilated Cardiomyopathy and Hypertensive Heart Disease, possibly Pregnancy-Associated Cardiomyopathy. We initiated the treatment with Furosemide drip at 5 mg/hour as well as heart failure medication such as Spironolactone 25mg, Forxiga 10 mg, Concor 1.25 mg, Ramipril 2.5 mg. We also gave KSR tablets to correct the mild hypokalemia. Improvement was seen with relieve of dyspnea. Patient then moved to inpatient ward for further monitoring. We recommended patient to stop breastfeed until completion of the heart failure therapy.

## Discussion

Cardiovascular conditions associated with pregnancy have major morbidity and mortality amongst the general. PPCM has been the leading cause of non-obstetric maternal mortality.(Davis et al., 2020; Sliwa et al., 2021) PPCM is defined as new-onset heart failure occurring during the last month of gestation to the first five months following delivery with no determinable cause. Our patient presents after 7 months of pregnancy, with notable experience of dyspnea since 4 months postpartum. Upon physical examinations we also found wet rales in two thirds of lung field with no leg edema. Women with PPCM typically present with symptoms of congestion, including dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, jugular venous distention, displaced apical impulse, presence of S3, pansystolic murmur consistent with functional mitral regurgitation, pulmonary rales and edema of the lower extremities (Akbar et al., 2019). Less commonly, women present with cardiogenic shock that requires inotropic or mechanical circulatory support. Uncommon presentations are symptomatic or severe arrhythmias, arterial thromboembolism causing neurological deficits. (Davis et al., 2020; Honigberg & Givertz, 2019; Iorgoveanu et al., 2021)



Electrocardiogram (ECG) is widely available, powerful diagnostic tool for patient with potentially cardiac related complaint, particularly in patients suspected with PPCM. At time of diagnosis the ECG is abnormal in almost all women with PPCM (almost 50% had significant electrocardiogram abnormality such as Q-wave abnormality, ST segment depression, T-wave inversion, bundle branch block, second or third degree AV block, frequent ectopy, brady- or tachyarrhythmia. But normal ECG does not rule out PPCM.(Cooney et al., 2022; Davis et al., 2020; Sliwa et al., 2021) Our patient's ECG shows tachycardia 100 beats per minute with inverted T in V6. A prolonged QTc and sinus tachycardia at baseline were independent predictors of poor outcome in PPCM at 6 months and 12 months respectively. In which were associated with increased risk of death or readmission to hospital. (Cooney et al., 2022; Hoevelmann et al., 2019)

Chest X-ray role in diagnosis of PPCM is to identify alternative cause of breathlessness or hypoxia.<sup>1</sup> PPCM can produce normal chest X-ray, but commonly showing cardiomegaly as we see in our patient due to predominantly LV enlargement, features of pulmonary congestion, pleural effusion and interstitial infiltrates.(Hilfiker-Kleiner et al., 2012; Sliwa et al., 2021) Our patient

echocardiography shows left ventricle with eccentric hypertrophy and severe left ventricular (LV) dysfunction with 18% Ejection Fraction. Echocardiography should be performed in any case suspected for PPCM as the main diagnostic modality to confirm the presence of cardiac dysfunction and quantify severity.(Davis et al., 2020; Sliwa et al., 2021) Echocardiography may demonstrate LV and RV dilatation or dysfunction, functional mitral or tricuspid regurgitation, pulmonary hypertension, and left or biatrial enlargement.(Davis et al., 2020) It also can be used to exclude other alternative cause of heart failure such as congenital heart disease, primary valvular disease, inherited or acquired cardiomyopathy.(Sliwa et al., 2021)

Delayed presentation to healthcare services makes most cases difficult to predict if there are any significant reduction in heart function. Delays in diagnosis also associated with increased incidence of preventable complications and worse outcomes as well as lower rates of recovery.(Cooney et al., 2022; Davis et al., 2020) With the known EF of 18%, immediate actions are needed to prevent further deterioration and to preserve the remaining function. We initiated therapy with IV furosemide, dyspnea was relieved and improvement in rales was noted. For maintenance we prescribed diuretics

furosemide IV drip 5mg/hour, overlapping with intermittent furosemide 2x40 mg on the next day. ACE inhibitors, beta blockers and potassium sparing diuretics were given as a standard heart failure treatment. We gave the patient KSR tablets for 3 days to treat the mild hypokalemia.

We also gave SGLT-2 inhibitor as the new pillars in HF therapy.(DeSa & Gong, 2021) SGLT2i previously known as diabetes therapy has several cardioprotective effects through several mechanism including improvement in ventricular loading secondary to reductions in preload (mediated by osmotic diuresis and natriuresis) and afterload (lowering of arterial pressure and stiffness), providing alternative cardiac energy supply in the form of cardiac ketones, direct inhibition of the sodium/hydrogen ( $\text{Na}^+/\text{H}$ ) exchanger in the myocardium (leading to reduction in or reversing of cardiac injury, hypertrophy, fibrosis, remodeling, and systolic dysfunction), reduction in LV mass and improvement in diastolic function through inhibition of cardiac fibrosis, improvement in endothelial dysfunction and stimulation of increased glucagon secretion (improving cardiac performance by either increasing cardiac index and fuel availability or decreasing peripheral vascular resistance).(Lam et al., 2019)

Recent research has introduced bromocriptine as an additional therapy for

PPCM and administering bromocriptine should always be accompanied by anticoagulation treatment at least at prophylactic dose to reduce thromboembolic risk.(Davis et al., 2020; Laksono et al., 2021; Sliwa et al., 2021). Bromocriptine is a dopamine agonist that inhibits the release of prolactin. By reducing prolactin, the formation of proapoptotic 16-kDa from prolactin can be prevented, consequently inhibiting the progression of PPCM.(Hilfiker-Kleiner et al., 2012) In this patient, we did not administer bromocriptine considering that the patient has been 7 months postpartum, suggesting that her prolactin serum has decreased compared to the beginning of the postpartum period.

Patient's child has slowly been weaned from breast milk, started receiving complementary foods (MP-ASI) and has been drinking formula milk, so we encouraged patients to stop breastfeeding for a while in order to safely administer heart failure medications. Preventing lactation may be considered in patients with severe heart failure to avoid high metabolic demand of lactation and breastfeeding and enable safe treatment with heart failure drugs. (Sliwa et al., 2021) However the decision whether to breastfeed in PPCM in women with moderate LV dysfunction must consider the benefit of breastfeeding for the infant and the safety of PPCM medications

during lactation. Beta blockers, Ace inhibitor enalapril and captopril, as well as spironolactone are compatible with breastfeeding. Loop diuretics can be used during lactation but over diuresis may lead to decreased milk production. (Davis et al., 2020)

There are several predictors for PPCM prognosis, LV size > 6 cm and an EF <30% at the time of diagnosis are important predictors for left ventricle recovery. LVEF <30% was associated with lower rates of recovery and increased risk of adverse events.(Cooney et al., 2022; Davis et al., 2020; Sliwa et al., 2021) However PPCM is also associated with higher rate of recovery compared to other forms of HF with reduced LVEF, 50-80% of women with PPCM recover to normal range left ventricular systolic function (LVEF  $\geq$ 50%), with most of this recovery occurring within the first six months. Meanwhile delayed recovery may occur up to 2 years following diagnosis.(Honigberg & Givertz, 2019; Sliwa et al., 2021) About fifty percent of patient experience improvement with standard medical treatment for heart failure. 25% develop chronic HF, while the rest succumb to the disease during its course. Our patient was stable after being treated for 3 days in a regular ward and discharged in a stable condition. At the 1-month follow-up in the outpatient clinic after hospitalization,

the patient had no complaints and could engage in activities with some limitations.

Patients are advised to avoid further pregnancies if their EF remains low during monitoring. If a patient wishes to become pregnant again, they should wait at least 5 years until their EF can return to normal. After recovery, optimal duration of medication treatment is unknown. Medications have to be weaned gradually with close observation to prevent deterioration in LV function.(Kearney et al., 2018; Sliwa et al., 2021) ARNI or ACEi, Beta blockers, and MRA should be given in guideline based dosages and not discontinued during the first year after complete recovery of LV function.(Davis et al., 2020) Stepwise discontinuation of the therapy might be considered. Diuretics should be tapered if patient no longer have symptoms and signs of congestion.(Davis et al., 2020)

## Conclusion

Peripartum cardiomyopathy is a rare, idiopathic, life threatening cardiomyopathy. PPCM should be suspected in any peripartum women presenting with symptoms and signs of heart failure. Careful history taking and supporting examinations are important to help physicians determine the diagnosis. Echocardiography is crucial in PPCM in order to evaluate cardiac functions and rule

out other cause of cardiomyopathy. Early management and prompt treatment with medications adjusted for pregnancy and lactation may prevent adverse outcome, improve clinical symptoms and improve the overall cardiac functions. Long term follow up is important for patients with PPCM, since the optimal duration of medications after recovery is still unknown.

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## Criticism of different approaches to Islamic medicine in Iran

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### ABSTRACT

**Background:** Subject and objectives: Using the capabilities of Islamic civilization is one of the topics that has attracted the attention of contemporary Islamic thinkers. In this context, various opinions have been presented about whether medicine is Islamic or not among Iranian thinkers. In this article, we seek to examine the negative and positive opinions about the nature of Islamic medicine. The purpose of this article is to find a precise definition of Islamic medicine and provide a correct solution in using this treatment model.

**Result:** This research deals with the study of Islamic medicine through descriptive-analytical and documentary methods. In this research, a complete search of electronic banks, related books, and internet sites was conducted and all acceptable articles were reviewed completely and systematically. There are different views on the nature of Islamic medicine, each of which has looked at the issue from its own angle, some agree with it and some oppose it.

**Conclusion:** Islamic medicine has very good capacities, although there are serious criticisms against it. Islamic medicine is a specialized science, and a common opinion should be reached about its limits and conditions, and a system should be designed and drawn for it. The revival of Islamic medicine will contribute to the development of the modern Islamic civilization.

### Introduction

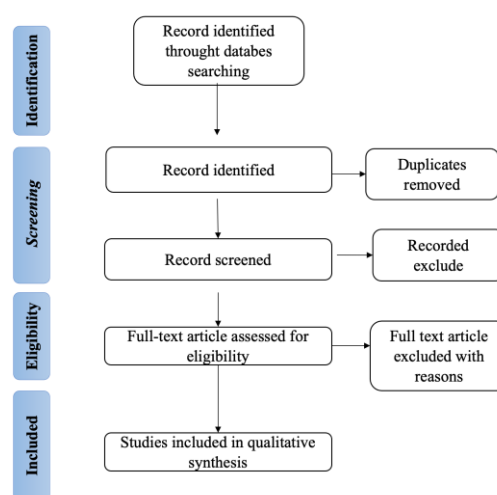
Islam generally encourages Muslims to science and scientific progress. Medical science is no exception to this rule. The relationship between Islam and medicine has always been described as intimate (Ebrahimnejad, 2011). Muslims are also eager to use the latest medical advances. Muslims consider medical advancements as God's creation and physicians as the enabler

of God's handiwork (Inhorn & Serour, 2011). The dominant and respected paradigm in the contemporary Muslim world is still the western biomedical model (Adib, 2004). However, shortcomings of new medicine, failure to treat some diseases and problems caused by chemical drugs caused some people to pay attention to traditional medicine. In Iran, modern medicine is generally used for treatment,

however, people have a special affection for traditional medicine. There are limited clinics for traditional medicine. Some of them have an official license from the Iranian Ministry of Health, while others treat patients without a license. There are many shops in different parts of the cities that sell medicinal plants, which are known as Attari. Many people go to them to buy medicinal plants, and sometimes even to consult them for the treatment of diseases. Iranian thinkers consider Islamic medicine to have a high capacity to treat diseases and encourage Muslims to use Islamic medicine methods, and they introduce it as a contributing capacity in the revival of Islamic civilization. Considering the development of the debate on the possibility of Islamization of medicine in Islamic countries, in this article, we seek to explain the nature of Islamic medicine and explore the positive and negative opinions in this field.

In order to investigate the researches about supporters or opponents of Islamic medicine or traditional medicine, an internet search was conducted with keywords including Islamic medicine, Arabic medicine, and Islamic civilization. A complete and comprehensive search was conducted in online electronic databases in Farsi and English languages. The reviewed databases are: Scopus, ISI, ISC, EBM reviews, PubMed, Google scholar, Iran

medex, SID, Noormax, and google. Also, existing conferences in the field of Islamic medicine and Islamic civilization were searched and used. In this search, finally more than 70 articles were found, the full text of relevant articles including original articles, review articles, and congress articles were prepared and studied and scanned. After reviewing the articles, those that were closer to the subject of the research were selected and used.



## Results

### *The nature of Islamic medicine*

For a better understanding of scientific topics, first of all, it is necessary to have a single understanding of the topic. Many definitions have been used for Islamic medicine and different terms have been proposed by scholars related to this field, although some of these definitions overlap, such as Arabic medicine, Prophetic medicine, Imam's medicine, traditional

medicine. For this purpose, we first state the definitions proposed in this field.

#### *Arabic medicine*

Islamic civilization founded a new medical system by using the medical traditions of Greece, Iran and India, which western thinkers mostly call it Arabic medicine (Mohammadi, 2018). This naming is because a large amount of works of Islamic medicine are written in Arabic, and they have called the doctors who write Arabic as Arabs. Of course, this is not limited to medicine, they have also used this method in the fields of science, philosophy, industry, and art. Since most of the Islamic writers in the fields of medicine, philosophy and other sciences were non-Arab, and even non-Muslim who were engaged in activities in the Islamic culture and civilization. While many famous doctors in this field, such as Ibn Sina, Razi and Majosi, were Iranians, not Arabs, although they mostly wrote in Arabic. Other doctors like Hunayn ibn Ishaq was Christian, and Ibn Maymun was Jew, but they lived within the Islamic culture and civilization. So, it is better to call them Islamic sciences, not Arabic sciences (Ullmann, 2010, p. 8).

Pre-Islamic Arabs were familiar with some experimental cases in the treatment of diseases, and they mainly used methods such as medicinal treatment and prayers. Jafariyan believes that the method of prayer among the ignorant Arabs was rooted in

Jewish teachings, but gradually after the rise of Islam, Muslims replaced the Quranic verses with Jewish prayers (Jafariyan, 2017, p. 224). It should be noted that what is called Arab medicine does not mean pre-Islamic Arab medicine.

#### *Islamic medicine*

In this definition, Islamic medicine refers to a science that comprehensively deals with health and the treatment of diseases and does not need other knowledge like modern medicine from the East and the West. This approach is proposed in the discussion of Islamization of sciences, and on this basis, as Islamic economics or Islamic management is defined as a science, Islamic medicine can also be defined in this format. This giving identity to medicine is based on Islamic worldview and values. Based on this definition, an independent system is introduced for health and treatment which has a different method and attitude from other modern human sciences, and it considers all aspects of human existence, from before birth to death (Ayazi, 2018).

Of course, the criticism that has been made to this view is that, so far, no claimed unified system of this science has been presented, and it is only emphasized on scattered and in some cases coherent religious propositions. The question is, how and by what criteria do you want to consider



these scattered religious propositions as a systematic science?

A group of historians use the term Islamic medicine for the medicine of the golden period of Islamic civilization, namely the era of Razi and Bu Ali. In fact, these people consider medicine at the golden period of Islamic civilization as Islamic medicine (Noormohammadi, 2009).

In short, Today, what has been common among Islamic societies, especially in Iran after Islam, and has been taken from the culture of these regions and has been believed in, is called Islamic medicine, and some books by Ibn Sina and Razi are examples of that (Ayazi, 2018).

#### *Prophetic medicine (al-Tibb al-Nabawi)*

Prophetic medicine is the medical school derived from prophetic traditions. In other words, a collection of teachings related to health and treatment of diseases, which are derived from the Qur'an and the traditions of the Prophet. A question arises that from what date concepts such as prophetic medicine or Islamic medicine were introduced in Islamic literature?

About the Islamic hadiths, it should be said that among the hadiths that were available to the hadith scholars in the third century, there are also some traditions about the benefits of certain foods and their medicinal properties, as well as the rulings related to them in terms of halal and haram. Since hadiths have been classified by topic,

a section has been dedicated to medical traditions, and hadiths were compiled under the title Bab al-Tab (chapter of medicine) or Kitab al-Tab (book of medicine). This method gradually progressed until in the fourth century, works were written under the title of prophetic medicine. As Book of Medicine in Sahih Bukhari, in the third century, and Al- Tibb al-nabawi by Abu Bakr Ibn al-Sunni al-Dinawari (364H/974AD). (Jafariyan, 2017, p. 225)

#### *Traditional medicine*

A group of scholars considers Islamic medicine as equivalent to traditional medicine, and they defend the views of Muslim doctors, which are based on the four temperaments of Greeks and Romans, as Islamic medicine (Noormohammadi, 2009). Some define traditional medicine as a collection of ancient medical traditions mixed with folk beliefs (Mohammadi, 2018).

Traditional medicine is a concept that is often used against modern and new medicine, and it does not necessarily mean what the claimants of Islamic medicine say. In traditional medicine, a specific interpretation of the physiology of the body has been presented, the basis of which is based on temper and four humours (akhlate arba'a) and herbal medicine (Ayazi, 2018).

One of the characteristics of traditional medicine is that it is universal, so that, makes it possible for people to access public

health care (AlRawi, et al., 2017). According to this definition, traditional medicine cannot be used in the same sense as Islamic medicine, because Islamic medicine is derived from the revelation and words of the infallibles and has sanctity, while in traditional medicine, some methods and medical treatments are given that may not have such sanctity. On the other hand, traditional medicine was common before Islam and even among non-Muslim nations, such as China and India.

However, some argues that these categorization of medicine to traditional and modern is only useful in depicting of the historical development of this science, not the meaning and nature of that (Aramesh, 2018).

#### *Muslims medicine*

Pirouzmand has called it as Muslim medicine. In fact, Islamic medicine is any method and experience of medicine founded by Muslims. Therefore, it cannot be attributed to Islam and called Islamic medicine, but it is Muslims medicine, not Islamic medicine (Noormohammadi, 2009).

The criticism that has been made to this view is that, the claimants of Islamic medicine ascribe the methods and propositions of this science to religion, not to Muslim scholars, also, they give special sanctity and godliness to these propositions (Ayazi, 2018).

#### *Tibb al-Aimma (Imam's medicine)*

This term is taken from one of the oldest medical books that has a Shiite approach. In the name of Tibb al-Aimma (Medicine of the Imams), which Abu Attab and Hussain, the sons of Bastam, narrated it. This book is an example of a combined approach of prayer plus medicine (Jafariyan, 2017, p. 222).

#### *Eastern medicine*

Ali Akbar Velayati suggests the title of Eastern medicine as an alternative to traditional medicine. Because he believes that in the past, it was not customary to use the term traditional medicine in contrast to modern medicine. As we do not have traditional mathematics and physics, it is better not to use traditional medicine and use oriental medicine instead. Because this reduced the value of traditional medicine in front of modern medicine. (Velayati, 2018)

#### *Medicine in Islamic civilization*

Some scholars use the term "medicine in Islamic civilization" as a more appropriate term. This definition refers to the medicine that expresses the services of Muslim doctors and their innovations in the medical knowledge of the world. The problem with this term is that with this concept, Islamic medicine will find more library and historical use (Noormohammadi, 2009).

Others believe that the meaning of the term Islamic in Islamic medicine is a

cultural force arising from the Islamic civilization, which brought together many cultural currents in one place and pushed them forward (Mohammadi, 2018).

### ***Does Islam have an independent medicine?***

The first debate that is raised about the Islamic nature of medicine is whether medicine is basically in the realm of religion. Was the purpose of the prophet's mission such things? In response to this question, it has been said that what is certain is that there are verses and traditions related to health and hygiene. As in the Qur'an, it is forbidden to eat wine or corpse, or man is ordered to eat good and clean foods, and avoid overeating.

But the point is whether the teachings of the Qur'an have recommended the health of the body and the prevention of diseases in the direction of human guidance, or that the Qur'an wants to express a specific medical system. From Islamic point of view, because the body is introduced as a tool for upgrading of the soul, the role of a healthy body becomes very important in moral and spiritual perfection of man (Majlisi, 1983, p. 40). This is a minimum perception of Islamic medicine. According to this view, Islamic medicine is not like modern medicine as a systematic science, rather, it is a set of statements that are recommended in the field of health. This is a general

attitude to health, even the detailed instructions and examples that are stated in the religion are to emphasize this general attitude, for example, recommending the use of arak wood to maintain oral and dental hygiene does not mean the only desirable method, but other methods can also be used (Ayazi, 2018, p. 488).

### ***Islamic teachings regarding health***

There is no doubt that Islam has provided many teachings in the field of medical issues. On the other hand, it is not possible to consider all these teachings to be applicable to all times, places and moods. Considering that the title of medicine is a title that has a special meaning. Therefore, Islamic medicine needs to be an independent medicine. So, in order to prevent possible abuses and misrepresentations, it is better to use "Islamic teachings regarding health" instead of Islamic medicine. By doing this, both abuses will be prevented and the glory of this group of teachings will be preserved. (Nemati & Khairi, 2019)

### ***The humanistic theory of medicine***

Another theory is the humanistic theory of medicine. According to this theory, medicine is a human science, not a divine one. This group limits the scope of religion's involvement in ethics, rulings and beliefs. Because they consider the nature of human

sciences to be different from natural sciences (Ibn-Hindu, 1989, p. 33). The Qur'an and the revealed teachings are the only guides for mankind, not the explainers of sciences such as chemistry, medicine or physics. If traditions and matters related to medicine were narrated by the Prophet or imams, it was because of their experiences and transfer of the knowledge that had a history even before Islam.

Among the supporters of this theory are Ibn al-Matran (d. 1191), Ibn Hindu (d.1032). Contemporary Muslim thinkers such as Imam Khomeini (Khomeini, 2010, p. 434) and Ayatollah Misbah (MisbaheYazdi, 2013, p. 210) also deny the medical nature of Islamic teachings. This discussion has been discussed before Islam. Ibn Abi Usaybi'ah has mentioned the opinions of some of those who derived medicine from experience in the book of Uyun al-Anba fi Tabagat al-Atebba (Ibn-Abi-Usaybi'ah, 1980, p. 155).

The problem with this theory is that there is a group of verses and traditions that express the general principles of health and they cannot be denied. For instance, there are many rulings about purity and impurity, and there is no doubt that they are revealed. These rulings also have health aspects such as impurity of blood and urine, and avoiding all forbidden meat animals etc. (Ayazi, 2018, p. 509).

### ***Ancient Greek medicine and Islamic medicine***

Another theory is the transfer of Greek, Indian and Iranian medical knowledge to the Islamic world. Manfred Ullmann is a supporter of this theory. He does not consider the advent of Islam to be effective in changing the state of medicine, and he believes that there is no mention of medicine in the Quran. Of course, he accepts the medical orders attributed to the Prophet, and he refers to collections of hadith in Sahih Muslim and Sahih Bukhari in this regard, but finally, he is concluded that these teachings and recommendations only complete the image of the Jahili period about the medicine. According to Ullmann, the folk medicine of the Arab Jahili era became importance in Islam, and because Muslims thought that these were the teachings of Muhammad, they collected them and mixed them with later hadiths and then interpreted them using the concepts Greek medicine. The final result of the integration of these methods was Prophetic Medicine, and this new Islamic medicine had to stand in opposition to the Hellenistic medicine, which fanatical Muslims were suspicious of it as a science of pagan (Ullmann, 2010, pp. 18-19).

Some Muslim thinkers also believe that many principles and methods of prominent Muslim doctors such as Ibn Sina and Razi were taken from Greek medicine

(MisbaheYazdi, 2013, p. 210). Ibn Khaldun also considers Islamic medicine to be the same as primitive Arab medicine, and he believes that these sciences have nothing to do with Divine Revelation, and they are based upon individual experiences of Civilized Bedouins (Ibn-Khaldun, 1967, p. 150).

### ***Islamic medicine: medicine based on reason, revelation and experience***

According to this definition, the explanation of the human health system is based on reason, revelation and experience. In other words, a set of laws and orders related to human health that originates from revealed sources and human experience, history and information, insights and natural tendencies (Ayazi, 2018, p. 493). According to this definition, if doctors adopt a treatment method that is not in the verses and traditions, it is still referred to as Islamic medicine, because it is accepted by religion.

### ***The divinity of Islamic medicine***

In contrast to the above view, there is the view of the divinity of medical science. Belief in the divinity of medical science is one of the key points of traditional medicine supporters. This view, not only has many fans in the contemporary era, but also in the past, some of well-known scholars raised this view and defended it, like Mohammad

Ghazali Toosi (Badawi, 1977, p. 27), Ibn Kathir (Ibn-Kathir, 2001, p. 503), Fayz Kashani (FaizeKashani, 1994, p. 57).

Tabrizian, one of the supporters of this theory draws five stages for treatment in terms of Islamic medicine; the first stage of it is the belief that treatment is only in the hands of God and that the doctor or medicine is a medium, the second step is to acknowledge the existence of the Prophet of Islam as the best doctor for mankind, the third stage is acceptance and belief in the prescribed medicine, the fourth step is to choose a doctor and finally the fifth step is to start the treatment (Tabrizian, 2006, p. 24).

According to this point of view, it is possible to realize the medical system with an Islamic approach (Falavarjani & Pajuhandeh, 2022). Proponents of this view must show that Islamic medicine has answers and methods for all medical problems, and Islamic medicine does not need new medical sciences, and it has favorable results in practice and scientific experience (Ayazi, 2018, p. 507).

Some consider Islamic medicine to be a medicine in which God's halal and haram are respected and Islamic dos and don'ts must be taken into consideration. In this view, special attention is paid to the human soul and the spiritual dimension of man in his excellence and health. In this definition, a comprehensive view of human being is

taken and human health is considered in different physical and mental dimensions

The criticism that has been made on this approach of Islamic medicine is that by adding ethics to a knowledge, it cannot be considered Islamic. Rather, to define a science, the foundations, and methods must be clear (Ayazi, 2018, p. 492).

### ***Narrative medicine***

In narrative medicine, the science of medicine is a divine science, the basis of which is hadiths, and its source of knowledge is the revelation and knowledge of the Prophet. Sheikh Mufid believes that due to the multitude of medical traditions the existence of narrative and Islamic medicine is possible (Mufid, 1993, p. 144). By extracting the basics of Islamic medicine from verses and traditions, Tabrizian has tried to provide medicine based on Islamic teachings (Tabrizian, 2006, p. 23).

Some opponents of narrative medicine believe that quantity and quality of existing medicine narratives are not to the extent that it can be possible to present a comprehensive medical system with it. In addition, various motivations for falsifying medical hadiths, along with the weak citation of a large number of these hadiths, have distorted their validity (Karbasizadeh, 2012). Sheikh Sadouq also believed in such an approach (Sadouq, 1993, p. 115).

Jafariyan believes that the sources of narrations in narrative medicine are sometimes personal experiences and sometimes beliefs left over from before Islam. Methodologically, narrative medicine relies on hadith-based and non-rational insight, and the attribution of medical traditions to the Prophet has also created a kind of holiness for them. Another important point is that the jurists have never defined what is obligatory and what is forbidden, based on these hadiths. Even they have mentioned the medical traditions in the ethics section (Jafariyan, 2017, p. 242).

### ***Adverse consequences of prayer therapy***

Some belief in spatial Quranic healing effect (Elkadi, 1985), and in general in positive effect of prayers and supplications on the psyche of the patient especially when it is combined with conventional remedies (Nagamia, 2010). Proponents of this view believe that there are many prayers in Islamic traditions for the treatment of diseases. There are also many cases of intercession with the Qur'an, remembrance and charity in hadiths (Tabrizian, 2006, p. 98).

On the other hand, empirical research shows that some Islamic medical activities that take place in the form of prayer and Quranic faith-healing activities have the

potential for adverse consequences (Adib, 2004).

However, some believe that according to Islam's emphasis on rationality, the definition of Islamic medicine is far beyond such common notions (Zarvandi, 2022).

## Conclusion

A few points about the conclusion of the discussion can be mentioned:

1. In this article, different definitions and approaches about Islamic medicine were mentioned along with criticisms.
2. The definition of Islamic medicine can certainly vary depending on the perspective, which may be historical, religious, scientific, geopolitical, etc.
3. Islamic medicine as a science including specialized knowledge, professional abilities, moral, religious and spiritual insights and values, new technologies with an emphasis on the inherent human dignity.
4. If someone says that there is no attention to medicine in Islam, he does not have correct information about Islam.
5. Islamic medicine has very good capacities, although there are serious criticisms against it. Attention should be paid to the existing criticisms and the shortcomings of the Islamic medicine should be removed. For example, Islamic medicine requires acceptable scientific methods and indicators.
6. Modern and ancient medicine both have advantages and disadvantages that cannot be rejected in general or both cannot be fully approved. Criticism in the method of treatment or the effectiveness of drugs is raised in traditional medicine as well as in modern medicine. At least some of the problems or gaps in modern medicine can be corrected by using traditional medicine.
7. There is no doubt that Islamic doctors have benefited from the writings of Greek doctors, but it must be accepted that they have added many information and findings to the previous collections. These findings either had a religious them, which had reached them through hadiths, or were the personal experiences and findings of Muslim doctors.
8. Today, herbal medicine is accepted in most countries. Considering the disadvantages of chemical drugs, it can be a suitable alternative in the treatment of many common diseases. This can be under the full

supervision of the country's pharmaceutical system.

9. Islamic medicine should be considered separate from the prescription of herbal medicine in traditional drugstores. A person who works in traditional medicine pharmacies and has a little familiarity with the properties of medicinal plants is not necessarily an expert in Islamic medicine.
10. Islamic medicine is a specialized science and it should be removed from the general and customary state. It is suggested that instead of rejecting this science in general, proper organization should be done in teaching it and how to practice medicine, and a system should be designed and drawn for it.
11. The elements that should be used in the design of the comprehensive system of Islamic medicine are:
  - a. Philosophical and Islamic attitude in the design of Islamic medicine
  - b. Dynamic structural design for traditional medicine
  - c. Presenting a suitable and up-to-date operational and executive model
  - d. Targeting according to the current situation in dealing with modern medicine.

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## Parasitic Disease and COVID-19 Syndemics in Indonesia: Biomedical Aspects

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ARTICLE INFO	ABSTRACT
<p><b>Keywords:</b> Syndemics, Parasitic disease, Covid-19, biomedical, Tropical disease</p> <p>Submitted: Sept 3<sup>rd</sup> 2023 Reviewed: Sept 12<sup>th</sup> 2023 Accepted: Oct 26<sup>th</sup> 2023</p>	<p><b>Background:</b> Syndemics happened while two or more coinfections have dangerous interaction and lead to a harmful outcome than for either single infection. In Indonesia, during COVID-19 pandemic, it has deal with a doble burden presume to neglected tropical disease (NTD) control. Parasitic disease as a part of NTD must be a concern in Indonesia along pandemc. There are still few articles that review the biomedical aspects of co-infection COVID-19 with parasitic diseases in Indonesia, whereas an understanding of biomedical aspects can encourage knowledge about pathogenesis which will make an earlier diagnosis.</p> <p><b>Results:</b> This review summarize how parasites may serve as protective agents or risk factors in pandemic and, vice versa, how the COVID-19 may disturb the prevention and misdiagnosis of parasitic disease in Indonesia. Co-infection COVID-19 with malaria increass the burden of severe clinical manifestations and poor prognosis due to exaggerated proinflammatory response. Coinfection triggers TNF and IL-6 to activate coagulation cascade leading to micro-thrombosis and coagulopathy. Besides, helminthiasis causes vary configuration of immune-modulation, thereby lowering susceptibility to other infections and tolerating COVID-19 better. They modify Th2 respons to limit pro-inflammatory cytokines, such as IL-6 which is observed in severe cases of COVID-19. T-cell hypoactivation in SARS-CoV-2 and <i>W.bancrofti</i> will cause relatively mild manifestation of COVID-19.</p> <p><b>Conclusions:</b> In parasite infection, the IL-4 may elevate and induce shadow memory CD8+ T-cell (TVM cell) for CD8 response rapidly agains virus. It control human IL-4 or IL-10 that leads to the maturation of Th2 cells and down-regulation of the inflammation respons of IFN-<math>\gamma</math>, IL-17 and TNF-<math>\alpha</math>. These mechanisms allow us to blockade the cytokines storms observed in COVID-19 cases.</p>

### Introduction

Synergistic endemics happened while two or more coinfections have dangerous interaction and lead to a harmful output than for other single infection. For instance, Epstein Barr Virus (EBV) and malaria co-infection may leads to Burkitt's lymphoma

because EBV loads can be increased by malaria which stimulate B-cell proliferation. Besides that, HIV-infected person confluence a lot frequency of increased HIV viral load subsequent severe manifestation of *Plasmodium falciparum* infection. Some of HIV-parasite

coinfections were correlated with worsened immunosuppression and increased HIV viral load. (Hussein, et al. 2020)

Many kinds infectious agents can independently and simultaneously invade host body. Because parasites and microorganisms share mechanisms of pathogenesis, raising up allergic or immune reactions and inflammatory processes, it is reasonable that coinfections can lead to under-diagnosis and misestimates of the true prevalences of single infectious agent. That coinfections can led to a harm course of manifestation. The emergence of new infective agent gives a defiance for both the health care system and researchers effort to estimate its long-term health and epidemiological problems. That agent were followed by happening risk factors, lead to a more harmful symptoms and need new a diagnostic approach. One of currently come snarl was the SARS-CoV-2 disease in this recent pandemic. (Gluchowska, et al. 2021)

COVID-19 which caused by SARS-CoV-2 which has rapidly deployment to elevate than 200 countries worldwide, resulting in 596.873.121 people being infected and 6.459.684 deaths (as of August 30<sup>th</sup>, 2022). Amongst Southeast Asian countries, Indonesia was one of the aloft elevating rates of COVID-19 incidences. Based on data gotten from the Indonesia Ministry of Health on September 1<sup>st</sup>, 2022, Indonesia has 6.354.245 COVID-19

confirmed cases and 157.541 deaths. (Kemenkes, 2022)

Prior to the COVID pandemic, it was a distinct category of contagious disease that got a few considerations, in spite of affecting more than 140 nations and infecting a lot of people, called by Neglected tropical diseases (NTDs). There are 15 parasitic and vector-borne disease which included in the category of NTDs based on the 10<sup>th</sup> Meeting the Strategic and Technical Advisory Group for NTD: Dengue, Chagas, chikungunya, trypanosomiasis, soil transmitted helminthiasis (STHs), onchocerciasis, lymphatic filariasis, schistosomiasis, echinococosis, taeniasis/ neuro-cysticercosis, food-borne trematodiasis, chromoblastomycosis, mycetoma, visceral and cutaneous leishmaniasis. (WHO, 2022)

Most prevalent NTDs were founded in low-income nations, including Asia, Africa, and Latin America. NTDs were as usual found in tropical area because of their climate and humidity, which is appropriate habitats for the expansion of the disease. People whose have little accessibility to pure water and whose get along at district no right management regarding human waste were potential to be infected. As long as the pandemic, work to eradicate NTDs has been upset. In 2021, WHO suggest some recommendation concerning this emergency condition, substantially propose

the use of continuous health promotion, community-based engagement, and participative case find out. Eradication of NTDs has to implicate such potent cooperation between citizens and health stakeholder. Hence, WHO push authorities of local health to reinforce NTDs platforms, health campaigns and surveillance management. (UNICEF, 2020)

COVID-19 interfere the program, for example ITNs and SMC distribution. Malaria diagnostic and management were also interfered because of the hazard faced by health workers who serve during pandemic. Resolution makers will be necessary to produce complicated choices to make sure COVID-19 and continuous malaria endemics were did when lowering the risk to communities and health workers. The community-based action towards malaria diagnosis, prevention, and treatment has important character to present in respons to COVID and were critical to match individuals on-going health care, especially for sick people. Applying approaches of delivery would need to be gotten for some action changes in the contexture of pandemic. (Hussein, et al. 2020)

Indonesia encounter a double burden as a tropical country. For example, the management of NTDs concatenated with the present of COVID-19 will remain a public health problem. In October 2022,

some province in Indonesia suffered the rainy season, that escalate the any vector borne disease survival rate, like helminths and mosquitoes that bring causative agent. Furthermore, based on the Indonesia Ministry of Health, three parasitic NTDs were exist in Indonesia, including lymphatic filariasis, schistosomiasis, and STHs. (Risksedas, 2019) This review will present the readiness of Indonesia in facing NTDs along the pandemic based on biomedical aspect.

## Results

### *Biomedical Aspect of COVID-19 and Helminthiasis*

Because SARS-CoV-2 infectious disease manifested by fever accompanied by cough and difficult to breath, it may be misdiagnosed for other respiratory disease. In other side, identical symptoms are monitored in some parasitoses. Parasitic infection not only cause malnutrition and anemia, destroy tissue, influence immune system, but also support viral infectious and disturb vaccines effectiveness. Nevertheless, immune-modulation of parasite will be take care of us from organ damage by minimizing inflammation responses. (Mohamed et al, 2020)

### *Filariasis*

Filarial worms are a species of nematode that causes an infectious disease

called filariasis. Vectors transmitting these parasite include *Culex sp*, *Anopheles sp*, *Aedes sp* and *Mansonia sp*. The species that cause the most cases in Indonesia are *Brugia malayi*. Currently, WHO data show that 892 million people from 48 countries in 2019 were suffered filariasis, and they need therapy to quit the transmission. This parasite may infect person by infective stage of larva from mosquito bites. Moreover, children more often to be infected and experience silent decay in their lymphatic system. (WHO, 2022)

In tropical regions with many species of vectors like Indonesia, filariasis was still a health issue. In 2020, it were 591 recent filariasis cases, where 10.679 prolonged cases from the prior year. The Papua province possess the first number of chronic cases, followed by East Nusa Tenggara, East Java, West Papua and Aceh. The amount of filariasis cases in 2020 is 10.845 cases. (Figure 1) Beside that, the incidence in Indonesia filariasis is <1% for 10.000 resident in 2019. (Kemenkes, 2020)

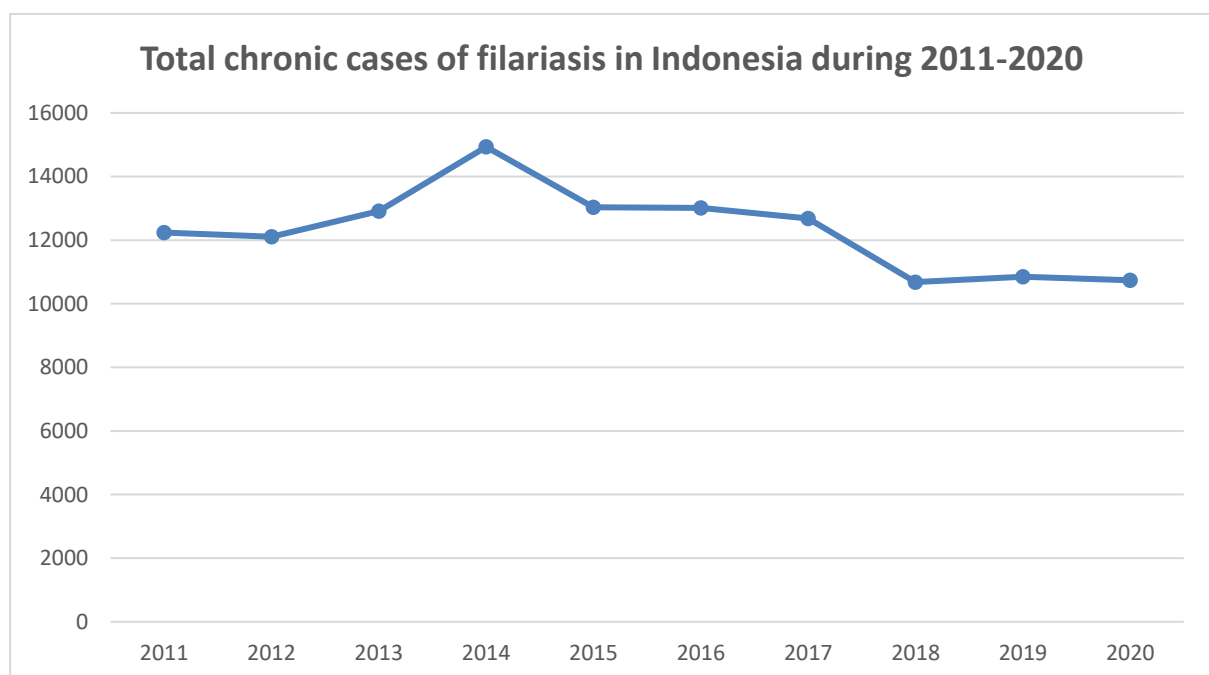


Figure 1. Total Filariasis Chronic Cases during 2011-2020 in Indonesia

An obligatory effort to eradicate lymphatic filariasis was been tried via large-scale therapy within at-risk community annually. A combination of diethylcarbamazine, albendazole and ivermectin regimen have been suggested by WHO to overcome filariasis in endemic

countries. This method may destroy the microfilariae in the blood of infected individual so that the transmission may be stopped. Indonesia have worked to eradicate filariasis since fifty years ago, but it still faces challenge. For example, lack of personnel of health worker, cooperation

related the geographical boundaries in Indonesia, low of health promotion, lack of awareness and inadequate medication. (Kemenkes, 2020)

The WHO recommended to delay community-based program on April 1, 2021, as well as case surveillance action and mass drug therapy promotion in tropical countries with NTD up to farther notice. Accordingly, the preparation of interim MDA which used on filariasis eradication programs were postponed to. Nevertheless, WHO purpose to anatomize effect of delaying delivery of MDA at 2030 by thinking others way to empowering program, later intend to decline the bad effects of the pandemic. Relatively, by postponing this program, the WHO is speed up progress by annual MDA or through elevating access to the drug until 65% of the population at risk. (WHO, 2022)

Elephathiasis is examined etiology of chronic morbidity, infirmity and permanent disability, lead to societal stigma. The early stadium is signed by lymphangitis, chest pain, coughing, and fever. Leucocytosis and massive blood eosinophilia are also present. Likewise, infection of *Wuchereria bancrofti* that cause tropical pulmonary eosinophilia was also signed by eosinophilia, body weight loss, chest pain, fever, and coughing. CT-scan of the thorax shows bronchiectasis, calcification,

mediastinal lymphadeno-pathy, and trapped air. (Mullerpattan et al, 2016)

### *Soil Transmitted Helminths (STHs)*

STH disease still slender in some rustic areas in Indonesia. A study at Sampang District on 2020 showed an elevated incidence (71,3%) of STH disease among toddlers. (Kurniati et al, 2020) Another research in Central Sumba Regions showed that the STH incidence was 91% of disease occurred in children. (Mau F, 2019) In addition, there are still 23 countries where preventive chemotherapy (PC) coverage is under the target of WHO as of 2019. One of them is Indonesia. Beside that, compare to that in 2018, the world PC coverage is decline from 60% to 57%. (WHO, 2021)

COVID-19 pandemics impended the detention of NTD, a condition that was a great health issue for subtropical and tropical regions, where parasite infection, like NTDs and STH are frequent and co-incidences are commonly occur. This situation will lead to a bad outcome, which is called to as syndemic (synergistic endemics). (Gutman, et al. 2020) Commonly, STH infection arrange host IL-10 and IL-4 cytokines, which resulting in downregulation of proinflammatory response of TNF- $\alpha$ , IL-17, IL-6 and IFN- $\gamma$ . This regulation permit us to inhibit the helminth both systemically and locally. Nevertheless, IL-6 storm monitored in

COVID-19 cases was prompt to prevent the inhibition. This condition will go on in person whose infested by parasites and remain in rural area with mass drug administration was not held regularly. (Trasia RF, 2020)

In resolving to the pandemic, Indonesian Ministry of Health has suggested guidance. The objective of this regulations are suggestion for cooperation of crss-sectoral in spreading efforts to stop SARS-CoV-2 transmission, applying emergency situations and daily services for children along the pandemic. Daily health services for children were done by implementing the triage strategies, physical distancing, transmission control and prevention. In districts where the government applies imposing Pemberlakuan Pembatasan Kegiatan Masyarakat (PPKM), the administration of preventive chemotherapy is held by applying health protocol for control of COVID-19 and physical distancing. Those programs are held by school-based community and integrated health service (as known as Pos Pelayanan Terpadu in Indonesian). (Kemenkes, 2021)

Ascariasis is largely disseminated infestation of the ileum caused by *Ascaris lumbricoides*. Some infective stage of its larva are released in the host ileum. From this, they penetrate the abdominal wall and

adjourned via vascular to alveoli, where it molt and grow. Throughout transmission, the human may suffered muscle pain, paleness, chills, dyspnea, breathlessness, fever and coughing. A prevalent symptoms are Loffler's syndrome, a self-limiting pulmonary eosinophilia correlated with lung inflammation. (Lamberton, et al. 2017) The adjourning larvae may stimulate lung-granuloma and tissue-granuloma conformation with eosinophils, neutrophils, and macrophages, lead to peribronchial inflammation and hypersensitivity, with bronchospasm and elevated bronchial mucus production. (Cheepsattayakorn et al, 2016)

Hypereosinophilia was a primary manifestation of ascariasis enabling to differentiate with leucopenia associated COVID-19. The thorax roentgen will show pulmonary infiltrates. In severe ascariasis, a group of helminths may blockade a segment of human ileum. These may suffer colic or abdominal cramping and vomitus. (Lamberton, et al. 2017)

The migration of hookworm in human bloodstream resulting in symptoms which are be confusd with COVID. On this incidence, th infective larva permeate thrugh skin, entering vein, and carried away to lungs and heart. The unique signs made by moving larva are identical to pulmonary ascariasis, involving Loffler's syndrome, expectoration and coughing, aside from



symptoms of bronchitis: wheezing, malaise, fatigue, headaches, general weakness, joint pain, muscle aches, and fever. Then if cough up and swallowed, larva feed on blood in small intestine, lead to iron-deficiency anemia or protein deficiency, which can result in facilitation co-infection, like SARS-CoV. Existence of adult helminth in ileum can result in loss of appetite, blood in feses, nausea, abdominal cramps, colic and severe pain. (Tan X, et al. 2019)

Diagnosis of strongyloidiasis must be done with attention. *Strongyloides stercoralis* invasiveness complies an identical way to *Ancylostoma* larvae infestation. Nevertheless, feature hang on the severity of infestation and manifestation diverge among cases. (Cimino et al, 2020) None the less, symptoms of pneumonitis or bronchitis, fever, coughing, and eosinophilia were particularly found when larva move to alveolus. Infestation of *Strongyloides* may be not apparent clinically. The common gastrointestinal feature such as stomachache, constipation, vomiting and nausea. Immunodeficiency individual is more tend to present with syndrome of hyperinfection because of disseminated strongyloidiasis and where parasitic burden elevated by autoinfection. The spread form is signed by the helminth may be found in atypical predilection, like

the central nervous system, heart, muscle, and liver. (Karanam, et al. 2020)

Doctors should be mindful that tocilizumab and corticosteroid therapy may make easier strongyloides infestation, lead to disseminated infection and hyperinfection. There ara two cases of Strongyloidiasis declared in COVID-19 patients: one in an old man who showed disseminated infection after methylprednisolone and tocilizumab therapy (Lier, et al. 2020), and another a woman from Italia after tocilizumab and dexamethasone treatment. (Marchese, et al. 2020) In endemic area, person infected by COVID-19 must be detected for *Strongyloides* infestation before therapy. A probable alternative for patients at risk was a colaboration of the administrating antiparasite prophylaxis and serological testing as prevention strategy. (Stauffer, et al. 2020)

A study suggest that effect of STH infestation on both Th2 and Th1 immunity is important be aware in designing vacines against SARS-CoV, especially in STH-endemic nations. These inference is promoted by showed something for the developing of Th2 immuno-pathology pathway and triggering Th1 response in controlling replication of virus. Chronic STH infections are founded to enhancing a type 2 respons of immunity such as IL-9, IL-6, and IL-5, resulting in suppressiveness

of the immune respons againsts virus. Besides that, STH and COVID coinfection might lead to heavy outcome, especially in a population with malaria. (Fonte, et al. 2020)

STH infection requires many kinds of immunomodulation, lead to an elevated susceptibility to other infections, alteration in the severity of allergic, inflammatory and autoimmune disease. It was argued that STH infestation may resulting in good tolerance of SARS-CoV infection and inadequate responses to vaccines. (Maizels, 2020) The interleukin storm showed in heavy incidence of COVID is figured by pro-inflammatory cytokine, like IL-6. Nevertheless, it was probable which STH infestation might modifying the outcome of infection by modulating Th2 respons to

prevent the inflammatory substance. It will be especially happened at countries which STH infestations are still exist. (Siles-Lucas, 2021)

### *Schistosomiasis*

*Schistosoma japonicum* is the cause of schistosomiasis in Indonesia, which is also widely distributed in some other Asian countries. Schistosomiasis was endemic in two districts in Indonesia, Poso (Bada and Napu valley) and Sigi (Lindu valley), which are in the Province of Central Sulawesi. Statistic from 2012-2019 (Figure 2) declare a generality in the incidence of schistosomiasis in Central Sulawesi. The latest statistic show that the incidence of schistosomiasis has decline. (Nurwidayati, 2019)

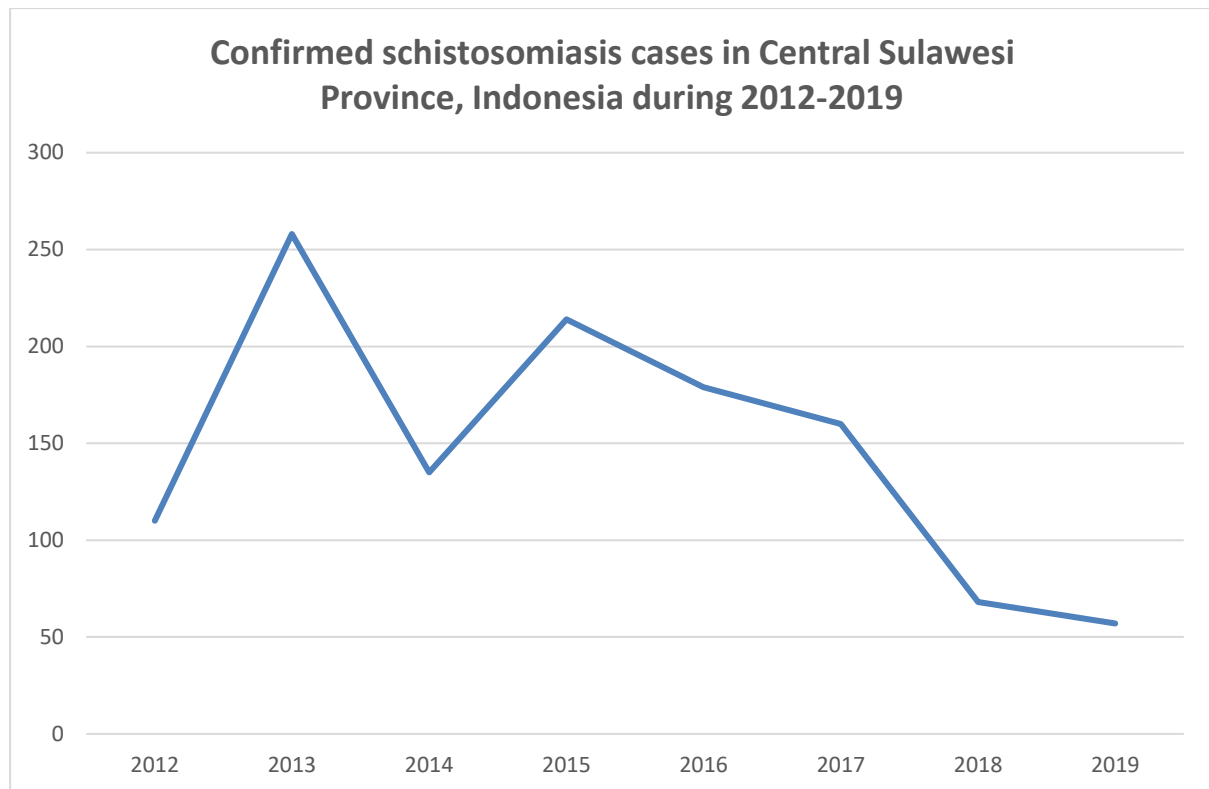


Figure 2. Confirmed Schistosomiasis Cases in Central Sulawesi, Indonesia during 2012-2019

Waters do an important part in spread and transmission of schistosomiasis. Host-to-surroundings transmission specially happen when infested person defecate on fresh water and contaminate it with their stool which contain worms egg. Then the larvae stage of the helminth may penetrate via host skin during contact with those waters. Cercariae is the free-swimming and short-lived larval stages of trematodes, it is shed by slug which play role as mediate host for worms. This larva need 5-6 week to differentiate to adult schistosoma. Then the big helminth may be in person vein for until three years. The mate Schistosoma may generate thousands eggs every day. A little amount of eggs may stimulate immune

reactions and destruction in human organ, while another egg was released from the body through stool. (CDC, 2022)

The manifestation of schistosomiasis is outcome of imune response to helminth's egg. Many people having no complain while he/she is first infested, but may suffered an itchy skin and rash during several days after becoming ill. Moreover, some systemic complain can develop within 1-2 months of transmission, such as cough, muscle aches, chills, and fever. Without appropriate therapy, these features may be prolong and exist during any months in host organs. (Colley, et al. 2016)

Clinical feature of schistosomiasis include diarrhoea, haematochezia, and

stomach ache. In heavy cases, enlargement of the spleen and liver can be happened. Magnification of the hepatic is usually correlated to hypertension of the stomach vein and liquid accumulation in the peritoneal cavity. Another side, schistosomiasis may exist as uro-genital manifestation too, by connected urinary infection feature like ureter and bladder fibrosis, and haematuria in severe cases. Uro-genital schistosomiasis happen in female and uniquely appear as nodules in the vulva, pain during sexual intercourse, vaginal bleeding, and genital injuries. (Nelwan, 2019)

Diagnostic methods for this commonly use worms detection from the urine and faeces with urine microscopy, antibody detection in the serum, antigen and DNA detection, or Kato-Katz technique. This Kato-Katz is the most widely used test because of its diagnostic sensitivity, easy to used, and cheap. Furthermore, immunological and serological based testing might be use in stating exposur to the transmission in nonendemic districts. (Ajibola, 2019)

Person respiratory system may be infected by flukes of schistosomiasis which establish similar feature to COVID-19. Most incidence of schistosomiasis is no complain or just appear as only rash. A study observed eight patients have pulmonary manifestation with reporting

dyspnea, dry cough, nausea, lymphadenopathy, loose faeces with blood, enlarged hepatic and vomiting, without fever or with nocturnal fever sometimes. The chronic infection was figured by blood in the urine or faeces, enlarged liver, anaemia, and abdominal cramp. Nodule is also appear in the lungs range at 2-15 mm in size and has grond opacity halo. The feature of intestinal schistosomiasis are non-specific, include malnutrition and dyspepsia. (Niemann, et al. 2012)

A study show a low amount of COVID incidence in districts when schistosomiasis is syndemic. This might suggested a probable protection effect toward COVID. [36] Similar to other flukes infection, Schistosoma obtain a hunch Th1 respons in earlier stadium of infection. [37] That has been observed which worms may enhanc mechanism of antiviral, resulting in a better viral load control. During helminthiasis, IL-4 may elevate and situation TVM cell so fast CD8 response agains antige encounter. Most possible, helminthiasis has stimulate the host imune reaction to thrive a safe mechansm base on inductive of high responsiveness virtual memory CD8+. These will counter the anti-inflammation impact associated to immunity type two, so that lead to more efficient anti-viral response. Low mortality of COVID in Africa can be correlated to immunomodulation of inflammatory proceses

by helminths released molecule. (Fonte, et al. 2020)

The treatment method of schistosomiasis in Indonesia consists of praziquantel dose regimen (60 mg/kg BW). In 2012, a research in Central Sulawesi showed praziquantel was suggested therapy toward all phases of schistosomiasis. Nevertheless, researches on other drugs were still needed because the time of evaluation was so long. (Nurwidayati, 2019) Kemenkes has announced a promotion to eliminate schistosomiasis. Synergy and collaboration sectoral are significant, like community, government and public health. Before pandemic, treatment of schistosomiasis was difficult. The COVID can exacerbate NTDs that switched both human and financial resources. Great planning must be indicated to take care the collaborative among the prevention of both NTDs and pandemic. (Bapennas, 2019)

### ***Biomedical Aspect of COVID-19 and Malaria***

All species of *Plasmodium* obtain identical symptoms over infection, such as general malaise, body aches, vomiting, nausea, headaches, sweats, chills and fever, with the onset varies to the genus. Most serious feature is respiratory malaria which has similar manifestation with COVID at endemic districts. On some incidence,

bilateral pulmonary infiltrate may be shown on thorax roentgen. A study explained any cases of malaria with pulmonary infiltrates and bilateral fluffy pulmonary infiltrate. Infectious may result in the destruction of erythrocyte and anemia, which aggravate COVID-19 comorbidity and lead to poor prognosis. On the contrary, it has also been forecasted that pandemic can lead to more than 36% malaria mortality over five years opposed with the situation before pandemic. (Sanklecha, et al. 2013)

A significant factor in patient diagnosed malaria was ARDS. Besides that, the similarity of COVID-19 and malaria manifestation may lead to one disease being misdiagnosed, or the probability that comorbidity may be missed. Meanwhile, patient with malaria has anti-GPI antibody which may find SARS-CoV glycoproteins. This can make a good character against COVID or improve disease course. As shown, in districts where malaria is endemic, chloroquine and hydroxychloroquine prophylaxis can have curative or preventive effects against SARS-CoV-2. (Hussein, 2020)

Notified from many studies has observed which are interferon secreted by lymphocyte as immune reaction to transmission by any strain of malaria. This interferon has in vivo and in vitro efficacy against the corona responsible for COVID-19, SARS, and MERS. Glycosyl-

phosphatidyl-inositol (GPI) molecules targeted by IgG antibodies from malaria patients acts particularly via stimulating leucocytes, causing the proinflammatory cytokines release and triggering the expression of Toll-receptor (TLR) 4 and 2. SARS-CoV has vary glycoprotein (GPs). These might be knew by anti-GPI antibody leading to milder disease feature or protecting against viral infection. (Gomes, et al. 2016)

Because of the identically feature between COVID-19 and malaria, particularly headache, fatigue, shortness of breath and fever of acut onset, a COVID-19 patients might be mis-diagnosed as malaria on the contrary. Furthermore, complications such as multiorgan failure, septic shock, and ARDS could also ocur at both COVID and malaria. Primary step to find a COVID patients is the syntomatic surveillance, which are myalgia, headache, sore throat, dry cough, fever, dyspnea in at-risk population such as healthcare workers and person with a history of close contact with confirmed cases. Nowadays, individual suffered fever might be test for COVID-19 and then back house because of a nonreactive results, rejecting the probability of malaria. In other hand, febrile person might get test for malaria when she/he actualy has SARS-CoV-2 infection. A third probable condition is that an individual might has malaria and COVID-19

coinfection, but the treatment and diagnosis can result in missing the other. (Gostic, et al. 2020)

In malaria, when schizonts rupture and release merozoits in blodstream, this lead to chills and another features of malaria. Therefore, manifestation of malaria is because of the relase proinflammatory cytokine, such as IL-12, IL-6, IFN- $\gamma$ , and TNF. Several studies in endemic regions has conclude that it was important to has a balanc between host anti-inflammatory Th2 response (IL-10 and IL-4) and pro-inflammatory Th1 respons (IL-12, IL-6, IFN- $\gamma$ , and TNF). The massive Th1 response is often cause severe symptoms of malaria. Similar appears to COVID-19 cases, suggesting that comorbidity also result in massive immunological response which lead to heavy features and bad prognosis. (Jin, et al. 2020)

ARDS visible in nearly 25% of adults and 40% of children with malaria falciparum. It has some causes, such as metabolic acidosis, anaemia, coinfection with pathogen-related pneumonia and sequestraton of infested eritrosit (RBC) in the pulmonary capillary. The manifestation ranges from mild to severe upper respiratory symptoms. ARDS both in malaria and COVID-19 is because of inflammatory elevated permeability of capillary and endothelial damage. Due to this condition, Plasmodium – SARS-CoV-2

coinfections might result in fast decadence and bad outcome. Consequently, coinfection can lead to heavy COVID-19 and physicians must keep this in mind. (Jin, et al. 2020)

Some virus infection, such as SARS-CoV, release a pro-coagulan through induced any factor expression, bring about endotelial disfunction or activating of TLR. Increased D-dimer, prolongation of prothrombin time, and fibrin degradation products levels are correlated with a bad outcome. Relatively, malaria was also correlated with procoagulant state. The IL-6 and TNF activate coagulate cascades, which is similarly to the disease course. Disease of malaria is regularly correlated with complication of micro-thrombotic. Nevertheless, large vessels thrombosis such as pulmonary embolism and cerebral venous thrombosis have been observed. (Lippi, et al. 2020)

The release of molecule from breakdown endothelial cell or damage of activate platelet in malaria producing a

coagulan condition, same as mechanisms in COVID. Thus, Plasmodium-SARS-CoV co-infection can lead to more severe degree of coagulopathy. Hence, it requires increasing sensitisation on potent of malaria-COVID comorbidity. In view of that malaria testing is more available, which is better if health worker do test of malaria while they suffered on COVID. This condition is especially relevant for person in endemic country and travellers. It provides an opportunity to respond to several infectious diseases beforehand and decline avoidable mortality and complications. (Hussein et al, 2020)

### ***Effect of COVID-19 on Parasitic Disease Diagnostic and Prevention Program***

The WHO released a general suggestion on April 2021 to disrupt all actions for control of NTDs program, in spite of high prevalence of human disease. (Figure 3)

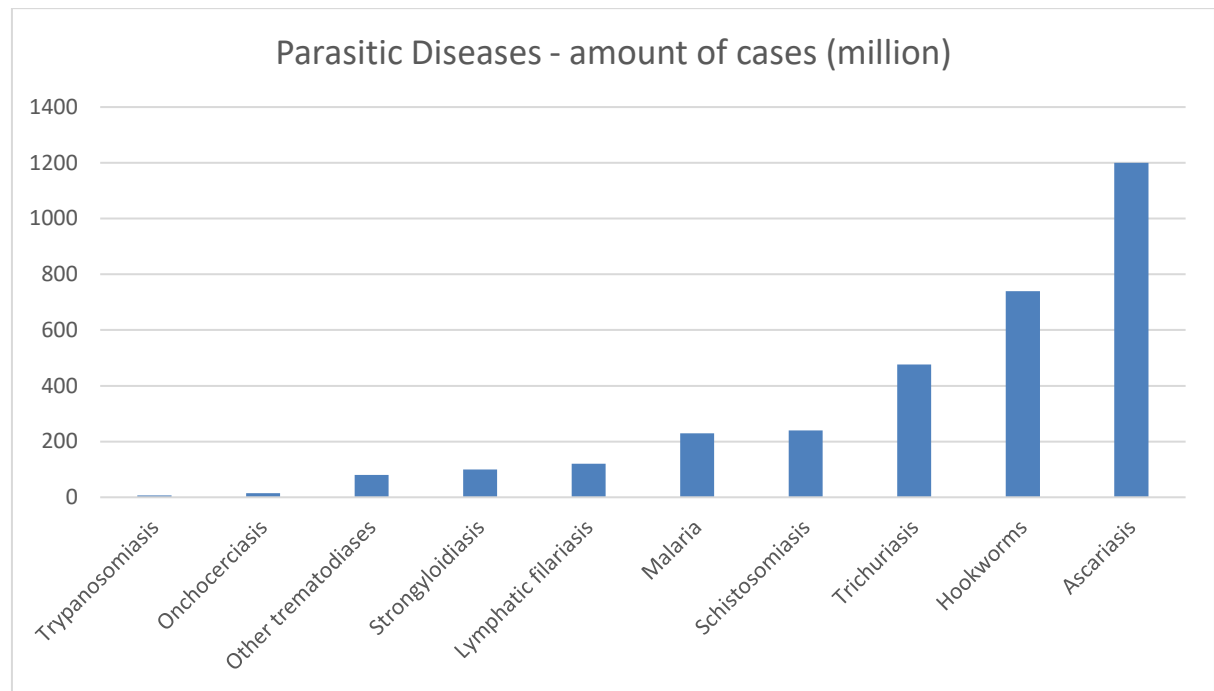


Figure 3. Estimation of Existing Parasitic Disease Worldwide (source: WHO/CDC)

These have reversely impact roadmap of any NTD, include that concerning parasite infestation, have result in disappear of some achievem. Furthermore, parasite infection has been widely excluded from the tasks of health services at the regional and national levels. Nevertheless, as malaria prevention program is threatened by COVID-19 pandemic, there was a constan purpose to evade malaria outbreak. A study conclude that pandemi might resulting in extra 205 milion malaria incidence and 378.900 deads at Africa. (Sherrad, et al. 2020)

STH diseases (STDs) and schistosomiasis are two other NTDs which control and prevention programs have impact by local and global respons effort to lower dissemination of COVID. Even

though an interference in the prophylaxis therapy of STD would just temporarily effect improvement toward WHO 2030 target, program must be started as early as possible to lessen impact on mortality. When this interference, aditional time would be need to deal with the increasing infestation level. (Malizia, et al. 2021)

Parasitological diagnostics has influenced by the COVID-19 pandemic. Because a lot of laboratory are need perform SARS-CoV test, it have to postpone or minimize its particular parasitology testing duty, that have important effect on amount of confirmed case of human parasitic. The lessened in the amount of order and diagnostic test of parasitologic was noticable in some laboratory. (Gluchowska, et al. 2021)



Plasmodium infection is a considerably endemic disease in east of Indonesia. Outbreak of COVID may lead to disruption in health-care system on malaria, indecorous treat and non-treated malaria incidence, consequence in elevate in morbidity and mortality. Malaria prevention measure which might lower the load on health-system also in background of COVID such as presumptif malaria therapy and MDA. (Hussein, et al. 2020)

There are modalities to convey these intercession. The seasonal malaria chemopreventive and insecticide-treated nets were presented through population-large promotion while other intercession were accompanied through patient centre mode. Execution of these malaria program was influenced by the lockdown and travel restrictions during the pandemic. The implementation of these programs have to examine the weightiness of both maintaining the safety of health care workers and decreasing malaria-related deaths. Action should be managed in the way which keep away meeting of resident without dwelling by precaution. Action which elevate risk of COVID or were not easy to applicated with no break protectif measure should be interrupted. (WHO, 2020)

To confirm repercussion of malaria service, national malaria program should pick up COVID-19-related recommendations which enhance malaria control service by

confirming safety to service teams, patients, and clients, while doing case management action and malaria prevention to the most extent probable. For example, ensuring the best testing and management of malaria patients. Malaria therapy and prevention was more significant along COVID pandemic than under normal conditions. So that, all procedur must done when keeping safety to patients and health worker in the situation of SARS-CoV-2 transmission. (WHO, 2021)

The latter-day strategy of Indonesia government to decrease contagion of COVID consist of implementation of health protocol, such as wash hand, stay at home, minimize outdoor activities, wear masks, physical distancing, suspend travel activity, and stay updated in relation to COVID-19. Furthermore, large-scale physical distancing has been implemented widely in districts with high prevalence, based on Government Regulation. The total amount of tests done until September 3<sup>rd</sup>, 2022 is 6.280.183 tests. The fiasco to decline the transmission of SARS-CoV-2 lead to highest active case, which is 176.367 case on September 3<sup>rd</sup>, 2022. The current update on September 3<sup>rd</sup>, 2022 show number of BOR is at their worst also, with most severe rating report in Jakarta is 79%. The real case of COVID-19 in Indonesia seems like to be underestimated because of lack testing. The large gap between the amount of suspected

cases and person tested indicates that capacity of testing in Indonesia still limited. (WHO, 2022)

As aforesaid, there are four parasitic NTDs in Indonesia which need the beginning of a specific eradication program. Because of pandemi, Indonesian require to perform smart effort to efficient manage of NTDs. Nevertheless, there is no guideline for strategic to overcome NTD in Indonesian along pandemic. There is also no number of NTDs cases reported during pandemic. Next health police stakeholders must use these in care, because the accessibility of data as baseline was significant in creating a new strategy. A research in Jakarta show an elevation in deaths due to COVID with up to 59% compared with the previous year. Even though, the fatality rate is less than developed countries because of Indonesia demographics, which is dominated by adult age group. On the whole, there was no hesitation that surveillance for new cases NTDs detection would be interfered during the pandemic, like surveys for STH and filariasis. (Elyazar, et al. 2022)

To reduce death cases due to late response, Indonesia must strengthen its means at control of NTD. Team work was key for success control of NTD during the pandemic. The citizens and government must cooperate on case tracing, and may use the integrated data centres. If online

networking was limited in endemic districts, another effort may be the use of short message services. (Martindale, et al. 2019)

## **Conclusion**

The in spite of being a fatal disease, COVID-19 remains be misdiagnosed as other infection because of its novelty, especially affecting respiratory system, such as schistosomiasis, malaria, strongyloidiasis, and filariasis. Along COVID pandemi, Indonesian yet deal with any defiance for the control of NTDs, particularly parasitic disease, such limit observation on follow-up of MDA in filariasis, miscoordination in eradication STDs or delayed evaluative of medication use for schistosomiasis. (Fauziah et al, 2021) This article prompt to the Indonesia goverment to reinforce its work in NTD controls via other design, like collaboration on stakeholder in detecting recent cases. Tracing, testing or treatment to decline the COVID-19 transmission should be remedy, so that gap of COVID-19 suspect and confirm case may be declined. If it happen, then NTD control and case detection of parasitic infection may be done efficiently.

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## Health Issues of Nigerian Muslim Pilgrims in The Immediate Post-Covid-19 Era Hajj Year 2022– Part II (Non-Communicable Diseases)

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### ABSTRACT

**Background:** Hajj is an important rite in the life of devout Muslims, requiring the devolvement of physical and material resources in its execution. Limitations posed by COVID-19 on the performance of Hajj make the year 2022 hajj to be an atypical one compared to other years' international hajj. Nigerian pilgrims are peculiar as a low-and middle-income country (LAMIC) with the highest number of Muslim pilgrims from Africa. The objective of this article is to review the health implications of Hajj and peculiarities of the post- COVID 19 era, regarding non-communicable diseases in Nigerian pilgrims based on literature, the interaction of authors with pilgrims, and the experiences of an author as a pilgrim.

**Results:** Commonly encountered non-communicable respiratory, cardiovascular, nutritional, gastrointestinal, endocrine, reproductive, neurological, and musculoskeletal health issues in Nigerian pilgrims were explored. Preventive health strategies by individual pilgrims, the national medical team of National Hajj Commission of Nigeria (NAHCON), the Ministry of Health (MOH) of the Kingdom of Saudi Arabia (KSA) and other stakeholders involved directly or indirectly in conducting Hajj rites were appraised. This includes but not limited to illness screening, chronic illness management, life style modification, medication adherence, and accident prevention.

**Conclusions:** It was concluded that the efforts of the Kingdom of Saudi Arabia, as well as Nigeria authorities on Hajj health services, are commendable, though there are still a lot of areas that need to be improved upon. Significant importance should be given to pre-hajj and post-hajj screening of pilgrims for communicable health issues in pilgrims to enable optimal execution of hajj task and maintenance of pilgrims' health beyond hajj period.

### Introduction

This piece should be regarded as part of a two-series publication, the

complementary part was focused on communicable health issues while this part objective is to elaborate the non-

communicable diseases among Nigerian pilgrims and the necessary mitigating efforts.

Regarding Nigeria, other low and middle-income countries (LAMICs) as well as high income countries, pilgrims have so many prevailing health issues even in the pre-COVID-19 era aside from communicable diseases. These include increased risk of stampedes and injuries, fire outbreak, disease transmission, worsening of non-communicable diseases, complications of exposure to unaccustomed climate such as heat stroke, sunburns, harmattan, dehydration, psychological illness, health hazards from food and environmental hygiene (Memish et al., 2012). Challenges of crowd management, safety, security, and emergency preparedness, are posed. Provisions need to be made for these health factors and it will involve non-health specialists including venue engineers, event planners, security personnel etcetera. to enable the successful performance of hajj rites as well as ensure optimal health of every member of the global community within and beyond the geographical area of the pilgrimage rites. The optimal health still needs to be maintained or improved upon after completion of hajj rites and remain in the cyclical path till the onset of the next hajj season which is usually about 11 days less

than the same date of the preceding year in the Gregorian calendar.

Non-Muslim imperial European powers were actively involved in hajj management before the emergence of the Saudi petrodollar and modern hajj management which is now being done entirely by the Muslims. Saudi Arabia's safety, security, environmental and health policies have evolved after several decades of conducting hajj rites for the Muslim populace (Memish et al., 2012), improving on this will serve as a useful mode of risk management and international collaboration in mass gatherings.

## ***General Health***

### ***Screening***

Screening for non-communicable diseases such as hypertension, diabetes, obesity, hyperlipidemia, bronchial asthma, neoplasm, osteoarthritis, and mental, neurological as well as other systemic illnesses must be done through detailed but focused history taking, purposeful methodical physical examinations, and relevant cost-effective simple laboratory investigations. Pilgrims should be encouraged to disclose their health status by revealing any chronic medical or surgical conditions they have had in the past or which they are currently on treatment for. This will enable appropriate health education and care for the respective



pilgrims. Long-term medications are usually required for most chronic illnesses, such pilgrims should be advised to visit their specialist at least a month before departure date, to allow ample time for pre-travel medical fitness evaluation, medication review, and refill stock of medications that can last up to two months. Copies of appropriate prescription forms should be available and presented when necessary to avert altercation with drug law enforcement agencies during departure as well as at the entry port.

Individuals with pre-existing illnesses of the respiratory system like bronchial asthma and chronic obstructive airway diseases (COPD) should take necessary precautions to avert symptom recurrence. Stress from intense activities, respiratory infective pathogens (Saifuddin et al., 2020) cold air from abuse of air conditioners (D'Amato et al., 2018) can lead to symptoms exacerbation. Most Nigerian families can not afford and maintain air conditioner. Fans are used more in Nigerian homes for adequate ventilation. The affluent Saudi community employs the use of air-conditioners in hotel rooms and Masjids. Cold air in winter/ harmattan season is known to be associated with airway hyper-responsiveness, air pollution, bio-contaminants proliferation, and other negative effects, especially on the lungs. Cold water/ beverages consumptions can

also be irritating to upper airway. There is risk of exacerbation of asthma and COPD when the air temperature drops too quickly by 2 to 5 degree Celsius without gradual adaptation in individuals that are not accustomed to such (D'Amato et al., 2018).

Inhalers and other necessary medications should be carried along with their recent prescriptions during the journey to enable early intervention during symptom exacerbation before hospital presentation. Lukewarm water or warm beverages are preferred to cold water as a thirst quencher in people at risk of airway disease (Saketkhoo et al., 1978).

### ***Cardiometabolic system***

Evaluation of cardiovascular risk factors is essential component of pre-hajj medical screening. People with a history of stroke, systemic hypertension, diabetes mellitus, and hyperlipidemia are placed on appropriate treatment and given health education to keep their illness in a stable and controlled state. The incidence of cerebrovascular accidents has been reported to be lower in Iranian pilgrims during hajj compared to the natives in home country. This was attributed to the proper screening for cardiovascular risk factors and intervention efforts that mitigate illness progression and complications (Reza Azarpazhooh et al., 2013).

Authorities of the KSA Ministry of Health (MOH) should be commended for placing Automated Electrical Defibrillators (AED) (figure 1) at strategic places in the premises of the sacred mosques for use in resuscitation during emergencies like cardiac arrest and syncope attacks. The security personnel in the premises of the Grand Holy Mosque (as well as other mosques) should be trained on the basic life support skills and the usefulness of AED in such emergencies before the arrival of an ambulance for conveyance to the hospital.



**Figure 1.** Automated Electrical Defibrillators (AED) Stationed at Strategic Places in the Precincts of Grand Holy Mosque

As part of hajj preparations, intending pilgrims should engage in regular exercise (Shaikh-omar et al., 2013) to enable them to be fit to perform the rigorous and physically

demanding tasks of hajj without getting exhausted easily. Junk food is considered as high in fat, salt and sugar (HFSS) (Asif, 2016) with little dietary fiber, protein, vitamins, minerals, or other important nutrients. They are considered unhealthy for people with cardiovascular risk factors such as hypertension, diabetes, hyperlipidemia, and obese individuals. These HFSS foods are usually distributed as free packaged meals for pilgrims by some Saudi Philanthropic agencies. Pilgrims from Nigeria and other LAMICs benefit from these meal packs to supplement their dietary needs without any regard or consideration for the effect on their cardiovascular health. Pilgrims with cardiovascular risk factors should be educated to avert getting these meals but can get the fresh fruit and vegetable packs that are also distributed by the philanthropists for their nutritional supplementation.

Pilgrims need to take into cognizance the necessary dietary modifications occasioned by their health. Hypertensive individuals are to abide by the necessary salt restriction in their diet, refined sugars should be avoided by diabetic individuals as much as possible. Catering institutions that got contracts for mass meal supply to pilgrims should be notified and instructed by the company for the Mutawwifs of Non-Arab African countries (MU'ASSASA) of the

need to prepare special dietary needs/dishes for these categories of people.

### ***Nutrition and Gastrointestinal System***

Peptic ulcer disease (PUD) is reported as one of the commonest illnesses among Nigerian pilgrims (Abubakar, 2022). Eating habits may be a focus of concern here as some food items may precipitate symptoms recurrence (eg caffeinated beverages) and should be taken with caution. The stress of the journey may also induce or precipitate PUD in the predisposed.

Zamzam is a readily available water source in the precinct of the Holy Mosque, prescribed in the religion to be consumed immediately after completion of sa'ay. It is also used for nutritional and medicinal value based on prophetic recommendations for quenching thirst, and hunger and a healing for several ailments. Modern plumbing and the hydrological system have made the claims of possible contamination or pollution of Holy Zamzam water from Hagar's well a thing of the past (Memish et al., 2012). A recent subject of controversy is the claim of unsafe high concentrations of arsenic and nitrates in Zamzam water. The possible carcinogenicity of arsenic as a heavy metal calls for caution as raised by British Broadcasting Corporation (BBC) in hot health and sociopolitical debate in May 2011 (Lyrin, 2011)



**Figure 2.** Bottled Zamzam Water by the Custodian of the Two Holy Mosques

Arsenic is a heavy metal, beneficial though to a large extent but has also been described to be carcinogenic (WHO, 2018). Organ toxicity (eg Nephrotoxicity, hepatotoxicity) which are a typical occurrence in acute and chronic heavy metal poisoning like lead, and mercury is not demonstrable during five-week comparative study on experimental animals that were fed with Zamzam water and the control group. (HA et al., 2021) Arsenic has also been used in some cancer chemotherapy. it's not unusual for a chemotherapeutic agent to be found to be carcinogenic (Harris Curtis, 1976). Such paradoxical and bidirectional effects have been described in several classes of drugs. (Smith et al., 2012) A multi-center study of about 30 samples of Zamzam water was obtained from the precincts of the Holy Mosque in Makkah as well as from pilgrims

from several countries, and were analyzed for different micronutrients, minerals, heavy metals, and other constituents. There was no significant difference between the constituents of all the samples even after two-year storage. The concentration of Arsenic and lithium were demonstrably higher than WHO allowable limits in all the samples. The higher lithium concentration may be beneficial for mood stabilization and suicide prevention (Shomar, 2012). A possible rejoinder for higher concentration of arsenic and the scriptural recommendation of healing properties of Zamzam water is the demonstration of the presence of antioxidant minerals like selenium, magnesium, manganese, and strontium which concentration probably counteract the oxidative effect of high arsenic concentration (Aljuhani, 2021).

Ingestion of Zamzam water for the few days or weeks of the annual Hajj and Umrah pilgrimage by pilgrims is unlikely to precipitate carcinogenesis or organ toxicity as demonstrated in experimental animals (HA et al., 2021). Consistent use is more likely for the Meccan dwellers who are more likely to make use of the water on several occasions due to proximity, availability, and the belief in its healing properties. Retrospective epidemiological data may need to be garnered to know if any form of cancer (or other features of heavy metal poisoning) is more prevalent in

Meccans than dwellers of other places that have no access to Zamzam water.

### ***Central Nervous System***

#### ***Cerebrovascular accidents (CVAs)***

Incident of Cerebrovascular accidents was found to be about 8.9/per 100,000 pilgrims during the 2015 hajj, with peak occurrence on the day of Eid-ul-Adha and an 11.6% case fatality rate (Almekhlafi et al., 2017). Azarpazhooh et al estimated the adjusted incidence of first-ever stroke (FES) amidst Iranian Hujajs and compared it with the non-pilgrims Iranian population in a Mashhad city of Iran. The incidence of FES was generally lower than that of the non-pilgrim populations (Reza Azarpazhooh et al., 2013). Hypertension, diabetes mellitus, hyperlipidemia, and other risk factors for CVA should be assessed and controlled before allowing pilgrims to proceed on hajj.

#### ***Epilepsy***

Epilepsy is a common neurological illness as well. Affected pilgrims are better stabilized on antiepileptic drugs (AEDs) before being certified fit to proceed with Hajj by the medical team (Saad, 2017). ‘

#### ***Psychiatric Illnesses***

The prevalence of mental illnesses among Hajj pilgrims ranges between less than 1% (Raja et al., 2017) and 7.2 %

(Alzahrani et al., 2021). Patients with Major mental illnesses (like Schizophrenia and related disorders, bipolar, depressive, and anxiety disorders) should be encouraged to disclose their illness to the medical team who should advise or refer such pilgrims to a psychiatrist for assessment of their fitness to proceed on Hajj. An illness remission state must be attained before proceeding on hajj. The stock of medication and prescription notes should be carried along as done for other chronic ailments during the hajj journey for ease of refill and sustaining the maintenance dose to avert recurrence. It is not uncommon for mental illness to recur due to the strenuous nature of hajj rites. Early warning signs and relapse signatures characteristic of the patient illness should be identified and the patient educated on the need for early presentation and early intervention to avert full relapse.

### ***Psychoactive Substance Use/Misuse***

Hajj season is an opportunity for people who abuse a psychoactive substances to abstain from their addictive behavior as much of their time and attention should be dedicated to worship and not recreational drug use/activities. Consumption of alcoholic beverages is a punishable offense in Islam, the same applies to buy, selling or using in the Kingdom of Saudi Arabia as well as most other Islamic countries of the world. Smoking is prohibited in most holy

sites to avert the exposure of other pilgrims to passive smoking and prevent fire accidents in congested settings/mass gatherings. Most other psychoactive substances are considered khamr (intoxicants) whose consumptions are also sinful in Islam and should be avoided to enable the attainment of the desired spiritual benefit of the hajj. There are anecdotal reports that consumption of Zamzam water reduces addictive behavior possibly because of its sub-therapeutic lithium content (Sudhir Gadh, 2020). Lithium concentration of Zamzam water may be of therapeutic value in people with suicidality, mood, other behavioral disorder, and lead neurotoxicity (Brown et al., 2018).

### ***Emotional Distraught***

Some intending pilgrims could not perform the 2022 Hajj due to the stringent measures dictated by the COVID19 pandemic, and the limited period is given to prepare for the operation by the Hajj Ministry of Saudi Arabia, which make NAHCON title it as an “emergency hajj” (Abubakar, 2022). Such people are emotionally distraught as this translated to missing the hajj chance for three consecutive years. NAHCON put measures in place to ensure that such individuals should be given topmost consideration during the subsequent year (2023) hajj year.

### ***Musculoskeletal System***

Prevalence of musculoskeletal pain was reported to be as high as 80.46% among pilgrims of different nationalities that were interviewed at various sites of hajj rites such as Grand Holy Mosque, Mina, Arafat and Muzdalifah (Alshehri et al., 2021). The painful conditions (especially lower limb pain) are more prevalent in females, older age groups, and the obese (Alshehri et al., 2021). Disorders of the musculo-skeletal system are next to respiratory tract infection in order of commonality of hospital presentation amidst Nigerian pilgrims (Abubakar, 2022), same was reported in a study of Pakistani pilgrims presenting in Pakistani Hajj Medical Mission` Hospital and Dispensary in Meccas (Raja et al., 2017). This is due to the need to walk in performing most tasks by pilgrims. Some pilgrims also miss their ways and end up walking long distances in search of their destinations. The language barrier makes it difficult for most pilgrims to get appropriate guidance from Saudi security personnel. Making use of a wrist straps which can be read by the Saudi personnel, and the use of maps (including google Maps) can ameliorate this. Pilgrims should also try to make use of the free transport systems (eg train services) provided by Saudi authorities.

Footwear should not be tight fitting (note that shoes and socks are not allowed for

men). It is advisable to use old footwear than new ones to avoid soring and blisters during rigorous tasks like tawaf and sa'ay. Voluntary health workers (VHW eg Red Crescent Society of Saudi Arabia) are readily available and accessible on most walkways to the sites of performance of rigorous rites to assist people that have muscle cramps, osteoarthritis, sprains etcetra.

People with disabling illnesses and advanced age should be informed about the permissibility of delegating a healthier younger person to perform the Hajj on their behalf. This will reduce the burden of illness, cost, and associated discomfort. Stampedes, accidents, injuries, and exhaustion are a common occurrences during the hajj (Al-Harathi & Al-Harbi, 2001). This can be minimized by following Islamic guidelines of rites performance, adoptions of permissible options, devices, and technologies.

Most activities can be done at convenient periods of different parts of the day. Pilgrims can be grouped into batches of genders, regions, or nationalities in performing tasks like the stoning of satan effigy to avert congestion, fall, and stampede that may occur during the task. People with physical disabilities are permitted to do the stoning at an earlier part of the day or delegate a healthy person to perform it on their behalf while able-bodied

pilgrims are encouraged to do their stoning by mid-day. The use of wheelchairs, electronic carts etcera is permissible for the disabled. These are available for rent at some cost which may not be affordable to most Nigerian pilgrims.



**Figure 3.** Pilgrims performing strenuous Hajj rites on Electric Scooters

Adoption of apps and online portals (like tawakalna, absher, eatmarna, maqam, etc all available for free download on play store) enable pilgrims to book an appointment for timing specific period one want to do task like visitation of Holy Rawdah; the sacred place between the mimbar (pulpit) and the house of the noble prophet PBUH in Medinah during the ziyara (visitations). This has been tried as part of technological approaches for easing hajj tasks. Some recognized limitations therein include non-

compatibility of some devices with the apps, the requirement of valid and specific types of credit cards, affordability, and availability of internet access.

### ***Reproductive {urogenital} system***

#### ***Pregnancy and Pilgrimage***

Islam encourages accompaniment by one's legally married spouse(s) in the hajj ritual, sexual cohabitation is however a forbidden act during Hajj and can nullify the validity of Hajj. Separate accommodation facilities are provided for each gender during hajj. Pregnancy is not a contraindication for pilgrimage. The pregnancy test is part of a routine tests conducted for women during pre-hajj medical screening. Pregnant women are encouraged not to perform Hajj to avert possible complications that may arise due to the strenuous nature of the rites. At least, a case of miscarriage was reported among Nigerian pilgrims in the Hajj year 2022 (Gbadamosi, 2022) despite the inclusion of pregnancy tests and ultrasound scanning as parts of pre-hajj medical screening. There are possibilities that such women get fecundated after the conduct of the pregnancy test. It may therefore be recommended during pre-hajj health education that married female pilgrims should practice sexual abstinence or be on contraceptives after the conduct of medical screening, especially during the menstrual

cycle preceding their departure for Hajj, if there are no other gynecological reasons against such.

### **Menstruation**

Menstruating women have some limitations in performing most of their worship generally in *Islam* as seen in solat (prayer) and sawm (fasting). However, most of the Hajj and Umra activities are not limited by menstruation factors except Tawafs which is one of the obligatory aspects of the pilgrimage rites. It however allowed for women to defer the period of performance of compulsory Tawafs (tawaful ifada) till the cessation of menstruation, while other forms of the (voluntary) tawaf (eg Tawaful wada: farewell tawaf) may be left undone. It is also allowed for a woman to take medications (eg norethisterone, combined oral contraceptive pills) that can suppress/postpone her menstruation cycle during the Hajj period till a later time to enable prompt/timely performance of these rites. This should be done after discussing such with her gynecologist to avert the possibility of any adverse effect that may arise upon the use of such medication (Islam et al., 2019).

### **Dehydration**

To avert dehydration from extremely hot arid weather, pilgrims are advised on the

need for frequent water drinking. Bottled Zamzam and non-Zamzam water are readily available, and freely distributed in the city of Mecca and the precinct of the Holy Mosques. Dysuria may be a feature of urine hyper concentration in an individual that is not taking enough water. Heat stroke characterized by a sudden loss of consciousness can result from excessive heat. Pilgrims are therefore advised to make use of an umbrella to avert heat from intense sunshine.

### **Conclusion and Recommendation**

A holistic approach to healthcare is applicable in a mass gatherings like hajj as it is for other aspects of the health sector. The tremendous and continuous developmental efforts by the Ministry of hajj and Umrah and the Ministry of Health of the KSA is commendable. Continuous improvement in services, technological innovations, adaptations, collaborations, and training avenues like the Hajj University concept in KSA, Hajj Institute of Nigeria, {HIN} (Aljoudi, 2013; Usara, 2022) should not cease.

Health education of pilgrims during pre-hajj seminars and workshop needs to be given priority among Nigerians and other LAMICs. Pilgrims should be encouraged to disclose their health status and assured that this may not necessarily prevent them from performing hajj but may serve to improve



their health during hajj. Warm water/ beverages should be made available the same way as cold water is made to be readily available as a thirst quencher, prophylactic and therapeutic modality for people who are prone to respiratory illnesses (Saketkhoo et al., 1978) .

Only twelve Nigerian pilgrims reportedly died during the 2022 Hajj and this is the lowest mortality (3/10000) in the preceding ten years (Aremu, 2022). Despite strong scriptural admonition of performing Hajj when one is healthy, so many wheel-bound pilgrims partake in Hajj and Umrah. Some sick pilgrims anecdotally give advance DNR (do-not-resuscitate) directives/orders if they go into cardiac arrest that they may attain the spiritual benefits of dying during the hajj (Memish et al., 2012). This has big ethical and religious implications. To avert such occurrence, people deemed unfit for hajj should be sermonized of the permissibility of a younger /healthier person to perform the hajj on their behalf while they will still get the spiritual benefit/reward as documented in the authentic hadith of the Noble Prophet Muhammad PBUH.

Pilgrims should be advised (if not mandated) to undergo post-hajj health screening. Similar importance given to pre-hajj screening should be accorded to post-hajj screening to mitigate the risk of disease

transmission in the native countries of all pilgrims.

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