PREVALENCE OF MALARIA AMONG COVID-19, EXHIBIT SEVERITY, MANAGEMENT, AND OUTCOME

Manal Adam Motkhatr[1], Musa Mohamed Khier[1], Sufian Khalid Mohamed[2], Mohamed Osman Elamin[3], Wahaj A Khan[4]*, Hatim Matooq Badri[5], Ahmed A Osman[6]

1. *Faculty of Medicine, University of Khartoum, Khartoum, Sudan.*
2. *Faculty of Medicine, University of Nile Valley, Khartoum, Sudan.*
3. *Department of Health Education and Promotion, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Makkah, Saudi Arabia.*
4. *Department of Occupational Health, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Makkah, Saudi Arabia.*
5. *Department of Environmental health, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Makkah, Saudi Arabia.*
6. *Faculty of Medicine, University of Kassala, Khartoum, Sudan.*

ARTICLE INFO

ABSTRACT

Coronavirus disease (COVID-19) is an infectious disease caused by a new coronavirus strain. Malaria is a parasitic disease caused by protozoan parasites of the genus Plasmodium, transmitted by mosquitoes of the genus Anopheles. The dual infection of malaria and COVID-19 is not fully understood or reported. We aimed to identify the association between malaria and COVID-19, its severity, management, and clinical outcome. This is a prospective hospital-based study conducted in isolation centers in Khartoum state during the period from October to December 2020. We used the total coverage method as a sampling technique to include participants from Khartoum isolation. We included 143 participants chosen from three centers. Data were collected from the patients and their files for those who met inclusion criteria using a questionnaire as a study tool filled out by the principal researcher. All participants in this study were COVID-19 patients diagnosed by PCR. Malaria was diagnosed in 115 patients (80.4%), and fever was the most common presenting symptom that occurred in all patients followed by fatigability in 125 (87.4%), cough in 115 (80.4), and headache in 83 (58.1%). This study found an association between malaria and COVID-19. And revealed that there is a better outcome for the patient with malaria and COVID-19 compared to those without malaria (p-value=0.036). This study revealed that there is a significant relation between COVID-19 and malaria, also it reveals that anti-malaria treatment may improve patients' clinical outcomes. Owing to widespread COVID-19, PCR tests were considered for any patient who had malaria.

Introduction

Coronavirus disease-2019 (COVID-19) is an infectious disease caused by a new coronavirus strain [1]. COVID-19 causes mild to moderate respiratory disease, many patients recover without requiring special treatment, on the other hand; older patients and patients with comorbidities (like diabetes, cardiovascular disease, chronic respiratory disease, and cancer) are more likely to suffer from serious forms of the disease [2]. Coronaviruses (SARS-CoV) were responsible for an outbreak of severe pneumonia in China, in November 2002 which infect more than 8000 people before it had been controlled, coronaviruses (MERS-CoV) also were responsible for another outbreak which start in June 2012 in Saudi Arabia leading to infection of more than 2000 people [3]. In December 2019 Coronaviruses (COVID-19) start another outbreak, which began in Wuhan (China) before it spread to other countries [4].

Corresponding Author: Wahaj A Khan; Department of Occupational Health, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Makkah, Saudi Arabia. E-mail: wakhan@uqu.edu.sa.

Malaria is a parasitic disease caused by protozoan parasites of the genus Plasmodium, transmitted by mosquitoes of the genus Anopheles—is among the top ten causes of death in low-income countries and represents one of the great global health challenges [5]. About 100 countries worldwide have achieved disease elimination and are now malaria-free [6, 7]. The co-infection between malaria and COVID-19 is not understood or fully reported [8]. However, there are some associations between COVID-19 and malaria [9]. COVID-19 disturbs the continuity of the preventive measures conducted against malaria; also, malaria testing and treatment are disturbed due to risks of infection to healthcare workers during the pandemic [10]. There is a low prevalence of COVID-19 in malaria-endemic areas, this fact suggests an association between the two diseases and stimulates researchers to conduct studies to get answers [11].

In Sudan, COVID-19 and malaria are common febrile conditions and both of them have a high morbidity and mortality rate [12]. Both of the diseases put a high burden on the health care system in Sudan. According to our best knowledge, there is no published data from Sudan covering this area.

In this study, we aimed to identify the association between Malaria and COVID-19, its severity, management, and clinical outcome.

Materials and Methods

This was a prospective hospital-based study conducted in isolation centers in Khartoum state, Sudan (Royal Care Hospital, Ibrahim Malik Hospital, and Alshaab Hospital). The study was conducted from October to December 2020. We included all patients diagnosed with COVID-19 from October to December 2020 and patients who accepted to participate in this study. We exclude any patients who refused to participate in the study and patients who came from other isolation centers. We used the total coverage method as a sampling technique to include 143 participants from Khartoum isolation centers namely Royal Care Hospital Isolation Center 94 (65.7%), Ibrahim Malik Hospital Isolation Center 27 (18.9%), and Alshaab Teaching Hospital 22 (15.4%).

Data were collected from the patients and their files for those who met inclusion criteria after taking written consent using a questionnaire as a study tool filled out by the principal researcher. Study variables included the socio-demographic data of the patients with COVID-19 (age, gender), results of blood film for malaria (BFFM) presence of co-morbidity, and the possible outcome of the patients.

Data Analysis

Data were analyzed using Statistical Packages for Social Sciences (SPSS) version 24. Frequency listings and percentages were used to describe categorical variables. The P-value was considered significant if $p < 0.05$.

Ethical Consideration

Ethical clearance was obtained from the committee of the Sudan Medical Specialization Board (SMSB) and EDC. Approval to conduct this study was obtained from the administration of included centers. Written informed consent from patients was obtained before participation.

Results and Discussion

A total of 143 participants were enrolled in this study from various age groups. Patients had a history of several diseases most notably diabetes mellitus (55%) **(Table 1)**. The patients experienced several presentation symptoms most notably fever (100%) **(Table 2)**. Study participants suffered from a variety of complications, most notably sepsis (52%) **(Table 3)**.

Table 1. Co-morbidities distribution among study participants (N=143)

Co-morbid illness	Frequency (%)
Diabetes mellitus	79 (55.2 %)
Hypertension	34 (23.8 %)
Asthma	22 (15.4 %)
Renal disease	24 (16.8 %)
Chronic Obstructive Pulmonary Disease	1 (0.7 %)
Cardiovascular	41 (28.7 %)
Malignancy	4 (2.8 %)
None	3 (2.1 %)

Table 2. Presenting symptoms of the study participants (N=143)

Presenting symptoms	Frequency (%)
Fever	143 (100 %)

Fatigability	125 (87.4 %)
Cough	115 (80.4 %)
Headache	83 (58.1 %)
Vomiting	8 (5.6 %)
Diarrhea	19 (13.3 %)
Shortness of breath	72 (50.3 %)
Tachypnea	62 (43.3 %)
Oxygen saturation less than 93	52 (36.4 %)
Loss of appetite	1 (0.7 %)
Shock	1 (0.7 %)

Table 3. Complications among the study participants (N=143)

Complications	Frequency (%)
Severe pneumonia	22 (15.4 %)
Respiratory failure	14 (9.8 %)
Organ failure	3 (2.1 %)
Sepsis	75 (52.4 %)
Septic shock	3 (2.1 %)
None	45 (31.5 %)

There was a significant association between age and the outcome (p = 0.00) (**Table 4**). There was a significant difference between the outcome of patients with Malaria and COVID-19 compared to those without Malaria (p = 0.036) (**Table 5**). There was a significant association between medications received for Malaria and the outcome (p = 0.000) (**Table 6**).

Table 4. Association between age and the outcome of the participants (N=143)

Age groups (in years)	Death	Discharge in a good condition	Full recovery	Total	P-value
25-30	0	0	1	1 (0.7 %)	
35-40	0	2	1	3 (2.1 %)	
40-45	0	4	4	8 (5.6 %)	
45-50	1	7	4	12 (8.4 %)	
50-55	0	8	6	14 (9.8 %)	
55-60	0	17	15	32 (22.4 %)	0.00
65-70	4	12	8	24 (16.8 %)	
70-75	4	13	1	18 (12.6 %)	
75-80	11	6	3	20 (14 %)	
80-90	9	0	1	10 (7 %)	
Above 96	1	0	0	1 (0.7 %)	

Table 5. Outcome of patients with malaria and COVID-19 compared to those without Malaria (N=143)

Patient test for Malaria	Outcome			Total	P-value
	death	Discharge in a good condition	Full recovery		
Negative	11 (7.7%)	11 (7.7%)	6 (3.5%)	28 (18.9%)	
Positive	19 (13.3%)	58 (40.6%)	38 (26.6%)	115 (80.4%)	0.036*
Total	30 (21.0%)	69 (48.3%)	44 (30.8%)	143 (100%)	

Table 6. Medications received for Malaria and the outcome cross-tabulation (N=143)

Medications received for Malaria	Outcome			Total	P-value
	Full recovery	Discharge in a good condition	Death		
Artemether-lumefantrine	39 (27.3%)	49 (34.3%)	9 (6.3%)	97 (67.8%)	
Artesunate intravenous	0 (0%)	10 (7%)	10 (7%)	20 (14%)	0.000
None	5 (3.5%)	10 (7%)	11 (7.7%)	26 (18.2%)	

Total	44 (30.8%)	69 (48.3%)	30 (21%)	143 (100%)

In this study, about four-fifths of the study participants had malaria. More than two-thirds of the participants were discharged in good condition. This study found an association between malaria and COVID-19 [13]. According to WHO reports, this finding is high when compared to reports from Nigeria (25%), the Democratic Republic of the Congo (11%), Mozambique (5%), and Uganda (4%) [7]. It is important to mention that most of the malaria cases and death occurs in sub-Saharan Africa, about 92% of global cases of malaria occur in the African region. In 2019, there were an estimated 229 million cases of malaria worldwide and about 409,000 deaths [6]. This study found that fever was the most common clinical presentation followed by fatigability, cough, headache, Tachypnea, Oxygen saturation of less than 93, and other clinical presentations [14]. This finding is consistent with another study where fever (58.66%) was the most common clinical presentation followed by: cough (54.52%), dyspnea (30.82%), malaise (29.75%), fatigue (28.16%) and sputum/secretion (25.33%), Neurological symptoms (20.82%), dermatological manifestations (20.45%), anorexia (20.26%), myalgia (16.9%), and other clinical presentations [15]. In this study, Artemether-lumefantrine was the most commonly used drug [16]. The development of resistance to drugs poses one of the greatest threats to malaria control and results in increased malaria morbidity and mortality [17]. Resistance to currently available anti-malarial drugs has been confirmed in only two of the four human malaria parasite species, Plasmodium falciparum, and Plasmodium vivax. Due to resistance against most of the anti-malaria, artemisinin-based combination therapies (ACTs) become widely used, and Artemether-lumefantrine is the most commonly used combination [18, 19].

In this study, more than four-fifths of the participants were admitted to ICU [20]. This finding is comparable to a meta-analysis study conducted by Semagn Mekonnen Abate *et al.*, in which the rate of ICU admission among patients with coronavirus varied from 3% to 100%. Some studies suggest a better outcome and a lower risk of COVID-19 in malaria-endemic areas, however; the underlying mechanism has yet to be investigated [21, 22].

This study found that there is an association between age and outcome [23]. Centers for Disease Control and Prevention (CDC) reported that the risk for severe illness with COVID-19 increases with age, with older adults at the highest risk [24].

This study found an association between malaria and COVID-19, also, this study found that there is a better outcome for the patient with malaria and COVID-19 compared to those without malaria [25]. Several studies conducted in different countries found an association between COVID-19 and malaria. However, this association required more studies to reveal the mechanism of the effect of malaria on COVID-19 [10, 26].

Conclusion

This study revealed that there is a significant relationship between COVID-19 and Malaria, also it revealed that anti-Malaria treatment may improve patient's clinical outcomes.
Considering the wide spread of COVID-19, we consider doing COVID-19 tests for every patient with a positive Malaria test, and start the COVID-19 protocol.

References

1. Sarraf DP, Gupta PP, Keshwar S. Public's knowledge and beliefs towards universal safety precautions during COVID-19 pandemic in Nepal: a web-based cross-sectional study. J Drug Deliv Ther. 2020;10(3-s):133-41.
2. Hughes MM, Groenewold MR, Lessem SE, Xu K, Ussery EN, Wiegand RE, et al. Update: characteristics of health care personnel with COVID-19—United States, February 12–July 16, 2020. Morb Mortal Wkly Rep. 2020;69(38):1364.
3. Gastanaduy PA. Update: severe respiratory illness associated with Middle East respiratory syndrome coronavirus (MERS-CoV)—worldwide, WHO, 2012–2013. MMWR. Morb Mortal Wkly Rep. 2013;62(23):480.
4. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020;395(10223):470-3.
5. Baranitharan M, Tamizhazhagan V, Kovendan K. Medicinal plants as potent power for malaria control. Entomol Appl Sci Lett. 2019;6(1):28-44.
6. Newby G, Bennett A, Larson E, Cotter C, Shretta R, Phillips AA, et al. The path to eradication: a progress report on the malaria-eliminating countries. Lancet. 2016;387(10029):1775-84.
7. Shrivastava SR, Shrivastava PS. Identifying the path and the areas of focus to accomplish malaria eradication: World Health Organization. BLDE Univ J Health Sci. 2021;6(1):98.
8. Eid MM. Co-Infection with COVID-19 and Malaria in a Young Man. Dubai Med J. 2021;4(1):104-6.

9. Davidescu L, Ursol G, Korzh O, Deshmukh V, Kuryk L, Nortje MM, et al. Efficacy and Safety of Masitinib in Corticosteroid-Dependent Severe Asthma: A Randomized Placebo-Controlled Trial. J Asthma Allergy. 2022;15:737-47. doi:10.2147/JAA.S337284

10. Hussein MI, Albashir AA, Elawad OA, Homeida A. Malaria and COVID-19: unmasking their ties. Malar J. 2020;19(1):1-0.

11. Zoller M, Irlbeck M, Zwissler B. Coronavirus disease 2019. Der Anaesthesist. 2020;69(4):223-4.

12. Mahajan R, Marcus S. Low-dose radiation therapy for COVID-19 pneumonia. Clin Cancer Investig J. 2021;10(1):1-4.

13. Suhartati T, Fatimah N, Yandri Y, Kurniawan R, Bahri S, Hadi S. The anticancer, antimalarial, and antibacterial activities of moracalkon a isolated from Artocarpus kemando Miq. J Adv Pharm Educ Res. 2021;11(4):105-10. doi:10.51847/9NHxpCqzUD

14. Tudoran C, Velimirovici DE, Berceanu-Vaduva DM, Rada M, Voiţă-Mekeres F, Tudoran M. Increased Susceptibility for Thromboembolic Events versus High Bleeding Risk Associated with COVID-19. Microorganisms. 2022;10(9):1738.

15. da Rosa Mesquita R, Junior LC, Santana FM, de Oliveira TF, Alcântara RC, Arnozo GM, et al. Clinical manifestations of COVID-19 in the general population: systematic review. Wien Klin Wochenschr. 2021;133(7-8):377-82.

16. Damanhouri ZA, Alkreathy HM, Ali AS, Karim S. The potential role of Fluoroquinolones in the management of Covid-19 a rapid review. J Adv Pharm Educ Res. 2021;11(1):128-34. doi:10.51847/FE1iOIPTwD

17. Eltayeb LB. An update about Coronaviruses with Emphasis on Newly Emerged COVID 19. J Biochem Technol. 2020;11(3):14-20.

18. Derbie A, Mekonnen D, Adugna M, Yeshitela B, Woldeamanuel Y, Abebe T. Therapeutic Efficacy of Artemether-Lumefantrine (Coartem®) for the Treatment of Uncomplicated Falciparum Malaria in Africa: A Systematic Review. J Parasitol Res. 2020;2020:1-4.

19. WHO. Responding to antimalarial drug resistance. WHO. 2018.

20. Al Husain ZZ, Alqahtani NH, Dahan MA, Softah AA, Alghamdi YA, Alsolami KF, et al. An Overview on X-Ray Diagnostic Findings in Covid-19 Patients. Arch Pharm Pract. 2021;12(2):130-3.

21. Iesa MA, Osman ME, Hassan MA, Dirar AI, Abuzeid N, Mancuso JJ, et al. SARS-CoV-2 and Plasmodium falciparum common immunodominant regions may explain low COVID-19 incidence in the malaria-endemic belt. New Microbes New Infect. 2020;38:100817.

22. Rusmini M, Uva P, Amoroso A, Tolomeo M, Cavalli A. How Genetics Might Explain the Unusual Link Between Malaria and COVID-19. Front Med. 2021;8:499.

23. Rahman AA, Khoso MH, Shaikh Z, Malik E, Siyal FJ, Rahoojo A, et al. Myths and Realities: Novel Study on COVID-19 among the Medical students of Rural University of Sindh. Arch Pharm Pract. 2021;12(1):16-20.

24. Mehra A, Grover S. COVID-19: A crisis for people with dementia. J Geriatr Ment Health. 2020;7(1):1.

25. Ghamri KA. Coronavirus Disease 2019 (COVID-19) and Pregnancy: A Review of the Current Knowledge. Int J Pharm Res Allied Sci. 2022;11(2):92-9.

26. Park JY, Freer R, Stevens R, Neil S, Jones N. The accuracy of chest CT in the diagnosis of COVID-19: An umbrella review. Cent Evid Based Med. 2021.