Clinical Characteristics, Complications and Predictors of Outcome of Hospitalized Adult Sudanese Patients with COVID-19 and Malaria Co-Infection in Sudan, a Multi-Center Retrospective Cross-sectional Study

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Abstract

Background

Malaria and COVID-19 share several characteristics that could lead to cross-infection, particularly in malaria-endemic areas. Early COVID-19 symptoms might be misdiagnosed for malaria in clinical settings. Also, both diseases can cause fatal complications. So, laboratory testing for both diseases was recommended by the WHO.

Objectives

To study the clinical characteristics and outcomes of Adult Sudanese patients with COVID-19 and Malaria Co-infection.

Methods and materials:

This retrospective cross-sectional study was conducted from January 2021 to October 2021 in Wad Medani. A total coverage of all Sudanese patients above 18 years old with a confirmed diagnosis of co-infection with COVID-19 and malaria was included, and data was collected using a data collection sheet. Data was analyzed using R software version 4.0.2. Data were described and presented as mean $\pm$ Standard deviation (SD) and number (percentage). To find associated factors with in-hospital outcome, chi-square test, fisher exact test, and independent t-test or Wilcoxon rank-sum test were used.

Results

In this study, 156 participants were diagnosed with COVID-19 and malaria co-infection. Most of them were between 60-70 years (30.8%), the majority were males (59%). Shortness of breath (76.3%) and acute respiratory distress syndrome (35.3%) were the most common symptom and complication among co-infected patients, respectively. Ground glass opacity (n=47/49, 95.9%) is the most common result for CT scan. Atrial fibrillation was the most common abnormal ECG finding (n = 6/62, 9.7%). Overall mortality among all participants was (63/156, 40.4%).

Conclusion

High mortality rate was found among the co-infected patients. More attention is needed towards fighting COVID-19 and Malaria co-infection. There may be a link between Malaria and COVID-19.

Introduction

Malaria is a mosquito-borne infectious disease caused by a plasmodium-like eukaryotic protist¹. Malaria is one of Africa's most frequent endemic diseases, affecting 250 million people and killing one to three million people, usually children, in Sub-Saharan Africa². *P. falciparum*, *P. vivax*, two morphologically identical sympatric species of *P. ovale* (as suggested by recent data), *P. malariae*, and the monkey malaria parasite *P. knowlesi* are the five species known to cause malaria in humans. *P. falciparum* produces more deadly infections, and patients can quickly develop complications such as severe anemia, acute renal injury, cerebral malaria, spontaneous bleeding and coagulopathy, and others. Its incubation period is about 10–15 days³. In 2020 there were about 241 million cases worldwide, Africa accounts for 95% of all cases. Southeast Asia is ranked second, followed by the eastern Mediterranean region, which is ranked third⁴. It is one of Sudan's endemic diseases and a severe public health issue. So up to date, almost 1.8 million malaria cases have been documented across Sudan⁵. Fever, headache, generalized fatigability, nausea, and vomiting are typical clinical manifestations of malaria. The severity of an infection is determined by a number of factors, including the plasmodium species, the patient's immunity, and the infected person's overall health and nutritional status^{6,7}. Malaria laboratory diagnosis by microscopic thin and thick film, which is the gold standard for malaria identification, as well as fast antigen testing (e.g. Immunochromatography (ICT) and Nucleic acid amplification procedures, may aid in the detection of acute conditions⁸.

SARS-Cov-2 virus, a single-stranded RNA virus belonging to the Coronaviruses family, causes COVID-19. The outbreak began in December 2019⁹ in Wuhan, China, and was declared a pandemic in March 2020 because of its rapid expansion¹⁰. More than 250 million instances of COVID-19 have been verified to date, with a total mortality estimated over 5 million cases. As of the 15th of December 2021, there are 45112 instances in Sudan, with 3252 deaths¹¹. When encountered, the major method of transmission is through respiratory droplets from person to person¹², with an incubation period of about 5 days¹³. COVID-19's most common clinical symptoms are fever and cough. Fatigue, myalgia, headaches, and diarrhea are some of the other common symptoms. The most prevalent laboratory finding is high C-reactive protein, followed by lymphopenia and leukopenia¹⁴. The real-time polymerase chain reaction (RT-PCR) is a standard approach for diagnosing COVID-19, although its sensitivity is only about 71%, compared to 98 percent for CT chest¹⁵. Bilateral, peripheral, lower-lobe ground-glass opacities and/or consolidation are typical findings of COVID patients on CT scans¹⁶. Fever (70 percent-90 percent), dry cough (60 percent-86 percent), shortness of breath (53 percent-80 percent), fatigue (38 percent), myalgias (15 percent-44 percent), nausea/vomiting or diarrhea (15 percent-39 percent), headache, weakness (25 percent), and rhinorrhea (7 percent) are among the most

common symptoms in admitted patients ¹⁷. Pneumonia and acute respiratory distress syndrome are two of COVID-19's most common consequences (ARDS). Additionally, COVID has been linked to acute liver, heart, and renal injury ¹⁸. Age, comorbidities, immunological response, radiographic findings, laboratory data, and signs of organ dysfunction are all characteristics that might help predict the severity of the disease ¹⁹.

Malaria and COVID-19 share several characteristics that could lead to cross-infection, particularly in malaria-endemic areas. Early COVID-19 symptoms, such as fever, myalgia, and exhaustion, might be mistaken for malaria in clinical settings. Adult respiratory distress syndrome (ARDS) is a complication of both of them ^{20,21}. In the meanwhile, many investigations have found that malaria and COVID-19 co-infection can be diagnosed by positive lab findings for both infections ^{22,23,24}. As a result, the World Health Organization (WHO) said that the existence of one disease does not imply the absence of the other. This implies the need to do laboratory testing for both disorders ²⁵.

Approximately 270 million COVID-19 cases have been reported worldwide, with over 5 million deaths. From January 3rd, 2020, Sudan has around 45 thousand confirmed cases and over 3,000 deaths so far. In 2020, an estimated 241 million cases of malaria will have been reported worldwide, resulting in roughly 627 thousand fatalities, with Africa bearing the brunt of the burden, particularly in the African Sub-Saharan area.

Aside from what has already been stated. Malaria and COVID-19 pose a serious threat to Sudan's already-fragmented health system. In addition, the mutual side effects of each of them add to the difficulty of determining the optimal care regimens for such deadly conditions. There was scarcity in literature regarding this topic, so we aimed at throwing a stone in a pond of water. In this study our aim was to assess the presenting symptoms of malaria and COVID-19 co-infection, to find complications of malaria and COVID-19 co-infection, to describe laboratory, X-ray, CT and ECG findings and to assess the predictors of outcomes of malaria and COVID-19 co-infection.

Methods And Materials

Study design and area:

This was a retrospective cross-sectional study which was conducted from January 2021 to October 2021 in Wad Medani (the capital of Gezira state) which is the second largest state in Sudan, with a total population of 4,133,048. This city, composed of 32 secondary and tertiary hospitals, receives patients from Gezira, Sinnar, Blue Nile, Kassala, Gadarif and White Nile states. Two isolation centers were involved in the study. The first (Soqatra isolation center) composed of 65 beds for mild to moderate cases divided into a general ward (45 beds) and a high dependency unit (HDU) containing 20 beds, 24-hour laboratory, pharmacy and 2 ambulances. The second (Mycetoma center) for critical cases with capacity of 10 ICU beds supplemented with 10 mechanical ventilators and 2 hemodialysis machines in addition to a laboratory, pharmacy and 2 ambulances. The two centers are referral centers that receive patients from all middle, eastern and southern Sudan states (6 states).

Participants:

We included all Sudanese patients above 18 years old with a confirmed diagnosis of co-infection with COVID-19 by RT-PCR and malaria by microscopy. All patients less than 18 years old or tested negative for COVID-19 were excluded.

Sampling:

A total coverage for all consecutive patients was done in this study during the period of data collection.

Data collection:

Data was collected by a well-trained general practitioner using a data collection sheet containing the following items:

1. Demographic data and risk factors.
2. Vital signs (diastolic blood pressure, systolic blood pressure, respiratory rate, pulse and oxygen saturation)
3. Presenting complaints of COVID-19 and malaria.
4. Complication of COVID-19 & Malaria.
5. Laboratory investigations (WBC, hemoglobin, platelets, lymphocyte, C-reactive protein, creatinine, blood urea nitrogen, D-dimer, random blood glucose)
6. Chest X-ray, CT and ECG findings.
7. Length of stay
8. In-hospital outcome (death or discharge)

Data analysis:

Data was analyzed using R software version 4.0.2. Data were described and presented as mean $\pm$ Standard deviation (SD) and number (percentage). To find associated factors with in-hospital outcome, chi-square test, fisher exact test, and independent t-test or Wilcoxon rank-sum test were used.

Ethical considerations:

Ethical approval was obtained from the Ministry of Higher Education, University of Gezira, Gezira state, Sudan. The ethical approval of each center's ethical committee was acquired. Both written and verbal consents were obtained from the participants or their guardians. Privacy and protection of the participant's files and information were of the highest priority.

Result

Characteristics of participants

In this study, 156 participants diagnosed with COVID-19 and malaria co-infection with mean $\pm$ SD of 65.2 ± 14.5 participated in this study. Most of them were between 60-70 years (30.8%) followed by 71-80 years (23.7%). Nearly half of participants were males (59%). Hypertension (37.2%) and diabetes (38.5%) were the most common risk factors. Mean respiratory rate was 29.8 ± 9.8 breaths per minute. All species of malaria were *Plasmodium falciparum* except one participant with *plasmodium vivax* (Table 1).

Clinical presentation and complications

Shortness of breath (76.3%), and fever (73.1%) were the most common symptoms among co-infected participants.

Regarding complications, acute respiratory distress syndrome (35.3%), Thrombocytopenia (16.0%), and acute kidney injury (8.3%) were reported as the most common complications of COVID-19 and Malaria co-infection.

Clinical investigations

Overall mean of total white blood cells and C-reactive protein were 11.5 ± 8.5 and 233.3 ± 746.0 , respectively. Other laboratory investigations were shown in Table 3.

Nearly more than two third of urine samples (82.7%) were normal. The mean concentration of blood urea nitrogen was 61.6 ± 43.8 (Table 3 and 4).

Bilateral consolidation was found in more than half of participants who requested chest X-ray ($n = 9/16$, 56.2%). But for CT findings, most participants were having ground glass opacity ($n=47/49$, 95.9%). ECG findings were found normal in more than half of participants ($n = 33/62$, 53.2%) and atrial fibrillation was the most common abnormal ECG finding ($n = 6/62$, 9.7%) (Table 4).

Predictors of outcomes

Overall mortality among all participants was (63/156, 40.4%). Shorter length of stay ($P = 0.003$), usage of respiratory support ($P < 0.001$), presence of acute respiratory distress syndrome ($P < 0.001$), presence of black water fever ($P = 0.031$), and low platelets count ($P = 0.035$) were found significantly associated with death in hospital (Table 1-4).

During using non-parametric tests, increased respiratory rate ($P = 0.037$) and High serum creatinine ($P = 0.035$) were found significantly associated with death in hospital (Table 1 and 3).

Discussion

In this study we report the presenting symptoms and outcome of Adult Sudanese patients co-infected with COVID-19 and Malaria who were admitted to two isolation centers in Wad Madani, Sudan. Understanding clinical features and outcome of COVID19 and malaria co-infections is essential for accurate diagnosis and predictability of treatment when a patient develops complications, in order to alleviate symptoms and reduce morbidity and mortality. To our knowledge, this is the first retrospective observational study providing clinical characteristics and outcome of COVID19 and Malaria co-infection in Sudan, and one of the few in the whole literature. We found that the most common symptoms seen on presentation among co-infected participants include: shortness of breath (76.3%) and fever (73.1%). We found the overall mortality among all participants to be 40.4% ($n=63$).

During this crisis period, a malaria case may be misclassified as COVID-19 due to symptoms that resemble COVID-19 such as fever, difficulty breathing, fatigue, and headaches of acute onset²⁶. At present, given the alertness occurring at the community, health center, nation, regional, and global levels, it is expected that COVID-19 will remain the main target of suspicion; even though co-infection may be present. Sudan faces a number of other infectious diseases that must not be ignored. COVID-19 places additional strain on the already overburdened and resource-constrained health services, which are struggling to keep in check the high burden of existing infectious diseases and non-infectious diseases, such as malaria -which can be misdiagnosed as COVID-19 if it exhibits similar symptoms. Challenges arise from the fact that people with fever are more likely to be tested for COVID-19 and sent home as a result of a negative result, and conversely, febrile patients may be tested for malaria when they are in fact infected with COVID-19; in other words, a patient may be infected with malaria and COVID-19 at the same time, and diagnosis and treatment of one may cause the other to be missed²⁶. Malaria has been reported to threaten nearly half of the world's population as of 2018⁴. The deadly strain of *Plasmodium falciparum* malaria poses a challenge because it has the potential to result in severe cases; in Africa, *P. falciparum* is the most prevalent and deadliest malaria parasite causing the most severe malaria cases overall^{27,28}. It's reported in literature that Malaria infections caused by *P. falciparum* account for approximately 90% of global Malaria mortality^{29,30}. Regarding prevalence of Malaria species in Sudan, the majority (91%) are cases of severe falciparum infection, while *P.vivax* accounts for 8 (%) cases³¹. Overall Malaria incidence in Sudan was 12.4 percent of all diseases that were reported, over 1.8 million cases are detected with a 13 per 10,000 mortality rate in 2019⁵ which is considered low in comparison to the mortality rate (4.8 per cent) in 2002³². Untreated malaria is a

leading cause of illness and death in the developing world due to the further infectiousness among community^{33,34}. On the other hand, up to 3.58 susceptible individuals can be infected by a single case of COVID-19³⁵. Given that both COVID-19 or Malaria can cause severe disease, and both are highly infectious; then, co-infection is expected to occur – especially in areas endemic with malaria like Sudan – and it's expected to be even more fatal than either of the two – COVID-19 or Malaria – isolated.

Overall mortality rate of COVID-19 – mono-infection - is approximately 1-14% in international studies, as well as 7.1% in Sudan^{36,37}. However, the overall mortality rate of a country is not always representative for every state in that country. The majority of COVID-19 cases are in Khartoum state – the capital of Sudan - where the majority of health facilities are available, yet most of the deaths of the disease have been reported from areas outside the capital³⁸. Regarding comparison of co-infection mortality rate against mortality rate of COVID-19 isolated-infection; the mortality rate in our study 40.4% (n=63) – which is done in Gezira state – is comparable to a study done in Al Gadarif state, Eastern Sudan; that showed a high mortality rate of COVID-19 – alone – of 37.5%³⁹. And regarding comparison with other co-infection studies, the overall mortality among our co-infected participants was 40.4% (n=63), in contrast to a cohort study done in Uganda that showed a mortality rate among COVID-19 and Malaria co-infected patients of only 3%⁴⁰. We believe that co-infection has a vital role prompting a high mortality rate due to the increased inflammatory response; also, we assume the mortality rate in our study to be inflated due to other factors; such as the lack of fundamental resources (lifesaving resources and adequate staff). *P. falciparum* overall mortality is difficult to obtain due to scarcity of data; but as stated in a study, *P. falciparum* mono-infection overall mortality in Sudan, was approximately 0.13% in 2019⁵. It is considered low in comparison with the high mortality of co-infection in our study (40.4%). The substantial disparity in death rates is most likely related to two factors: one being the long history of endemic malaria in Sudan, that gave most of the community the knowledge, awareness and immunity to avoid further severe infection, in addition to the cumulative experience gained by the health staff regarding responding to the infection; the other factor being the enhanced severity of disease during co-infection.

Other COVID-19 co-infections have been documented, for instance, the co-infection of Dengue virus and COVID-19 has been reported⁴¹. Dengue and Chikungunya – which are two zoonotic arboviral diseases - are endemic in Sudan, as well as malaria^{42,43}. Tropical and subtropical countries experience high levels of infection with Dengue virus and Chikungunya virus during the monsoon season, and co-occurrence has been documented⁴⁴. Malaria and dengue virus co-infection, as well as Malaria and Chikungunya virus co-infection have been reported in Sudan^{43,45}. A co-infection with any or all of Malaria, Dengue virus, and Chikungunya virus; with COVID-19 is predicted during the rainy season due to favorable breeding conditions for the mosquitoes, at the same time as the COVID-19 pandemic could have a significant impact on public health⁴⁶.

Fever, cough, and lethargy are frequent symptoms of COVID-19⁴⁷. Malaria symptoms are many; low-grade fever, shivering chills, and muscle pain, as well as gastrointestinal issues in children, are common first complaints. Such symptoms may appear abruptly, followed by heavy sweats, a high fever, and fatigue⁴⁸. There is scarcity in data regarding COVID-19 and Malaria co-infection, but a study reported that most of the patients with co-infection had fever as a presenting complaint, while some patients had headaches, difficulty breathing and sore throats on presentation⁴⁹. Regarding symptoms among our co-infected patients, we found shortness of breath (76.3%) and fever (73.1%) to be the most prevalent symptoms. Our findings align with a study done in Uganda, where fever (21%, n=70) and shortness of breath (19%, n=70) were the second and fourth most common symptoms among COVID-19 and Malaria co-infected patients, respectively⁴⁰. Although both symptoms are considered among the most to occur, there is a substantial difference between the prevalence of occurrence among the two studies. This might be due to the treatment seeking behavior of our patients, as many individuals wait until symptoms arise before seeking treatment.

As a general rule COVID-19 complications are mainly attributed to cytokine release syndrome or a cytokine storm. Complications regarding COVID-19 include: Coagulopathy, Cardiovascular complications and acute respiratory failure⁵⁰. Severe cases may experience dyspnea and hypoxia within a week of the commencement of the illness, which can lead to ARDS or end-organ failure⁵¹. Acute respiratory distress syndrome produces alveolar damage in the lungs, and the prognosis is worse when COVID-19 is the cause⁵². Concerning complications among our co-infected patients, we found the most common to be acute respiratory distress syndrome, in 35.3% (n=156) of patients. This is in contrast to a study where the most common complication among COVID-19 mono-infected patients was acute kidney injury followed by probable acute respiratory distress syndrome in 24.3% (n=73,197) and 18.4% (n=73,197) of patients respectively⁵³. The greater percentage in our patients could be ascribed to the enhanced severity caused by the synergistic co-infection pathogenicity effects. Regarding Malaria, the most common pathogenic mechanism is the hemolysis of the *Plasmodium*-infected red blood cell, which releases plasmodium endotoxin, resulting in high levels of tumor necrosis factor (TNF) generation and findings like fever⁴⁸. Malaria complications are diverse; the most common include: Cerebral malaria, acute renal failure, pulmonary edema, severe anemia, and bleeding⁵⁴. We found Thrombocytopenia to be present in 16% (n=156) of our patients. This is in contrast to a study, where Thrombocytopenia complicated 41.7% (n=12) of COVID-19 and Malaria co-infections⁵⁵. This may be attributed to the difference in sample size and further studies are needed to clarify the ambiguity.

In our patients, the overall concentration of total white blood cells was decreased, and C-reactive protein levels were increased. During malaria, white blood cell (WBC) counts are low or normal, a characteristic that is commonly regarded to represent leukocyte localization away from the peripheral circulation to the spleen and other marginal pools, instead of real deficiency or stasis⁵⁶. In African studies, serum CRP levels have been linked to parasite burden and consequences in malaria, particularly *falciparum* malaria⁵⁷. In up to 86 percent of severe COVID-19 patients, CRP levels were found to be significantly elevated. CRP levels were much higher in patients with severe disease courses than in mild or non-severe patients, hence it was employed for classification and treatment counseling in severe COVID-19 cases⁵⁸. Elevated D-dimer is a known predictor of COVID-19 infection severity; it's linked to an elevated risk of complications - such as deep vein thrombosis and pulmonary embolism - and is one of the most important determinants of

severity⁵⁹. The most common abnormality seen in patients with COVID-19, according to the literature, is sinus tachycardia. Other abnormalities include supraventricular tachycardias like atrial fibrillation or flutter, ventricular arrhythmias like ventricular tachycardia or fibrillation, various bradycardias, interval and axis changes, and ST segment and T wave changes⁶⁰.

Malaria's clinical outcome can be impacted by a wide range of factors, including parasite species, host genetics, innate and acquired immunity, access to adequate treatment, comorbidities, and antimalarial resistance. Infections can lead to various outcomes, such as asymptomatic illness, influenza-like symptoms, and organ dysfunction and death⁶¹. Regarding COVID-19 outcome, extended hospital admission and greater death can be due to multi-organ failure as well as various metabolic disturbances and respiratory insufficiency, in addition to the multi-system involvement^{62,63}. Older age, neutrophilia, and organ and clotting failure (eg, higher LDH and D-dimer) were all linked to the development of acute respiratory distress syndrome in COVID-19 patients hence death⁵¹. We found acute respiratory distress syndrome to be significantly associated with in-hospital mortality; 63.5% (n= 55) of our patients with acute respiratory distress syndrome died. This is similar to a study where mortality was 52.4% (n=84) among patients with acute respiratory distress syndrome⁵¹. The increased mortality rate is probably due to the increased inflammatory response due to the co-infection. Also, we found length of stay of 5.4 ± 4.3 days to be significantly associated with in-hospital death ($P = 0.003$); and this is similar to a systematic review where in terms of overall stay - those who died had a shorter stay than those who were discharged alive⁶³.

There is a possibility of a higher rate of COVID-19 co-infections during the ongoing pandemic; especially in areas endemic with infectious diseases like Sudan, hence more efforts should be done to raise the awareness of the community regarding both diseases – COVID-19 and Malaria – in addition to emphasis on the possibility of co-infection between COVID-19 and Malaria in specific, or COVID19 and other infectious diseases in general. A greater clinical suspicion of COVID-19 co-infection should be held; obtaining a correct diagnosis of a treatable infection, and identifying the presence of co-infections requires careful investigation, hence, it would be beneficial to provide malaria testing kits to the COVID-19 testing laboratories, thereby reducing missed opportunities for malaria testing. As a crucial component of helping to solve this difficult conundrum, convenient health infrastructure needs to be prioritized; lifesaving resources and an adequate number of qualified health workers are essential. Further research is needed for identification of etiology as well as better understanding of the pathophysiology behind COVID19 and Malaria co-infection.

Our study had several limitations, first, although our careful approach, the retrospective design in itself increased chances of bias; secondly we selectively included patients with COVID-19 and Malaria co-infection only, without including patients infected with COVID-19 or Malaria mono-infection, so our results cannot be directly compared between patients; lastly, due to inconvenience, we were not able to include isolation centers in other states, so findings cannot be generalized. Despite these limitations, our study has strong points, such as the large sample size of co-infected patients, and diagnostic and immunological tests, in addition to comprehensive laboratory, imaging, and ECG diagnostic techniques, among others.

Conclusion

Almost 2 in 5 of our participants died with acute respiratory distress syndrome being the most common complication significantly associated with mortality; such a high rate is regarded as a public health concern, and more attention needs to be focused towards fighting COVID19 and malaria co-infection. There may be a link between Malaria and COVID-19, since both diseases present with similar symptoms and complications, resulting in one of them being underdiagnosed therefore -undertreated.

Declarations

Ethical Approval and Patients' consent:

Ethical approval was obtained from the Ministry of Higher Education, University of Gezira, Gezira state, Sudan. The ethical approval of each center's ethical committee was acquired. Both written and verbal consents were obtained from the participants or their guardians. Privacy and protection of the participant's files and information were of the highest priority.

Consent for Publication:

All authors gave their verbal and written consents for publication.

Conflict of interest:

Authors report no conflict of interest

Funding:

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Data availability statement:

The data that support the findings of this paper is available with the corresponding author upon reasonable request.

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Not applicable.

Authors' contribution:

KAH, EAH, MSH and MMF: Proposal writing, Building questionnaire and Data collection and Analysis.

YFO, ABN, EHS and AMA: Writing first draft.

WAM and MYE: Did Examinations and Investigations and Supervised the study.

All authors wrote the final draft, revised the final draft and contributed significantly in this study.

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Tables

Table 1: Baseline characteristics, risk factors and vital signs in participants.

Variables	N	Overall, N = 156 ¹	Outcome		p-value ²
			Death, N = 63 ¹	Discharge, N = 93 ¹	
Age, years	156				
Mean ± SD		65.2 ± 14.5	67.1 ± 14.4	63.9 ± 14.6	0.2
Median (Interquartile range)		65.0 (57.8, 75.0)	70.0 (60.0, 78.5)	65.0 (55.0, 75.0)	0.11
Age (Groups)	156				0.7
20-30		4 (2.6%)	2 (3.2%)	2 (2.2%)	
31-40		4 (2.6%)	0 (0.0%)	4 (4.3%)	
41-50		20 (12.8%)	8 (12.7%)	12 (12.9%)	
51-60		27 (17.3%)	9 (14.3%)	18 (19.4%)	
61-70		48 (30.8%)	20 (31.7%)	28 (30.1%)	
71-80		37 (23.7%)	16 (25.4%)	21 (22.6%)	
81-90		16 (10.3%)	8 (12.7%)	8 (8.6%)	
Gender	156				>0.9
Female		64 (41.0%)	26 (41.3%)	38 (40.9%)	
Male		92 (59.0%)	37 (58.7%)	55 (59.1%)	
Marital status	156				0.7
Married		131 (84.0%)	53 (84.1%)	78 (83.9%)	
Single		10 (6.4%)	5 (7.9%)	5 (5.4%)	
Widow		15 (9.6%)	5 (7.9%)	10 (10.8%)	
Length of stay (Duration of illness), days	144				
		7.0 ± 5.3	5.4 ± 4.3	8.1 ± 5.7	0.003
		6.0 (3.0, 10.0)	4.0 (2.0, 7.0)	7.0 (3.0, 10.0)	0.003
Recent Travel history (last 2 month)	156	9 (5.8%)	6 (9.5%)	3 (3.2%)	0.2
Residence	149				0.4
Kordofan state		1 (0.7%)	1 (1.7%)	0 (0.0%)	
Wad Medani		148 (99.3%)	59 (98.3%)	89 (100.0%)	
Occupation	150				0.056
Housewife		26 (17.3%)	12 (20.0%)	14 (15.6%)	
Nonskilled labourer		13 (8.7%)	4 (6.7%)	9 (10.0%)	
Not working		65 (43.3%)	33 (55.0%)	32 (35.6%)	
Professional		20 (13.3%)	4 (6.7%)	16 (17.8%)	
Skilled labourer		26 (17.3%)	7 (11.7%)	19 (21.1%)	
Usage of respiratory support	152	47 (30.9%)	29 (46.8%)	18 (20.0%)	<0.001
Previous medical history	156				
Previous hospital admission		1 (0.6%)	1 (1.6%)	0 (0.0%)	0.4
DM		60 (38.5%)	21 (33.3%)	39 (41.9%)	0.3
Asthma		7 (4.5%)	4 (6.3%)	3 (3.2%)	0.4
COPD		2 (1.3%)	0 (0.0%)	2 (2.2%)	0.5
HTN		58 (37.2%)	26 (41.3%)	32 (34.4%)	0.4
Immunodeficiency		1 (0.6%)	0 (0.0%)	1 (1.1%)	>0.9
Cancer		5 (3.2%)	2 (3.2%)	3 (3.2%)	>0.9
Recent surgery		2 (1.3%)	0 (0.0%)	2 (2.2%)	0.5
Others		46 (29.5%)	24 (38.1%)	22 (23.7%)	0.052
Malaria species	145				>0.9
P. Falciparum		144 (99.3%)	59 (100.0%)	85 (98.8%)	
P. Vivax		1 (0.7%)	0 (0.0%)	1 (1.2%)	
Vital signs					
Pulse rate, beat/min	149				
Mean ± SD		96.6 ± 20.5	96.9 ± 21.1	96.4 ± 20.1	0.9
Median (Interquartile range)		93.0 (84.0, 107.0)	95.0 (86.0, 106.0)	90.0 (84.0, 109.0)	>0.9
Systolic blood pressure, mmHg	150				
Mean ± SD		124.3 ± 24.5	122.4 ± 29.5	125.7 ± 20.4	0.4
Median (Interquartile range)		120.0 (110.0, 140.0)	120.0 (109.0, 140.0)	130.0 (110.0, 140.0)	0.2
Diastolic blood pressure, mmHg	149				
Mean ± SD		73.6 ± 12.0	71.9 ± 13.1	74.8 ± 11.1	0.14
Median (Interquartile range)		70.0 (70.0, 80.0)	70.0 (70.0, 80.0)	75.0 (70.0, 80.0)	0.2
Respiratory rate, breath/min	124				
Mean ± SD		29.8 ± 9.8	30.7 ± 7.9	29.2 ± 11.0	0.4
Median (Interquartile range)		28.0 (24.0, 34.0)	30.0 (25.5, 34.5)	26.0 (22.0, 32.0)	0.037

¹ Median (IQR); Mean ± SD; n (%)² Wilcoxon rank sum test; Two Sample t-test; Fisher's exact test; Pearson's Chi-squared test

Table 2: Clinical presentations and complication of COVID-19 and malaria co-in

Variables	N	Overall, N = 156 ¹	Outcome		p-value ²
			Death, N = 63 ¹	Discharge, N = 93 ¹	
COVID-19 and Malaria general symptoms	156				
Fever		114 (73.1%)	46 (73.0%)	68 (73.1%)	>0.9
Cough		104 (66.7%)	43 (68.3%)	61 (65.6%)	0.7
Loss of smell		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Nasal obstruction		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Loss of taste		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Gustatory dysfunction		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Sore throat		3 (1.9%)	2 (3.2%)	1 (1.1%)	0.6
Shortness of breath		119 (76.3%)	48 (76.2%)	71 (76.3%)	>0.9
Chest pain		6 (3.8%)	1 (1.6%)	5 (5.4%)	0.4
Myalgia		1 (0.6%)	0 (0.0%)	1 (1.1%)	>0.9
Decrease level of consciousness		22 (14.1%)	12 (19.0%)	10 (10.8%)	0.14
Headache		10 (6.4%)	5 (7.9%)	5 (5.4%)	0.5
Chills		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Sleep disturbance		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Shivering		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Nausea		2 (1.3%)	1 (1.6%)	1 (1.1%)	>0.9
Vomiting		11 (7.1%)	6 (9.5%)	5 (5.4%)	0.4
Diarrhoea		9 (5.8%)	6 (9.5%)	3 (3.2%)	0.2
Others		18 (11.5%)	5 (7.9%)	13 (14.0%)	0.2
Complications of COVID-19 and Malaria Co-infection		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Acute respiratory distress syndrome		55 (35.3%)	40 (63.5%)	15 (16.1%)	<0.001
Heart failure		6 (3.8%)	1 (1.6%)	5 (5.4%)	0.4
Myocarditis		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Pulmonary embolism		2 (1.3%)	2 (3.2%)	0 (0.0%)	0.2
Dizziness		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Peripheral neuropathy		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Encephalitis		1 (0.6%)	1 (1.6%)	0 (0.0%)	0.4
Convulsions		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Stroke		3 (1.9%)	0 (0.0%)	3 (3.2%)	0.3
Gillian Barrett syndrome		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Acute kidney injury		13 (8.3%)	6 (9.5%)	7 (7.5%)	0.7
Sepsis		8 (5.1%)	5 (7.9%)	3 (3.2%)	0.3
Hypoalbuminemia		1 (0.6%)	0 (0.0%)	1 (1.1%)	>0.9
Hyponatremia		1 (0.6%)	0 (0.0%)	1 (1.1%)	>0.9
Dysenteric malaria		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Biliuoric malaria		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Choleric malaria		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Malaria induced hepatitis		3 (1.9%)	2 (3.2%)	1 (1.1%)	0.6
Malaria pneumonitis		2 (1.3%)	1 (1.6%)	1 (1.1%)	>0.9
Cerebral malaria		12 (7.7%)	6 (9.5%)	6 (6.5%)	0.5
Black water fever		9 (5.8%)	7 (11.1%)	2 (2.2%)	0.031
Algid malaria		4 (2.6%)	3 (4.8%)	1 (1.1%)	0.3
Thrombocytopenia		25 (16.0%)	9 (14.3%)	16 (17.2%)	0.6
Pulmonary edema		2 (1.3%)	1 (1.6%)	1 (1.1%)	>0.9
Anemia		11 (7.1%)	6 (9.5%)	5 (5.4%)	0.4
Cerebllities		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Gillian Barrett syndrome		0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others (Pancytopenia, psychosis, sepsis)		3 (1.9%)	0 (0.0%)	3 (3.2%)	0.3

¹ n (%)² Fisher's exact test; Pearson's Chi-squared test

Table 3: Laboratory investigations in participants.

Variables	N	Overall, N = 156 ¹	Outcome		p-value ²
			Death, N = 63 ¹	Discharge, N = 93 ¹	
Lab findings					
WBCs counts, × 10 ³ /L	155				
Mean ± SD		11.5 ± 8.5	11.7 ± 9.6	11.3 ± 7.8	0.7
Median (Interquartile range)		9.7 (6.8, 13.4)	9.9 (6.9, 13.0)	9.6 (6.7, 13.6)	0.8
Hemoglobin, g/dL	153				
Mean ± SD		11.9 ± 2.0	11.6 ± 2.2	12.1 ± 1.8	0.13
Median (Interquartile range)		12.0 (10.6, 13.3)	11.7 (10.3, 13.2)	12.1 (10.8, 13.4)	0.3
Platelets, × 10 ⁹ /L	148				
Mean ± SD		248.9 ± 175.9	212.0 ± 119.9	274.0 ± 202.4	0.035
Median (Interquartile range)		210.0 (134.8, 310.8)	194.0 (126.8, 247.5)	217.0 (144.2, 350.8)	0.091
Lymphocyte, × 10 ³ /L	116				
Mean ± SD		3.5 ± 7.3	4.3 ± 9.8	3.1 ± 5.4	0.4
Median (Interquartile range)		1.2 (0.8, 2.0)	1.2 (0.6, 2.0)	1.3 (0.9, 2.0)	0.5
CRP, mg/dl	114				
Mean ± SD		233.3 ± 746.0	143.7 ± 92.2	289.6 ± 947.6	0.3
Median (Interquartile range)		233.3 ± 746.0	143.7 ± 92.2	289.6 ± 947.6	0.3
Median (Interquartile range)		105.5 (72.5, 200.0)	108.5 (83.2, 244.2)	93.5 (65.2, 198.8)	0.3
Creatinine, mg/dL	144				
Mean ± SD		1.7 ± 2.0	1.8 ± 1.4	1.6 ± 2.3	0.5
Median (Interquartile range)		1.1 (0.9, 1.7)	1.2 (0.9, 2.1)	1.1 (0.9, 1.5)	0.035
Blood Urea nitrogen, mg/dL	65				
Mean ± SD		61.6 ± 43.8	69.5 ± 41.6	56.0 ± 45.1	0.2
Median (Interquartile range)		49.0 (33.0, 71.0)	59.0 (43.5, 76.5)	44.0 (32.0, 68.5)	0.069
D-dimer, mcg/mL	113				
Mean ± SD		4,102.3 ± 3,656.7	4,276.0 ± 3,916.9	3,974.1 ± 3,477.6	0.7
Median (Interquartile range)		2,510.0 (1,200.0, 6,939.0)	2,459.4 (1,327.8, 7,164.2)	2,662.0 (1,189.0, 6,238.0)	0.7
Random blood sugar, mg/dL	82				
Mean ± SD		197.9 ± 118.5	195.9 ± 105.3	199.5 ± 129.1	0.9
Median (Interquartile range)		158.5 (125.2, 238.8)	156.5 (127.2, 228.2)	165.5 (120.8, 238.8)	>0.9
SpO2, percentage	147				
Mean ± SD		79.7 ± 16.0	76.8 ± 17.9	81.6 ± 14.4	0.078
Median (Interquartile range)		85.0 (72.0, 90.0)	80.0 (66.0, 88.0)	85.0 (74.0, 92.0)	0.1

¹ Median (IQR); Mean ± SD² Wilcoxon rank sum test; Two Sample t-test

Table 4: Urine analysis, Chest X-ray, CT and ECG findings.

Variables	N	Overall, N = 156 ¹	Outcome		p-value ²
			Death, N = 63 ¹	Discharge, N = 93 ¹	
Urine analysis	156				0.093
Bilirubin		1 (0.6%)	1 (1.6%)	0 (0.0%)	
Granular cast		1 (0.6%)	1 (1.6%)	0 (0.0%)	
Normal		10 (6.4%)	1 (1.6%)	9 (9.7%)	
Not done		129 (82.7%)	52 (82.5%)	77 (82.8%)	
Protein		3 (1.9%)	2 (3.2%)	1 (1.1%)	
Pus cells		7 (4.5%)	4 (6.3%)	3 (3.2%)	
RBCS		1 (0.6%)	1 (1.6%)	0 (0.0%)	
Sugar		4 (2.6%)	1 (1.6%)	3 (3.2%)	
COVID-19 diagnosis tool	156				
RT-PCR		99 (63.5%)	37 (58.7%)	62 (66.7%)	0.3
CT		54 (34.6%)	21 (33.3%)	33 (35.5%)	0.8
Clinical		13 (8.3%)	7 (11.1%)	6 (6.5%)	0.3
Chest Xray findings	16				0.019
Bilateral consolidation		9 (56.2%)	0 (0.0%)	9 (75.0%)	
Bilateral infiltration +suspected diaphragmatic hernia + lung collapse		1 (6.2%)	0 (0.0%)	1 (8.3%)	
Bilateral peripheral lung consolidation		1 (6.2%)	1 (25.0%)	0 (0.0%)	
Cardiomegaly + Right side consolidation		1 (6.2%)	1 (25.0%)	0 (0.0%)	
Congestion +consolidation		1 (6.2%)	1 (25.0%)	0 (0.0%)	
Midzone bilateral consolidation		1 (6.2%)	1 (25.0%)	0 (0.0%)	
Right side middle lobe consolidation		1 (6.2%)	0 (0.0%)	1 (8.3%)	
Right side pleural Effusion		1 (6.2%)	0 (0.0%)	1 (8.3%)	
Respiratory investigation COVID related CT chest	49				
Ground grass opacity		47 (95.9%)	21 (100.0%)	26 (92.9%)	0.5
Pleural effusion		1 (2.0%)	0 (0.0%)	1 (3.6%)	>0.9
Patchy or lobar consolidation		3 (6.1%)	1 (4.8%)	2 (7.1%)	>0.9
Alveolar congestion and fibrotic change		1 (2.0%)	0 (0.0%)	1 (3.6%)	>0.9
ECG findings	62				0.035
Atrial fibrillation		6 (9.7%)	6 (23.1%)	0 (0.0%)	
Atrial tachycardia		1 (1.6%)	1 (3.8%)	0 (0.0%)	
Complete heart block		1 (1.6%)	0 (0.0%)	1 (2.8%)	
Hyperacute T-wave		1 (1.6%)	0 (0.0%)	1 (2.8%)	
Left anterior descending artery occlusion		5 (8.1%)	2 (7.7%)	3 (8.3%)	
Left anterior descending artery occlusion bradycardia		1 (1.6%)	1 (3.8%)	0 (0.0%)	
Left anterior descending artery occlusion + R-wave in v1		1 (1.6%)	1 (3.8%)	0 (0.0%)	
Left bundle branch block		3 (4.8%)	1 (3.8%)	2 (5.6%)	
Normal		33 (53.2%)	11 (42.3%)	22 (61.1%)	
Q-wave		1 (1.6%)	1 (3.8%)	0 (0.0%)	
Q-wave + T-wave		2 (3.2%)	0 (0.0%)	2 (5.6%)	
Right axis deviation		2 (3.2%)	1 (3.8%)	1 (2.8%)	
ST segment elevation		1 (1.6%)	0 (0.0%)	1 (2.8%)	
ST Segment elevation		2 (3.2%)	1 (3.8%)	1 (2.8%)	
T wave inversion		1 (1.6%)	0 (0.0%)	1 (2.8%)	
T wave inversion + left ventricular hypertrophy		1 (1.6%)	0 (0.0%)	1 (2.8%)	

¹ n (%)² Fisher's exact test; Pearson's Chi-squared test