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ORIGINAL ARTICLE

Prevalence study of Malaria among Travelers Coming from Endemic Areas to Egypt

Saber Shaker Mohamed[1*], Osaman M.Abdou Seleem[2], Samia E. Etewa[3], Ahmed Said Mohamed[2]
[1] Gastroenterology & Hepatology, Dar El-Shifaa Hospital,Cairo,Egypt
[2] Tropical Medicine Department, Faculty of Medicine, Zagazig University,Egypt
[3] Parasitology Department, Faculty of Medicine, Zagazig University,Egypt

Corresponding author:
Saber Shaker Mohamed
Email:
sabershaker1991@gmail.com

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ABSTRACT

Background : The aim of the work is to assess the prevalence of malaria in travelers coming from endemic areas to Egypt either Egyptians or foreigners within two months of their arrival to Egypt.

Methods: Sites of study were Zagazig city, Tropical Medicine Department and Medical Parasitology Department, Zagazig University, Sharkyah Fever Hospitals and Abbasiah Fever Hospital, Cairo. Considering that all participants fulfilled the inclusion and exclusion criteria were included in the study.

Results: During the study period, the registered participants were 300 and were included as a comprehensive sample. The positive malaria patients were 18 (6% of all participants).

Conclusion: Foreign-acquired malaria infections have been elevated to a major concern for Egyptian travelers to African countries. To reduce the danger of catching the disease while traveling, high-risk groups should be made more aware of and given access to effective prophylactic measures against exposure to mosquito bites and malaria parasites. Increased capability for imported case detection is required to reduce the burden of fatal cases, severe malaria, as well as prevent secondary malaria transmission among Egyptians. RDTs have been found to be simple and effective for the rapid detection of malaria, which may encourage Egypt to put control measures against imported malaria into place.

INTRODUCTION

Malaria can be considered the commonest parasitic disorder . Female Anopheles mosquitoes are responsible for spread of disease to human host [1].

Recently, there is a new increasing challenge to public health in countries not known endemic with malaria due to malaria positive travelers coming from malaria endemic countries. Global warming which made changes to invironment and weather led to increase the risk of malaria[1].

Since ancient times, Malaria has been known in Egypt. All Egyptian governorates showed endemicity with malaria, but this endemicity decreased at 1990. Egypt was included into Eastern Mediteranean Region(EMR) group 2 countries which refers to countries with strong malaria control. Malaria is successfully eradicated from Egypt during 2010-2013 while efforts is done to prevent malaria re-introduction[2].

Cases of locally-transmitted malaria have not been recorded in Egypt since June 14, 2014 in Aswan Govrnorate where 19 locally-transmitted *Plasmodium vivax* malarial cases were detected in one village[3].

The study aim is to assess the prevalence of malaria in travelers coming from endemic areas to Egypt either Egyptians or foreigners within two months of their arrival to Egypt.

METHODS

I. Technical Design:

Site of the study: Zagazig city, Tropical Medicine Department and Medical Parasitology Department,

Zagazig University, Sharkyah Fever Hospitals and Abbasiah Fever Hospital, Cairo.

Sample size: Considering that all participants fulfilled the inclusion and exclusion criteria in our study. The registered participants were 300 and included as a comprehensive sample.

Inclusion criteria: Travellers coming from malaria endemic regions either Egyptians or foreigners during the first two months of their arrival to Egypt and complaining of any symptom may be related to malaria fever, malaise, jaundice, pallor

Exclusion criteria:Persons that refused sharing the study,Travelers coming from areas not endemic for malaria,persons received antimalarial treatment.

II. Operational design:

Study type: Cross-sectional .

Process: All patients of the present study underwent the following:

1. History taking:

Basic data was obtained from each patient via questionnaires which included information regarding:Personal history: Age, sex and nationality, History of travelling abroad to endemic areas of malaria and history of previous malaria infection and period of stay in Egypt since arrival and Present history: headache,fever,rigors,sweating, darkening of urine and presence or absence of vomiting, bonnyaches, myalgia, diarrhea, abdominal pain, History of intake of anti-malaria drugs.

2. Clinical examination:

General: pallor, jaundice, sweating and dizziness & Vital signs: temperature, pulse, blood pressure and rate of respiration & Respiratory system examination ,cardiovascular examination ,eye examination, gastrointestinal examination and neuropsychiatric examination .

3. Laboratory investigations:

Collection of the samples and investigations:The following laboratory investigations were done to all patients: Rapid blood test for P. falciparum & P. vivax &Thin & thick blood films(Giemsa stained) & Renal function tests (serum urea- serum creatinine and BUN) & Liver function tests (ALT,AST, total and direct bilirubin) & Complete blood count (CBC) and Blood glucose level.

Time line: The study extended from September 2021 to August 2022.

Obstacles/limitations of the study:

Uncooperative persons who refused to give the consent for sharing in our study.

Ethical considerations: we have taken an approval from (Institutional Review Board, Faculty of Medicine, Zagazig University) (ZU-IRB#7061/18-8-2021). Every participant had been told in details about the nature and purpose of our study and signed their acceptance in awritten concent.

Statistical analysis: Data collection, tabulation and statistical analysis were done using Microsoft Office Excel 2010 for windows (Microsoft Cor., Redmond, WA, USA) and SPSS 22.0 for windows (IBM Inc., Chicago, IL, USA) and MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium). The mean±SD & median (range) were used to express continuous quantitative variables. While absolute frequencies (number) & relative frequencies (percentage) were used to express categorical qualitative variables. Shapiro Walk test was used to check for normality of continuous data. Comparison between two groups of non-normally distributed data was done using Mann-Whitney U test . Chi-square test was used to compare categorical data or Fisher's exact test when suitable. All tests were two sided. Statistical significance (S) was considered for p-value< 0.05,while Highly statistical significance (HS) was considered for p-value < 0.001, and statistical insignificance (NS) was considered for p-value ≥ 0.05 .

RESULTS

The study revealed that 61% of all participants were males, with the mean of age 27.01±9.71 years. Fever was present in 9% of participants. Malaria rapid diagnostic tests were positive in 6.7% of participants, with a positive gimemsa-stained blood smear in 6%. Antigenemia was found in 0.72% of participants, and both antigenemia and parasitemia were found in 6% .A percentage of 25.9% of participants with fever had no antigenemia or parasitemia .

The study involved a diverse group of participants, predominantly Sudanese (77.3%), Egyptians (11.3%), Chadians (5%), South Sudanese (2.3%), Nigerians (2.3%), central Africans (1%), Ghanaians (0.3%), and Chinese (0.3). Most participants (86.7%) were coming from Sudan, followed by Chad, South Sudan, Nigeria, Central African Republic, Saudi Arabia, and Ghana. Positive malaria patients were 18(6% of all participants) who were predominantly Egyptians (33.3%), followed by Sudanese (16.7%), Chadians (16.7%), Nigerians (16.7%), Central African (5.6%), Ghanian (5.6%), and Chinese (5.6%). The most common nationality among positive malaria patients was Egyptian .The country that most of positive malaria patients came from was Sudan(50% of patients) . The difference in gender was statistically insignificant. The study found that 62.3% of participants had a history of

previous malaria infection, with 72.2% of positive patients having a history. 97.3% of participants did not receive malaria prophylaxis medication (Table 1). 16 malaria patients were positive for plasmodium falciparum and only 2 were positive for plasmodium vivax .

The main presenting symptom for all malaria positive patients was fever(100% of patients). Rigors/chills were present in 6.3% of participants, 1.1% of non-infected subjects, and 88.9% of malaria positive patients. Common symptoms included bone aches, myalgia, abdominal pain, diarrhea, nausea, vomiting, and dyspnea. Diarrhea was present in 12.3% of participants, while nausea and vomiting were found in 5%. Dyspnea was present in 0.3% of malaria-positive patients, while oliguria was present in 0.3%. A disturbed conscious level was present in 0.3% of cases, primarily malaria-positive patients. Significant differences were observed between infected and non-infected participants in fever, chills, diarrhea, nausea, vomiting, pallor, jaundice, and splenomegaly (Table 2).

In our study, it was noticed that there was significant decrease in hemoglobin levels of malaria patients in comparison with non malaria positive participants. Anemia was present in 22.3% of participants(19.9% of non malaria positive participant and 61.1% of malaria patients), while leucopenia was found in 0.3%. Leukocytosis was found in 1% of participants, 0.4% of non-malaria positive participants, and 11.1% of malaria positive patients. Thrombocytopenia was found in 4.7 of participants, 0.4 of participants without malaria, and 72.2% of malaria patients. The difference between infected malaria patients and non-infected participants was highly statistically significant(Table 3).

In our study,the difference between infected malaria patients and non infected participants was highly statistically significant concerning; total serum bilirubin, serum creatinine level and international normalized ratio. The difference between infected malaria patients and non-infected participants cncerning aspartate aminotransferase level was statistically significant (Table 3).

The study found that the mean duration of hospitalization for malaria patients in Egypt was 6.05±2.28 days, with a mean of 6±4.83 days between arrival and symptoms appearance. The mean of period from symptoms appearance till diagnosis was 5.44±2.30 days. The most common antimalarial medication used was Coartem(artemether plus lumefuntrine), followed by Artesunate, Primaquine, Quinine, and Doxycycline. The mean fever clearance time was 1.83±0.85, jaundice clearance time was 3±1, and parasite clearance time was 3.77±1.00. All 18 malaria patients (100%) recovered without deaths.This may be explained by that almost all patients was middle aged with range (median) of 35 (20–58) years in the absence of comorbidities, but recrudescence was observed in 5.6% of cases,(Table 4).

Table (1): Comparison between patients with malaria and subjects without malaria regarding personal data,previous malaria infection and prophylaxis:

Personal data	**The studied cross section(N=300)**		**No malaria (N=282)**		**Malaria(N=18)**		**p-value (Sig.)**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Gender							
Male	183	61%	169	59%	14	77.8%	**0.132 (NS)**
Female	117	39%	113	40.1%	4	22.2%	
Age (years)							
Mean±SD	27.01±9.71		26.39±9.15		36.72±12.98		**<0.001 (HS)**
Median (Range)	23 (12–58)		23 (12–58)		35 (20–58)		
Nationality							
Egyptian	34	11.3%	28	9.9%	6	33.3%	**<0.001 (HS)**
Sudan	232	77.3%	229	81.2%	3	16.7%	
South Sudan	7	2.3%	7	2.5%	0	0%	
Chad	15	5%	12	4.3%	3	16.7%	

Nigerian	7	2.3%	4	1.4%	3	16.7%	
Central Africans	3	1%	2	0.7%	1	5.6%	
Ghana	1	0.3%	0	0%	1	5.6%	
Chinese	1	0.3%	0	0%	1	5.6%	
Coming from							
Sudan	260	86.7%	255	90.4%	5	27.8%	**<0.001 (HS)**
South Sudan	9	3%	8	2.8%	1	5.6%	
Chad	16	5.3%	12	4.3%	4	22.2%	
Nigeria	7	2.3%	4	1.4%	3	16.7%	
Central Africa	3	1%	2	0.7%	1	5.6%	
Ghana	2	0.7%	0	0%	2	11.1%	
Saudi Arabia	3	1%	1	0.4%	2	11.1%	
Previous infection with Malaria							
Absent	113	37.7%	108	38.3%	5	27.8%	**0.372 (NS)**
Present	187	62.3%	174	61.7%	13	72.2%	
Previous Malaria prophylaxis							
Absent	292	97.3%	275	97.5%	17	94.4%	**0.394 (NS)**
Present	**8**	2.7%	7	**2.5%**	1	5.6%	

Table (2): Comparison between patients with malaria and subjects without malaria regarding clinical presentation :

	The studied cross section (N=300)		**No malaria (N=282)**		**Malaria(N=18)**		**p-value (Sig.)**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Fever							
Absent	273	91%	273	96.8%	0	0%	**<0.001(HS)**
Present	27	9%	9	3.2%	18	100%	
Rigors/Chills							
Absent	281	93.7%	279	98.9%	2	11.1%	**<0.001(HS)**
Present	19	6.3%	3	1.1%	16	88.9%	
Dark urine							
Absent	286	95.3%	275	97.5%	11	61.1%	**<0.001(HS)**
Present	14	4.7%	7	2.5%	7	38.9%	
Boneache & Malagia							
Absent	284	94.7%	279	98.9%	5	27.8%	**<0.001(HS)**
Present	16	5.3%	3	1.1%	13	72.2%	
Diarrhea							
Absent	263	87.7%	253	89.7%	10	55.6%	**<0.001(HS)**
Present	37	12.3%	29	10.3%	8	44.4%	
Nausea& Vomiting							
Absent	285	95%	279	98.9%	6	33.3%	**<0.001(HS)**

Present	15	5%	3	1.1%	12	66.7%	
Dyspnea							
Absent	299	99.7%	282	100%	17	94.4%	**0.060(NS)**
Present	1	0.3%	0	0%	1	5.6%	
Oliguria							
Absent	299	99.7%	282	100%	17	94.4%	**0.060 (NS)**
Present	1	0.3%	0	0%	1	5.6%	
Pallor							
Absent	290	96.7%	280	99.3%	10	55.6%	**<0.001(HS)**
Present	10	3.3%	2	0.7%	8	44.4%	
Jaundice							
Absent	297	99%	282	100%	15	83.3%	**<0.001 (HS)**
Present	3	1%	0	0%	3	16.7%	
Hepatomegally							
Absent	287	95.7%	272	96.5%	15	83.3%	**0.036(NS)**
Present	13	4.3%	10	3.5%	3	16.7%	
Spleenomegally							
Absent	291	97%	282	100%	9	50%	**<0.001 (HS)**
Present	9	3%	0	0%	9	50%	
Disturbed consciousness							
Present	1	0.3%	0	0%	1	5.6%	**0.060 (NS)**
Absent	299	99.7%	282	100%	17	94.4%	

Table (3): Comparison between patients with malaria and subjects without malaria regarding complete blood count, liver function tests,kidney function tests and INR:

	The studied crosssection (N=300)		**No malaria (N=282)**		**Malaria (N=18)**		**p-value (Sig.)**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Hb (g/dl)							
Mean±SD	13.08±1.65		13.26±1.44		10.41±2.36		<0.001 **(HS)**
Median	13.20		13.45		11.05		
(Range)	(6–15.10)		(10.50–15.10)		(6–13.10)		
Anemia							
Absent	233	77.7%	226	80.1%	7	38.9%	**<0.001 (HS)**
Present	67	22.3%	56	19.9%	11	61.1%	
WBCs							
Within normal	296	98.7%	280	99.3%	16	88.9%	**<0.001 (HS)**
Leucopenia	1	0.3%	1	0.4%	0	0%	
Leucocytosis	3	1%	1	0.4%	2	11.1%	
Thrombocytopenia							
Absent	286	95.3%	281	99.6%	5	27.8%	**<0.001 (HS)**
Present	14	4.7%	1	0.4%	13	72.2%	
Total serum bilirubin(mg/dl)							

Mean±SD	0.70±0.45	0.65±0.14	1.52±1.58	**<0.001 (HS)**
Median	0.70	0.70	0.90	
(Range)	(0.40–6.10)	(0.40–0.90)	(0.50–6.10)	
AST (U/L)				
Mean±SD	33.96±8.27	34.22±8	29.94±11.33	**0.020 (S)**
Median	31	31	28.50	
(Range)	(18–61)	(23–55)	(18–61)	
ALT (U/L)				
Mean±SD	33.50±9.28	33.53±8.80	33.11±15.29	**0.475 (NS)**
Median	31	31	30.50	
(Range)	(14–79)	(15–59)	(14–79)	
S. Creatinine (mg/dl)				
Mean±SD	0.72±0.25	0.70±0.23	1.09±0.32	**<0.001 (HS)**
Median	0.70	0.70	1.00	
(Range)	(0.30–1.70)	(0.30–1.10)	(0.30–1.10)	
S. Urea (mg/dl)				
Mean±SD	31.29±6.30	31.13±5.48	33.83±13.94	**0.629 (NS)**
Median	30.00	30.00	28.50	
(Range)	(18–61)	(22–41)	(18–61)	
INR				
Mean±SD	0.93±0.26	0.92±0.26	1.09±0.11	**<0.001 (HS)**
Median	1.00	1.00	1.02	
(Range)	(0.00–1.30)	(0.00–1.01)	(1.00–1.30)	

Table (4): Descriptive statistics regarding management of the studied malaria cases (N=18):

Descriptive statistics	**The studied malaria cases (N=18)**	
	No.	%
Duration of Hospitalization (days)		
Mean±SD	6.05±2.28	
Median (Range)	5.50 (3–11)	
Time until symptoms appearance (days)		
Mean±SD	6±4.83	
Median (Range)	4.50 (1–18)	
Time between symptoms appearance & diagnosis (days)		
Mean±SD	5.44±2.30	
Median (Range)	5 (2–9)	
Duration of fever before starting treatment (days)		
Mean±SD	5.44±2.30	
Median (Range)	5 (2–9)	
Antimalarial medication		
Primaquine	2	11.1%
Quinine	1	**5.6%**
Doxycycline	1	5.6%
Coartem	15	**83.3%**
Artesunate	4	22.2%
Fever clearance time (days)		

Mean±SD	1.83±0.85	
Median (Range)	2 (1–4)	
Jaundice clearance time (days)		
Mean±SD	3±1	
Median (Range)	3 (2–4)	
Parasite clearance time (days)		
Mean±SD	3.77±1.00	
Median (Range)	4 (2–6)	
Outcome of disease		
Recovery & alive	18	**100%**
Died	0	0%
Recrudescence		
Absent	17	94.4%
Present	1	5.6%

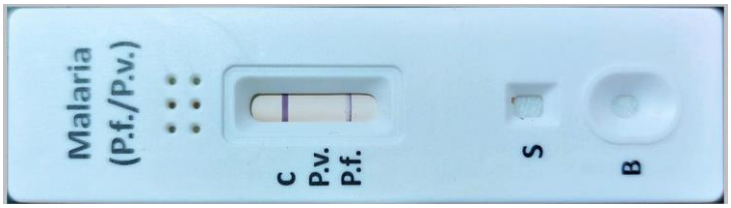


FIG (1): Aphotograph of malaria rapid diagnostic test (RDT) showing positive result for Plasmodium falciparum

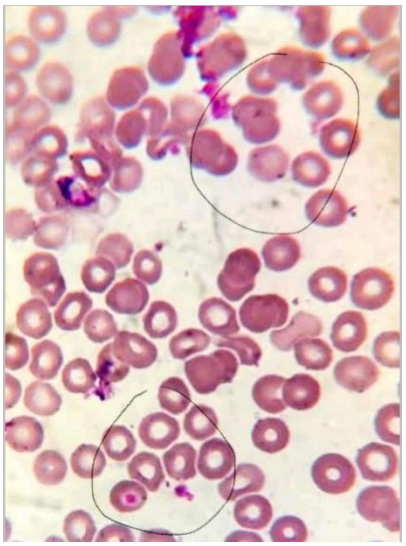
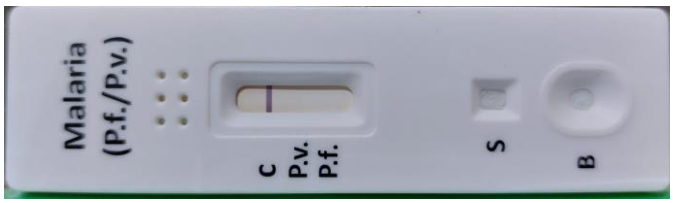
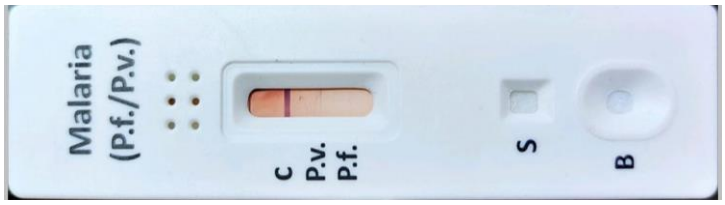


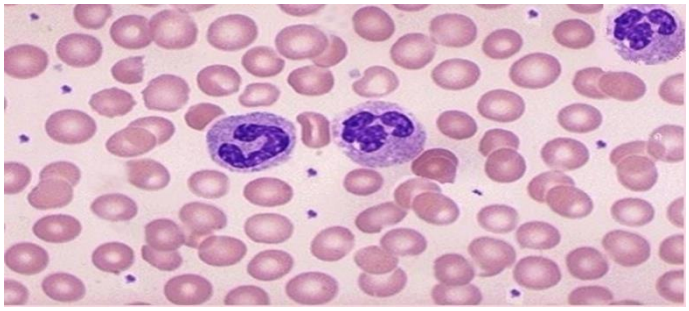
FIG (2): Aphotograph of Giemsa stained thin blood film showing Malarial merozoites in the peripheral blood. Note that several of the merozoites have penetrated the erythrocyte membrane and entered the cell.



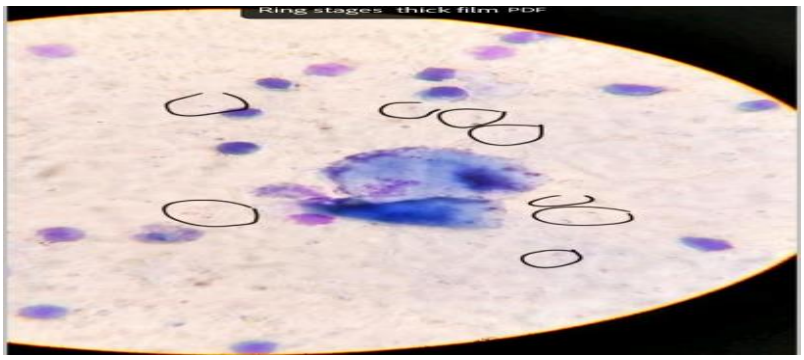
S1 : A photograph of malaria RDT showing negative result for both plasmodium falciparum and plasmodium vivax (control negative).



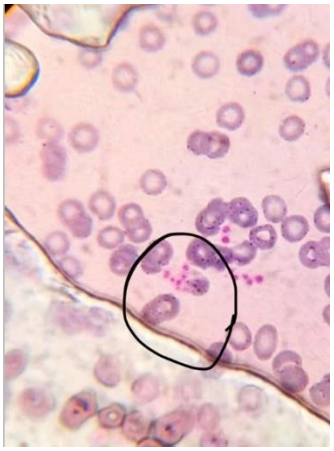
S2 : Aphotograph of malaria rapid diagnostic test (RDT) showing weak positive result for Plasmodium vivax



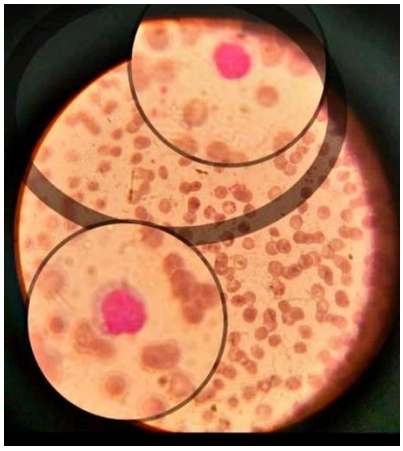
S3 : A photograph of normal blood film showing normal red blood cells, normal white blood cells and adequate numbers of platelets (control negative) Giemsa stain X 1000).



S4 : Aphotograph of Giemsa stained thick blood film showing Plasmodium falciparum multiple ring stages



S5 : Aphotograph of Giemsa stained thin blood film showing Plasmodium falciparum schizont



S6 : Aphotograph of Giemsa stained thin blood film showing Plasmodium vivax gametocyte

DISCUSSION

Malaria is one of major human parasitic diseases. Yearly, there is about three hundred million patients and two million deaths. Accurate and rapid diagnosis is essential to guarantee the effectiveness of disease management. Human malaria infection is caused by 5 species of plasmodium; P. falciparum, P. malariae, P. knowlesi. P. ovale and P.vivax. Most malaria infections occurring in Africa is caused by P.falciparum leading to global deaths[4].

Egypt faces a significant risk from imported malaria, which can reintroduce and spread the disease. Travelers coming from malaria-endemic areas can carry the parasite, and if not treated, local Anopheles mosquitoes can transmit it. Egypt must maintain surveillance, diagnostic techniques, and public health education to prevent the reappearance of malaria [5].

The purpose of that study is early detection of malaria infected cases for early management and proper control of infection. Early detection and management of infected cases decrease the possibility of transmission of infection.

Abo Hashim et al.[6] reported that a percentage of 28.6% of participants were females while 71.4% were males. 60 patients gave past history of previous malaria infection without data regarding type of plasmodium. Fever was found in 300 participants during sample taking.

D'Acremont et al. [7] reported that a percentage of 3.57%(25 patients) were positive for malaria among 700 travelers coming from areas known to be endemic for malaria. It was noticed that fever was the cardinal presenting symptom of positive patients for malaria . Plasmodium falciparum and Plasmodium vivax were the main two presenting species.

Our results are confirmed by Pasquale et al. [8] who stated that 11 patients travelled to Sudan, while 5 patients travelled to Nigeria,3 patients traveled to Ghana and one patient for each country of the following; Eritrea, South Africa, Togo, Guinea, Chad. Congo, Angola and Cameron. Being a part of Sub Saharan Africa; Sudan is considered one of the regions with the highest rates of malaria endemicity .

Checkley et al. [9] stated that the use of malaria oral prophylactic drugs was limited.The use of chemoprophylaxis was reported by 5711 out of 15933 individuals(35.8%). Apercentage of 5.7% gave history of regular intake of one of the effective drugs of malaria prophylaxis in Africa(doxycycline,mefloquine or atovaquone proguanil).

Mahittikorn et al. [10] showed that Plasmodium falciparum can cause anemia due to hemolysis and suppression of erythropoiesis. Malaria infection can lead to a decrease in hemoglobin levels, resulting in anemia. Life-threatening anemia can be a result of severe malaria. The severity of anemia in malaria can vary depending on factors such as the patient's age, their existing health status and the species of Plasmodium,. The severity of malaria infections can be assessed by using hemoglobin level as a diagnostic marker, particularly in research and clinical settings.

Kontoni et al.[11] reported variations in leukocytosis patterns in different malaria species. For example, Plasmodium vivax infections may show a more marked leukocytosis compared to

Plasmodium falciparum infections. Leukocytosis in malaria is generally considered a part of immune reaction to infection. An increase in white blood cell count, predominantly neutrophils, is observed as the body attempts to combat the malaria parasite. The severity of leukocytosis can vary between individuals and may correlate with the degree of parasitemia (parasite presence in the blood). More severe infections may lead to higher leucocytosis.

Bansal et al. [12] illusted that in astudy of 130 malaria patients, a percentage of 91% of them were found positive for P.vivax and 9% caused by P.falciparum. A percentage of 83% of patients was found to have thrombocytopenia. Although severe thrombocytopenia was considerably associated with P.falciparum;it was noticed that platelet transfusion was indicated in only one patient.

The results were compatible with Woodford et al. [13] who reported that hepatopathy due to malaria was found in a percentage of 2.4% of all cases. He stated that among patients suffered from abnormal LFTs, a number of 54 cases out of 861 showed normal or mild increase in LFTs on first day of diagnosis but developed moderate to severe increase later. He noted that all patients underwent assessment of LFTs showed elevated level of bilirubin. Bilirubin increasesd moderately for most cases,while 21 out of 861 patients showed severe increase.

Viriyavejakul et al. [14] stated that malaria positive cases showed markedly higher values of serum creatinine,total bilirubin and INR than non-infected participants. The study also found that the severity of malaria was associated with more abnormal LFT, KFT, and INR results.

Abo Hashim et al. [6] illustrated that a duration of 16.5 days(4 to 50days) was the average of period from arrival date of malaria positive patients coming from areas of malaria endemicity till appearance of malaria manifestations. While there was 6.6 days(4 to 20 days) as an average period between appearance of symptoms and definite diagnosis. Factors such as the specific strain of the parasite, the number of parasites transmitted during the mosquito bite and the individual's immunity can affect the incubation period. Early diagnosis through blood tests (such as microscopical examination of blood films or rapid diagnostic tests) is important for prompt treatment.

Bhutani et al. [15] stated that fever was the most frequent finding in patients with multi-organ dysfunction syndrome. A percentage of 97.22% of patients (105/108) suffered from thrombocytopenia. Other manifestations of severe malaria included;acute renal failure (17.59%), acidosis(22.22%), hemoglobinuria(30.55%) and hyperbilirubinemia(45.37%).

Potential conflicts of interest

Authors report no conflicts of interest .

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