‘’The Clinico-haematological Correlation In Malaria Patients AtDhiraj General Hospital - A Tertiary Health Care Centre’’

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ABSTRACT

INTRODUCTION

Malaria remains one of the chief health relatedissues in the tropics with the significant morbidity &mortality. Thrombocytopenia is the commonesthematological finding in malaria, but its clinical correlation with hematological parametersis being evaluated in various studies. In view of scarceness of data from Indian studies, we attempt to correlate the low platelet count with clinical outcome.

METHOD AND MATERIAL

The present study was hospital based observational and analytical study conducted at a tertiary care centre, Dhiraj General Hospital, Vadodara, Gujarat from August 2019- September 2019. Socio-demographic, clinical details, investigations were recorded on patient information sheet. Both thin and thick smears were stained by Field stain A & B and Giemsa stain respectively, studied under the microscope under oil immersion.

RESULT

In our study total of 85 cases of malaria were obtained within a period of 2 months in rainy season. Out of 85 suspected caes, 15 came out positive for malaria. Overall prevalence of malaria was found 17.6%.

CONCLUSION

Though the hematological changes in malaria cases in this study are not significantly different, our findings have added more information in the limited knowledge and sparse reports on clinico-hematological profile of malaria infected patients.

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KEYWORDS:

Clinico-haematological Correlation, Malaria Patients, Thrombocytopenia, Tertiary Health Care Centre

INTRODUCTION

Malaria is a life threatening infection caused by intra-cellular protozoa of the plasmodium species which is transmitted by bite of infected vectors called female Anopheles mosquitoes. Also malaria could be transmitted by congenital transmission, sharing needles and transfusion of infected blood. There are 5 species of plasmodium namedP. Vivax, P. Falciparum, P. Ovale,P. Knowlesiand P. Malariae. Amongst these P. Vivax and P. Falciparum pose the maximumhazard. *P. Falciparum* is supreme prevalent malaria parasite on the African continent. It is accountable for most malaria-related deaths worldwide. *P. Vivax*is the leading malaria parasite in most countries outside of sub-Saharan Africa.[1]

P. Vivax and P. Falciparum infections can cause complications like severe anemia, cerebral malaria with convulsions, ARDS, renal failure, circulatory collapse, hemoglobinuria, abnormal bleeding, thrombocytopenia, disseminated intravascular coagulation (DIC) and jaundice.[2]

Numerous studies have shown that wide-ranging hamatologicalterations mayhappen in malaria.[3,4,5,6] Alterations in the hematological parameters are thought to have the capacity to act as an adjuvant tool in strengthening the suspicion of malaria, by this meansstimulating a more meticulous search for malaria parasites.[4,5,7] Changes in physicochemical parameters of P. Falciparum infested blood may vary with level of malaria endemicity, presence of haemoglobinopathies, nutritional status, demographic factors and level of malaria immunity.[3]

Previous studies involving patients with complicated malaria had revealed that a reduced platelet count, reduced white blood cell counts and reducedRBC indices had relatively good sensitivities and specificities in predicting the presence of malaria infection.[5] In the last few decades, big advancements have been made in the sanitization, modifications or discovery of highly specific and sensitive diagnostic modalities for parasitic infections.

For diagnosis of malaria, the newer tests are based on serology assays [ELISA (FAST-ELISA)], and rapid antigen detection test (RDTs), molecular based approaches [real time polymerase chain reaction- RTPCR, loop-mediated isothermal amplification (LAMP), and the luminex], and proteomics technology (mass spectrometry). [1]

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The newer molecular and serological based malaria diagnostic methodologies provide superior specificityand sensitivity, but it is at a huge cost, in terms of infrastructure,equipment, and workforces which makes most of the newer diagnostic techniquesinappropriate to many areas in developing countries, where malaria is trulyhighly prevalent. Because microscopy is still considered by many as an imperfect gold standard, efforts have been made to examine role of hematological parameters in the diagnosis of malaria. Hematological profile along with microscopy will enable rapid diagnosis, speedy treatment and complications can be avoided. Some of the hospitals in the region, however, can afford to carry out a CBC for hematological valuesin patients suspected to havemalaria infection. The studies reported on this are sparse and data is limited. This study will add more information.

The effect of recent changes in environmental conditions experienced in many malaria endemic countries also, could affect disease incidences, transmission, prevalence, severity, and infection intensity amongst others.

The existence andoccurrence of malaria is meticulously related to naturally existing environmental / climate conditions. The incidence, severity and distribution of malaria are also affected substantially by human activities for example water and agricultural developments and by urbanization etc. Estimates indicate that 90% of the global burden of malaria is attributable to environmental factors. [1]

Even with all these efforts the malaria affects almost all the organs of body. But one of the principal components affected is blood. So, this work puts in an effort to associate the changes in blood.In the last few years efforts has been made to produce an effective malarial vaccination. These are still at the developmental stages [8].

AIMS

1. The aim isemphasizingvarious important indicators that possibly will be useful for public health monitoring of malaria infection
2. The study leads to early diagnosis, complicationanticipation based onhaematologicalparameters changes, closed monitoring of vital parameters and combination therapy helps to curtail the morbidity and mortality.

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OBJECTIVES

1. The objective of the study was to determine prevalence of malaria.
2. Toemphasis on haematological profiles of patients admitted with malaria in the tertiary care hospital.

MATERIAL AND METHOD

The present study was hospital based observational and analytical study conducted at a tertiary care centre, Dhiraj General Hospital, Vadodara, Gujarat from August 2019- September 2019. Total of 15 cases were studied.

Inclusion criteria –

- All cases of malaria diagnosed by either Peripheral blood smear (PBS) (thick + thin smears) or following Antigen detection sero-diagnostic test (Histidine rich protein 2 for Plasmodium falciparum / pLDH for any Plasmodium species) in our tertiary care hospital.

Exclusion criteria –

- Only the clinical diagnosis without rapid positive optimal test or peripheral smear study
- Known cases of bleeding disorder
- Patients who test positive for other infections like dengue, enteric fever, tuberculosis along with malaria.

The Ethical Committee clearance was taken prior to start study. Written informed consent for prospective cases was taken.

Socio-demographic, clinical details, investigations were recorded on PIS (patient information sheet).

3ml venous blood specimen was collected by venipuncture in EDTA vacutainer tubes and was analyzed using a Sysmex KX 21 hematology analyzer.

Hemoglobin level (Hb%), total white blood cell count (TWBC), differential Leucocyte count (DLC) and platelet count (PC) were recorded from CBC histogram. According to WHO guidelines, cases were categorized as anemia, leucopenia, leucocytosis and thrombocytopenia.[9] Subsequentlyafter sample has undergone to cell counter, at work station, two drops of capillary blood sample was added on a glass slide to prepare a thin and thick smear.

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Thick smear was de-hemoglobinised before staining. For this purpose adrop of blood on slide was kept with a drop of distilled water for 10 minutes, mixed,air-dried and heat fixed.

Both thin and thick smears were stained by Field stain A & B and Giemsa stain respectively, studied under the microscope under oil immersion.

Thin blood smear was studied for RBC morphology, differential count, platelets, detection of malaria parasite, its type (quantitative analysis) and density.

Thick smears were studied to get qualitative analysis for its morphology/ in case of scanty parasitemia/ in strong clinical suspicion of malaria.

Parasite density (Parasite Index- PI):

Parasitemia is number of parasitized RBCs / 1000 RBCs and is expressed as percentage. In a thin smear number of parasitized RBCs seen in 1000 RBCs (in 100Xobjective) were counted and the percentage was expressed. In this study 1µl of blood was considered to be equivalent to $5x10^6$ red blood cells and hence 1% PI is equivalent to 50000 parasites/ µl. Hyperparasitemia was categorized as > 100000 parasites / µl (i.e. >2%).Thus cases were categorized as < 2% (Low parasitemia) and > 2% (high parasitemia[10]

RESULT

In the present study total of 85 cases of malaria were obtained within a period of 2 months from August 19 to September 19. Out of 85, 15 came out positive for malaria in our set up.

Following table 1 and 2 shows details of malarial cases, its species, PI and socio-demographical details.

Table-1 :

Number of the cases based on species of malaria and parasitic index

Types of species	Number of cases	Number of cases (%)
P. Vivax	13	86.7
P. Falciparum	2	13.3
Mixed	0	0

Distribution of the cases based on parasitic index of malaria

Types of species	Parasitic Index

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	< 2 %	> 2 %
P. Vivax	12	1
P. Falciparum	1	1

Table-2. Number of the cases based on socio-demography of malaria

Gender of Patient		
Gender	Number of cases	Number of cases (%)
Male	11	73.3
Female	4	26.7
Residence of Patient		
	Number of cases	Number of cases (%)
Rural	15	100
Urban	0	0
Atmosphericfactor		
	Number of cases	Number of cases (%)
Pre-flood (before 31st Aug)	1	7.4
Post-flood (after 31st Aug)	14	93.6
Age		
Age in years	Number of cases	Number of cases (%)
≤ 16	3	20
17-30	9	60
31-50	2	13.3
≥ 51	1	6.7

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Following table 3 an 4 shows cases distribution based on clinical signs - symptoms and haematological parameters.

Table :3: Number of cases based on Clinical Presentation		
Symptoms		
	Number of cases	Number of cases (%)
Fever	15	100
Headache	15	100
Vomiting	9	60
Chills + Rigors (Typical Paroxysm)	11	73.3
General Weakness	10	66.7
Abdominal Pain	12	80
Signs		
	Number of cases	Number of cases (%)
Pallor	8	53.3
Splenomegaly	3	20
Hepatomegaly	1	6.7
Breathlessness	8	53.3
Bleeding manifestation	1	6.7
Jaundice	0	0
Convulsion	0	0

Table:4: Number of cases based on Haematological alteration		
Platelet count		
	No. of cases	Number of cases (%)
Normal (1.5-4.5 lacs/cumm)	2	13.3
Mild thrombocytopenia (1-1.5 lacs/cumm)	5	33.4
Moderate thrombocytopenia(0.5-1	6	40

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lacs/cumm)		
Severe thrombocytopenia(<0.5lacs/cumm)	2	13.3
Hemoglobin		
	Number of cases	Number of cases (%)
Normal	5	33.4
Mild anemia : Hb8%-10%gm	2	13.3
Moderate anemia: 6%-8%gm	6	40
Severe anemia:<6%	2	13.3
Total WBC count		
Normal	8	53.3
Leucocytosis	3	20
Leucopenia	4	26.7
ESR		
Normal	3	20
Increased	12	80
Differential count		
Neutrophil		
Normal	13	86.7
Neutropenia	1	6.7
Neutrophilia	2	13.3
Lymphocyte		
Normal	15	100
Lymphocytosis	0	0
Lymphocytopenia	0	0
Monocyte		
Normal	12	80
Monocytosis	3	20

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Eosinophil		
Normal	14	93.6
Eosinophilia	1	6.4
Basophil		
Normal	15	100
Peripheral blood smear		
	No. of cases	Number of cases (%)
Normal	10	66.7
Normocytic normpchromic	3	20
macrocytes	0	0
Dimorphic	2	13.3

DISCUSSION

In our study total of 85 cases of malaria were obtained within a period of 2 months. Out of 85 suspected caes, 15 came out positive for malaria.Overall prevalence of malaria was found 17.6%. In present study the male : female ratio was 2.75:1 and compared to Bhakshi*et al*., the males affected were more than female in our study. [10] The incidence of malaria was more in men than in women probably due to the working pattern i.e men are exposed to mosquito hits outdoors more than females.

Fever and headache was the predominant complaint in our study i.e is 100% of our patients presented with the fever and 73.3 % of the patients had chills and rigors. In the study conducted by Mehta et al fever was presented in 100% of patients and 96%in the studies conducted by Malhotra*et al*. [11]

It was also noted that 66.7% of our patients in our study had easily fatigability as their presenting complaint.

Vomiting was observed in 60% in the patients of our study conducted by Mehta and et al[12] it was also seen in 21% and 23% patients in the study conducted by the naval hospital cough and breathlessness was presenting complaint in 4.47% of the patients by study of Mehta *et al*. and the symptoms were noticed in 2% of the patients in our study [12].

Abdominal painwasobserved in 80%.

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Pallor was presented in 79% of the patients in the study carried out by Malhothra [11], it was noticed 53.3% in our study. The incidence of pallor was more pronounced in the patients with falcipurum and mixed infection which was 90%. It co-relates with the study by Sharma [13].

Splenomegaly was seen in 20% of the patients in the present study where as high incidence of spleenomegally was noted in a study conducted by rom which was 88.75 % in their study.Comparatively high incidence of 60 % was also observed by nand. [14,15]

Hepatomegally was noted in 6.7% of the patients in the present study. Studies by Ram and Murthy [15, 16] have shown an higher incidence of hepatomegaly in their work. It might be due to the fact that their study mainly concentrated on the subject such as malarial hepatitis and jaundice in malaria. The incidence in these studies was 79.5%and 91%in ram and murthy respectively where as in another study by nand the incidence was 3 % which was comparable to our study.[14, 15, 16]

Coma seizures or altered sensorium was not observed,may be due to short duration of study span. No mortality was observed.

In this study the proportion of falciparum malaria was 13.3% and vivaxinfection was 86.7%. In one study by Rajanastheinthe prevalence of falciparum was 76.2% whereasvivax malaria was just 23.8%. [17] In another study by Reddy *et al*. there was relatively high incidence of vivax malaria i.e 61.2 % and falciparum being 36.8 %. [18] In another study conducted by Bhakshin*et al*. the incidence of vivax,falciparum and mixed infection was 35% , 60% and 5% respectively. [10] From these interpretations we can conclude that incidence of particular species varies with geographical area, and the area where we have conducted the study is notendemic for falciparum is noted in my study.

Anemia was observed in 66.6 % of the patients in our study, the incidence of severe anemia (Hb<6gm%)was seen in 13.3 % and it was comparable to study conducted by Mehta et al. with incidence of 18% [12,19]. The overall incidence of anemia was higher in studies conducted by Sharma et al. where the incidenceobsrved was 86.7% [13]. The higher incidence could be explained by the fact that their study involved with cases of falciparum malaria only.

Leucocytosis was seen 20% of the total patients in our study. Similar observations were made in a study conducted by Sharma SK *et al*. [13] where the incidence of leucocytosis was 13.3%. All the patients who had leucocytosis had neutrophilia which indicates superadded bacterial infection. Leucopenia was seen in 26.7 %.

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Monocytosis was observed in 20% of patients in our study. It was observed N.K.D. Hakin*et al.* [20] in their study that monocytosis in patients especially those on antimalarial therapy may be an indicative of an anti-malarial effect by monocytes, thus monocytosis may enhance predisposition to a favorable outcome.

Eosinophilia was observed in 6.4% of cases in this study.

Here, thrombocytopenia was present in 53% of cases. In one study by Sharma S.K.*et al.* observed that 70% of the patients had thrombocytopenia.[13] Evidences of explanations for the thrombocytopenia happening in these cases have not been discovered.

In our study only 20 % had splenomegaly. It can be observed that only 66.6% of the patients with thrombocytopenia had splenomegaly. So hereby we can conclude that splenic sequestration is not only the cause of thrombocytopenia other causes such as immune mediated platelet destruction also play a role.

In our study 66.7% of the patients had normocytic normochromic picture on Peripheral blood smear. It was comparable to a study conducted by Sen et al. were halfpatients had normochromic normocytic blood picture [21]. Inour study 25%of the patients had microcytic hypochromic anemia. In our study prevalence of di-morphicanemia was seen in 13.3% of the cases similar results were also observed by Seen were the prevalence of dimorphic anemia was 20% in their study.

CONCLUSION

Though the hematological changes in malaria cases in this study are not significantly different, our findings have added more information in the limited knowledge and sparse reports on clinico-hematological profile of malaria infected patients.

Following are the gist points observed:

- The incidence is higher in males than females with peak in 2nd and 3rddecade.
- Fever and headache is the chief presenting complaint.
- Easy fatigability indicates severe anemia in malaria.
- A typical presentation is very common in the form of abdominal pain, arthralgia which was subsided after starting anti-malarial therapy.
- Splenomegaly is a vital sign in malaria, but absence of this doesn’t rule out malaria.
- Anemia is the common hematological abnormality found.

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- Thrombocytopenia is the most common finding in malaria.
- One observation was noticeable while collecting data that total cases of diagnosed dengue (NS 1/ IgM / IgG) were in significant number in our set up.
- Hence in each case of fever with thrombocytopenia, malarial infection should be considered in differential diagnosis in its endemic regions. Complications mighttake place in malaria so it is vital to know and perform hematological investigations to detect early complications, also to monitor the case and treat them effectively.

Limitations of the study and endorsement

The limitations of this study were :

- The study design is Cross sectional in nature,
- Small sample size and confounding factors that may affect hematological parameters, such as nutritional deficiencies and genetic backgrounds of patients, common bacterial, viral, and helminthic infections.
- We have not excluded these confounding factors.

We recommend studies on larger sample size and using experimental designs (case control, etc) and with exclusion of the confounding factors.

Our study on Malaria pattern wishes to create awareness at health sector level, municipal corporation level, panchayat level & individual level to take disciplinary action in monsoon season as well as government authority should find out the probable breeding sites of mosquitoes, slum areas, etc places which has to be cleaned regularly and water accumulation and stagnation should be avoided to prevent mosquito breeding.

Individual awareness can create miracle, if we try to fight malaria at individual level we can win the fight against this common infection which can convert into serious life threatening infection.

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