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Research On Hematological and Coagulation Profile in Plasmodium Vivaxand Plasmodium Falciparum Malaria Patients in Tertiary Care Hospital of Southgujarat

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ABSTRACT
Background:Malaria is a major health problem in many parts of India. Several factors have been attributed to increased morbidity and mortality in malaria with altered haematological and coagulation parameters playing an important role. This study was performed to find the correlation between the alteration of coagulation profile, hematological profile and degree of parasitemia.
Methods:In this cross sectional study we have assessed 104 cases of malaria who were admitted in SMIMER Hospital from November 2018 to April 2020. Clinical records of patients and their haematological and coagulation profile was investigated. Finally, the collected data was analysed using SPSS software Ver.16.
Results:104 cases of malaria were evaluated, 36 of these patients were female and 68 of those were male. The mean age of patients was 36 years. Anaemia was seen in 73% of the patients, 72.5% of patients with falciparum, severe anaemia was seen in 19.23% of thepatients. PT was increased in 21.15% of the cases and APTT was increased in 14.42% of thecases.BT was increased in 7.5% of the patients with P.Falciparum and out of these 5% had bleeding manifestations. 2 patients died because of multi organ dysfunction.
Conclusion:Our study showed that the incidence of malarial cases is higher in males than females with peak incidence in 3rd and 4th decade.Anemia is the most common hematologicalabnormality. Severe anemia is poor prognostic factor and it increased the duration of hospital stay and evenmortality. Overall P.Falciparum had higher incidence of anemia, thrombocytopenia, altered PT, aPTT.
KEYWORDS: Plasmodium vivax,Plasmodium malariae,Thrombocytopenia,Anaemia

I. INTRODUCTION

Malaria infection is a major public health problem in tropical areas. Global estimates suggest that the disease accounts for 300–500 million morbidity cases and contributes to approximately 3 million deaths annually [1]. Additionally, malaria parasitaemia is the leading cause of morbidity and mortality among children of the tropical and subtropical areas [2]. The tropical regions are thus affected by malaria due to the suitable breeding conditions such as high humidity, high temperature, and significantly high amounts of rainfall as well as the numerous stagnant waters it is marked with, that supports the life cycle of the vectors (mosquitoes) which transmit the parasites [1]. Several species of the plasmodium parasite exist but only four are parasites of man which are P. falciparum, P. ovale, P. vivax, and P. malariae.

Malaria plasmodia , a blood parasite , spend most of their complex life cycle intracellularly, primarily within their host–cell erythrocyte. Because of this association between the parasites and red cells, there are numerous consequences to the host's blood extending far beyond the direct effect of parasitized red blood cells, including severe anaemia, coagulation disturbances, leukocyte numerical or functional changes and spleen involvement and infrequently, disseminated intravascular coagulation . Haematological alterations that are thought to characterize malaria are related to the overt biochemical changes that occur during the asexual stage of the life cycle of the malaria parasite. Patients infected with malaria tend to have significantly lower platelet, leukocyte, lymphocyte, eosinophil, red blood cell, and haemoglobin (Hb) counts, while the number of monocytes and neutrophils was significantly higher than that in nonmalaria-infected patients Malaria infection in humans is associated with a reduction in the haemoglobin level frequently leading to anaemia, of which the most severe cases are seen in Plasmodium falciparum [3,4].

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Malaria infection also affects the haematopoietic physiology at any level and influences alterations in the haematological parameters resulting in numerous clinical presentations including anaemia [5,6]. This study therefore evaluated the haematological profile of adult individuals infected with the malaria parasite.

II. AIMS AND OBJECTIVES

1. To observe the incidence of alteration in hematological and coagulation profile parameters in malariainfection.
2. Correlation of hematological and coagulation profile of patients admitted in SMIMER hospital with the otherstudies.

III. MATERIALS & METHODS

The present study was conducted in Surat municipal institute of medical education and research, Surat, Gujarat. The study was carried out on 104 patients admitted during the period of November 2018-April 2020 these hospitals.A detailed history was taken followed by a detailed clinical examination to assess clinical severity and complications.All the patients in this study were proved to be cases of malaria by Peripheral smear examination (both thick and thin smear). These investigations were ordered before the antimalarial treatment was started.

Collected data were analyzed through SPSS version 20.0 (IBM Corp., NY). Descriptive variables were reported through mean with standard deviation and proportion. The association of the continuous variables was estimated by Student's t-test while that of the categorical variables was computed through Chi-square test. Pearson's correlation coefficient was used to find the correlation. $P < 0.05$ was considered significant.

The following investigations for haematological and coagulation
parameters were carried out:

- Haemoglobin estimation by cyanmethemoglobinmethod,
- RBC count by total and differential counts – using Neaberg'schamber.
- Total platelet count by modified Dacie Leursmethod.
- Whole blood clotting time by Lee whitemethod.
- Prothrombin time; activated partial thromboplastintime.
- PCV by Wintrobemethod

INCLUSION CRITERIA

1. Patients admitted under medicine department of our tertiary carehospital.
2. Peripheral smear positive for malaria(P.Vivax/P.Falciparum).
3. Willing to participate in thestudy.

EXCLUSION CRITERIA

1. Age < 18years.
2. Patients already having altered coagulationprofile.
3. Chronic liver diseasepatients
4. Fever due to any othercauses
5. Febrile thrombocytopenia of othercauses
6. Mix malariainfection

All the investigations were sent before the treatment was started.Once the patient was diagnosed to have malaria they were started on Anti-Malarial drugs according to the new WHO guidelines for treatment of Malaria. Other supportive treatment was given according to the patients conditions.

IV. OBSERVATION

Table No. 1SHOWING AGE DISTRIBUTION

Age group	Male	Female	Total	Percentage
20-30	30	11	41	39.42%
31-40	23	10	33	31.73%
41-50	7	7	14	13.46%
51-60	7	3	10	9.61%
>60	1	5	6	5.7%

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The numbers of males affected in our study were more compared to females. Total no of patients were 104 out of which 68 were male and 36 were female. In this study male: female ratio was 1.88:1. In this study the predominant age group affected was the age group between 20-40 years. More than 70% of the patients were young individual who were working age group. The numbers of people above the age of 60 years were very less i.e. 5.7%.There were no patients above the age of 70 years recorded in this study. The mean age in this study was 36 years.

Table No. 2 SHOWING NO. OF CASES OF P.VIVAX AND P.FALCIPARUM

Species	**No.**
P. Vivax	61.5% (64)
P.Falciparum	38.4% (40)
Total	100% (104)

Table No. 3 GRADING OF ANAEMIA IN P.VIVAX AND P.FALCIPARUM

Grading of Anemia	**P.Vivax (no of patients)**	**P.Falciparum (no of patients)**	**Total No.**
Mild anemia	23	7	30
Moderate anemia	16	10	26
Severe anemia	8	12	20
Total	47	29	76

Out of 104 patient 76 patients had Hb% less than 10.9 gm/dl. From 76 patients 30 had mild anemia (Hb-10-10.9gm/dl). 26 out of 76 had moderate anemia (Hb-7-9.9gm/dl). And 20 out of 76 had severe anemia (Hb-<7 gm/dl). Total 30 patients had mild anemia out of which 23 patients of P.Vivax and 7 patients of P.Falciparum. Out of 26 patients, 16 patients with P.Vivax and 10 patients with P.Falciparum had moderate anemia and out of 20, 8 patients with P.Vivax and 12 patients with P.Falciparum had severe anemia. Mean Hb for P.Vivax is 9.92±2.29 & Mean Hb for P.Falciparum is 9.18±2.59.

Table No. 4THROMBOCYTOPENIA IN P.VIVAX AND P.FALCIPARUM

Thrombocytopenia	**P.f (n=40)**	**P.V (n=64)**	**Total**	p value= 0.863
Present	34(85%)	51(79.68%)	85(81.73%)	
Absent	6(15%)	13(20.32%)	19(18.2%)	
Total	40	64	104	

Table No. 5 ASSOCIATION OF PARASITIC LOAD ON BLOOD AND PLATELET COUNT

Parasite load in blood	**Platelet**	
	Normal (no of patients)	**Decreased (no of patients)**
++++ (n=10)	0	10 (100)%
+++ (n=12)	0	12 (100%)
++ (n=46)	8 (17.4%)	38 (82.6%)

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+ (n=37)	11 (29.8%)	26 (70.2%)
Total (n=104)	18 (18.25%)	86 (81.75%)

In our study thrombocytopenia (<1, 50,000) was observed in 81.75% of the patients. Which are 85 out of 104 patients. Total 34 out of 40 patients of P.Falciparum showing thrombocytopenia&total51outof64patientsofP.Vivaxshowingthrombocytopenia.Total5 out of 34 patients, having severe thrombocytopenia (<50,000 / cumm) in case of P.Falciparum & 10 out of 51 patients of p vivax having severe thrombocytopenia. Mean value for P.Falciparum is 1.09 ± 0.42. As per table 18 there is association b/w parasite load inbloodandplateletcount.Asparasiteloadincreaseinbloodtherewasmoreprobabilityoflow platelet count. 10 out of 10 patients with +4 parasite load having low platelet count and also 12 out of 12 patients with +3 parasite load having low platelet count. Total 46 patients had +2 parasitic load out of which 38 patients had thrombocytopenia. And out of 37 patients with +1 parasite load 26 patients had thrombocytopenia.Mean value for P.Vivax is 1.10 ± 0.48.No statistically significant difference was seen regarding thrombocytopenia between P.Vivax &P.Falciparum (P value > 0.05).

TABLE NO. 6 SHOWING NO OF CASES WITH INCREASED APTT AND NORMAL APTT

aPTT	**P.Falciparum (n=40)**	**P.Vivax (n=64)**	
Increased	27.50%	17.18%	**P value =0.23**
Normal	72.50%	82.80%	

Mean aPTT was 30.7 seconds. It was increased in 14.42% (i.e. 15) of the total cases. It was found increased in 25% of (i.e. 10) patients with falciparum malaria & 7.81% of (i.e. 5) patients with vivax malaria had elevated aPTT.Normal value of aPTT is- 35 to 40 sec.Mean aPTT value for P.Vivax is 29.62±4.98 & Mean aPTT value for P.Falciparum is 32.56±7.98. There was no statistically significant difference seen. (P value =0.23)

TABLE NO. 7 SHOWING NO OF CASES WITH INCREASED PT AND NORMAL PT.

PT	**P.Falciparum**	**P.Vivax**	
	(n=40)	**(n=64)**	
Increased	27.50% (11)	17.18% (11)	**P value=0.008**
Normal	72.50% (29)	82.80% (53)	
Total	40	64	

It was increased in 21.15% of the total cases. The increase was noted in 27.5% of (i.e. 11) the patients with falciparum malaria. It was increased in 17.18% of (i.e. 11) patients with vivaxmalaria.Normal value of PT is up to 15 sec.Mean PT value for P.Vivax is 13.56±2.74 & Mean PT value for P.Falciparum is 15.26±3.61. Statistically significant difference is seen between P.Vivax and P.Falciparum. (P value is 0.008).

TABLE NO. 8 SHOWING NO OF CASES WITH INCREASED BT AND NORMAL BT.

BT	**P.Falciparum (n=40)**	**P.Vivax (n=64)**	**P value=0.049 (Fisher exact test)**
Increased	7.5% (3)	-	
normal	92.5% (37)	100% (64)	
Total	40	64	

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Bleeding time was increased in 7.5% of the total cases. Mean bleeding time was5.14 seconds. Bleeding time was increased in 7.5% of the falciparum cases. None of the pt with vivax malaria had increased bleeding time. Out of the 3 patients with increased bleeding time only 2 presented withbleeding. Normal value of BT: 2-7 min. Statistically significant difference is seen between P.Vivax and P.Falciparum. (P value is <0.05) in view of increase in bleeding time.

TABLE NO 9 : ASSOCIATION BETWEEN PARASITIC LOAD IN BLOOD AND COAGULATION PROFILE.

Parasite load blood	PT		aPTT		BT	
	Normal	Increased	Normal	Increased	Normal	Increased
++++(n=10)	0	10	3	7	8	2
+++ (n=12)	0	12	7	5	11	1
++ (n=46)	46	0	45	1	46	0
+ (n=37)	37	0	35	2	37	0
Total (n=104)	82	22	90	15	101	3

As per table 23 there is association b/w parasite load in blood and coagulation profile. As parasite load increase in blood there was more probability of deranged coagulation profile. Total 10 patients had +4 parasitic load out of which 10 patients had increased PT and 7 patients had increased aPTT and only 2 patients had increased BT. Total 46 patients had +2 parasitic load out of which only 1 patient had increased aPTT & none of the patient had increase in PT or BT. Out of 37 patients with +1 parasite load only 2 patients had deranged aPTT. Total 12 patients had +3 parasitic load out of which 12 patients had increased PT and 5 patients had increased aPTT and only 1 patients had increased BT.

TABLE NO. 10 NO. OF DEATHS.

	P.Falciparum	Pl. vivax	Total
NO OF DEATHS	2 (5%)	0	2(1.92%)

Overall P.Falciparum had higher incidence of anemia, thrombocytopenia, altered PT, aPTT, BT which may be the cause of high mortality in P.Falciparum than P.Vivax.

V. DISCUSSION

In our study the male to female ratio was 1.88:1 and compared to **Bhakshin et al**[7]females affected more in our study. The incidence of malaria was more in men than in women due to the working pattern i.e. men are exposed more to mosquito bites during outdoors work whereas females are less exposed.The working group is the age group which is predominantly affected, because this is the group which is exposed to the mosquito bites especially in the fields and outdoors. Also our study follows the age pyramid, in our country where the base is formed by young people and apex by the older age that constitute lesser percentage of the population. In a study by **Malhotra et al**[8]the percentage of people above fifty years was just 4%. Our study shows the percentage of people affected over 50 years was17.30%.The mean age in our study was more than the study done by **Sharma et al** and **Bhakshi et al. Mean age was 36 year in our study.**

Anemia was present in 73% of patients in our study. The incidence of severe anemia (Hb <7gm %) was seen in 19.23% of the patients and it was comparable to study done by **Mehta et al**[10]which had severe anemia incidence of 18%. The overall incidence of anemia was higher in studies conducted by **Sharma et al**[9]where the incidence was 86.7%. The higher incidence could be explained by the fact that their study involved with cases of falciparum malaria only. If we consider only falciparum cases even our study showed an incidence of 72.5%. Out of the 76 patients who had anemia only 39 patients had splenomegaly this indicates that there are other

factors other than splenic sequestration which could lead to anemia.

Thrombocytopenia was present in 81.73% of the cases in the present study. Thrombocytopenia was present in 85% of the cases with falciparum malaria in our study. In a study by **Horstmann et al**[11]the incidence of thrombocytopenia was 85%[66]. **Sharma S K et al** observed that 70% of the patients had thrombocytopenia. **Kuch et al**[12]had observed that 85% of the patients with falciparum malaria had thrombocytopenia[67]. In our study 79.68% of the patients with vivax malaria had thrombocytopenia. It was comparable to the study by **Horstmann et al**[11]where the incidence of thrombocytopenia in vivax malaria was 72%. There was no statistically significant difference seen for thrombocytopenia between p vivax and p falciparum. (p value=0.863)

In our study only 40 patients out of 85 had splenomegaly. It can be observed that only 47% 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.

Prothrombin time was increased in 21% of the total cases and it was increased in 27.5% of in cases with falciparum malaria. It was increased in 17.18% of the patients with vivax malaria. In a study conducted by **S.Roy et al**[13]PT was increased in 11.6% of cases. In a study of severe falciparum malaria cases by **R.Clemons et al**[14] PT was prolonged in 22.7% of the cases this was near similar to the observations in our study. There was statistically significant difference was seen b/w P.Vivax and P.Falciparum. (P value =0.008).In our study APTT was found to be increased in 14.42% of the patients. It was increased in 25% of the cases with falciparum malaria and7.81% of cases with vivax malaria. In a study conducted by **S.Roy et al**[13]APTT was increased in 16.6% of the patients this was similar to what we observed in our study. No statistically significance difference was seen regarding aPTT value b/w P.Vivax and P.Falciparum in our study. (P value = 0.23).

In our study 3 patients had increase in bleeding time. All 3(i.e.7.5% of falciparum cases) patients had P.Falciparum malaria. 2 out of these 3 patients had bleeding manifestations. In a study by **Sharma et al**[9] 6.7% of patients had increased bleeding time. In a study by **S Roy et al**[13]on falciparum malaria cases 5% of the patients had increased bleeding time. Our observations were comparable to both these studies. There was statistically significance difference seen in view of BT between P.Vivax and P.Falciparum. (P value <0.05).

In our study 55.76% of the patients had normocytic normochromic blood picture. It was comparable to a study by Sen et al61 where half the patients had normocytic normochromic blood picture. In our study 25% of the patients had microcytic hypochromic blood picture. This could be due to the prevalence of iron deficiency anaemia in our country**. Sen et al**[15] in their study also had microcytic hypochromic picture in 20% of cases..In our study prevalence of dimorphic anaemia was seen in 16.34% of the cases similar results were also observed by Sen et al where the prevalence of dimorphic anaemia was 20% in their study. Macrocytic hyperchromic anemia seen only in 3 patients.

Timely intervention in altered hematological and coagulation profile inmalaria patients may prevent complications like bleeding manifestation anddeath. This study was limited only to the patients of a tertiary care hospital with a small sample size that cannot be generalized to all population ofsociety.

Exclusion of other causes leading to alteration in hematological and coagulation profile in patients of malaria isrequired.

VI. CONCLUSION

Our study showed that the incidence of malarial cases is higher in males than females with peak incidence in 3rd and 4th decade.

- Anemia is the most common hematologicalabnormality.Thrombocytopenia is very common in malaria, but spontaneous bleeding israre.
- The higher incidence of P.Vivax in this study is due to the fact that
- PT and aPTT were prolonged in some cases, predominantly in falciparum but this does not result in spontaneous bleeding.
- BT was prolonged in 5% of the cases; most of them had spontaneous bleeding. It is also indicator of poorprognosis.
- Severe anemia is poor prognostic factor and it increased the duration of hospital stay and evenmortality.
- Overall P.Falciparum had higher incidence of anemia, thrombocytopenia, altered PT, aPTT.

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