

## A STUDY OF CLINICAL PROFILE OF MALARIA AND ITS ACUTE COMPLICATIONS CAUSED BY DIFFERENT SPECIES OF PLASMODIUM IN CHILDREN

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### ABSTRACT

#### BACKGROUND

Malaria is an insect-borne parasitic infection of tremendous global importance. India alone contributes 80% of south East Asia's malaria burden. Children are at the highest risk for severe disease and death between six months and five years of age.

#### MATERIALS AND METHODS

The aim of the study is to assess the clinical profile and complications caused by different species of plasmodium in children with malaria. This is a prospective, cross-sectional, observational study. Children from 1 month to 15 years of age diagnosed with malaria by standard laboratory tests are enrolled.

#### RESULTS

Majority of the study subjects belong to age group of <5 years (50.9%). 64% of the study subjects are boys and 36% are girls (36%). All the study subjects presented with fever (100%). Majority of the study subjects presented with splenomegaly (74.6%). The most common complication was anaemia (35.08%) followed by hepatitis (11.40%). Out of 40 anaemic patients, majority (62.5%) belong to <5 years age group. In smear for MP, PF is positive in 75.4%.

#### CONCLUSION

Cerebral Malaria, renal failure, bleeding diathesis, metabolic acidosis, pulmonary oedema, repeated convulsions, shock were noted only in Falciparum malaria. Mortality was 1.8% in this study. Majority of patients recovered.

#### KEY WORDS

Malaria, Species of Plasmodium, Acute Complications, Children

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#### BACKGROUND

Malaria is an insect-borne parasitic infection of tremendous global importance. According to the WHO, there were 214 million cases and 438, 000 deaths attributed to malaria in 2015<sup>1</sup>. A declining trend has been observed in the global incidence of malaria in recent years; in paediatric malaria also, the incidence decreased from 33% in 2000 to 16% in 2015.<sup>1</sup> India alone contributes 80% of south East Asia malaria burden.<sup>2</sup> India has by far the greatest estimated Plasmodium vivax burden of any country. Around 30% of all P. vivax cases in India occur in children aged 1–14 years, though these represent just 12% of the total population.<sup>3</sup> In a recent study by "million death collaboration", it was estimated that malaria accounts for 205, 000 deaths per year in India, with 55, 000 deaths occurring in early childhood.<sup>3</sup> Among the different human species of these protozoa, Plasmodium falciparum is responsible for most fatalities.<sup>1</sup>

Young children manifest this disease in many different ways, but the classic picture of malaria, with periodic fever, shivering, and sweating, is not observed. Children are at highest risk for severe disease and death between six months and five years of age: during this period children are most vulnerable as they have lost maternal immunity and they haven't yet developed specific immunity to infection.

Haematological and biochemical parameters are often abnormal: Features of severe or complicated malaria include respiratory distress, acidosis (pH <7.3), hypoglycaemia (<2.2 mmol/l), elevated aminotransferases, severe anaemia (Hb <5 g/dl), and high parasitaemia (defined as >5%–10% infected erythrocytes or more than 500 000 infected erythrocytes per microliter)<sup>4</sup>. Considering the above facts, the present study was undertaken to find out the spectrum of clinical manifestations, infecting species, age distribution and complications in children admitted with malaria.

#### Aim of The Study

To assess the clinical profile and complications caused by different species of plasmodium in children with malaria.

#### MATERIALS AND METHODS

This is a descriptive study conducted at Government District General Hospital, Vizianagaram, Andhra Pradesh, in the Department of paediatrics for a period of one year from June 2017 to May 2018. Children from ages of 1 month to 15 years of age diagnosed with malaria by standard laboratory tests are enrolled until sample size is attained after taking due

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consent. The study protocol is approved by Ethical committee.

**Inclusion Criteria**

1. Children from 1 month to 15 years of age admitted in paediatric ward diagnosed with malaria.
2. Diagnosis of malaria was done by using Smear for malarial parasite and/or RDT.

**Exclusion Criteria**

1. Children on empirical treatment for malaria but later found negative.
2. Children not willing to participate.
3. Children with other infections like enteric fever, meningitis, TB etc with coincidental smear positivity for malaria.

**Statistical Analysis**

Data entry and statistical analysis was performed with the help of Microsoft excel 2007 and SPSS version 20.0, while categorical variables are presented as number and percentages. Chi-square test is used to compare differences in categorical variables. The statistical significance level is fixed at p<0.05.

**RESULTS**

Age Category	Frequency	Percent
<5 YEARS	58	50.9
5-10 YEARS	41	36.0
11-15 YEARS	15	13.2
Total	114	100.0
Mean $\pm$ SD= 5.9704 $\pm$ 3.77861		

**Table 1. Age Distribution**

Majority of the study subjects belong to age group of <5 years (50.9%), followed by age group of 5-10 years (36%) and 11-15 years (13.2%).

Gender	Frequency	Percent
Girls	41	36%
Boys	73	64%
Total	114	100%

**Table 2. Gender Distribution**

64% of the study subjects are boys and 36% by girls (36%).

Locality	Frequency	Percent
Rural	28	24.6%
Tribal	83	72.8%
Urban	3	2.6%
Total	114	100%

**Table 3. Distribution of Children Based on Their Locality**

Majority of the study subjects belong to tribal locality (72.8%), followed by rural (24.6%) and urban (2.6%).

Symptoms	Frequency	Percent
Fever	114	100%
Headache	51	44.7%
Myalgia	34	29.8%
Vomiting	54	47.4%
Loose stools	26	22.8%
Abdominal distension	44	38.6%
Jaundice	9	7.9%
Bleeding	8	7.0%
Pallor	21	18.4%
Altered Sensorium	24	21.1%
Convulsions	7	6.1%
Dark urine	5	4.4%
Shortness of Breath	2	1.8%

**Table 4. Clinical Presentation of Malaria**

All the study subjects presented with fever (100%). 47.4% presented with vomiting, 44.7% with headache, 38.6% study subjects presented with abdominal distension, 29.8% with myalgia, 22.8% presented with loose stools, 21.1 % presented with altered sensorium, 18.4% presented with pallor, Jaundice observed in 7.9%, bleeding in 7.0%, convulsions in 6.1%, dark urine in 4.4% and shortness of breath in 1.8% of the study subjects.

Signs	Frequency	Percent
Pallor	52	45.6%
Icterus	12	10.5%
Hepatosplenomegaly	12	10.5%
Splenomegaly	85	74.6%

**Table 5. Clinical Signs of Malaria**

Majority of the study subjects presented with splenomegaly (74.6%), followed by pallor (45.6%), icterus (10.5%) and hepatosplenomegaly (10.5%).

Complications	Frequency	Percent
Anemia	40	35.08%
Hypoglycemia	4	3.50%
Cerebral Malaria	6	5.26%
Hepatitis	13	11.40%
Renal failure	4	3.50%
Bleeding diathesis	6	5.36%
Metabolic acidosis	4	3.50%
Pulmonary edema	2	1.75%
Repeated convulsions	1	0.87%
Shock	1	0.87%

**Table 6. Complications of Malaria**

In our study, the most common complication was anaemia (35.08%) followed by hepatitis (11.40%), Bleeding diathesis (5.36%), cerebral malaria (5.26%), hypoglycaemia (3.50%), renal failure (3.50%), metabolic acidosis (3.50%), pulmonary oedema (1.75%), repeated convulsions (0.87%) and shock (0.87%).

Complications	<5 Yrs		5-10 Yrs		11-15 Yrs		Total	P value
	n	%	n	%	n	%		
Anemia	25	62.5	12	30	3	7.5	40	0.15
Hypoglycemia	3	75	1	25	0	0	4	0.56
Cerebral Malaria	6	100	0	0	0	0	6	0.04*
Hepatitis	2	15.4	7	53.8	4	30.8	13	0.01*
Renal failure	2	50	1	25	1	25	4	0.74
Bleeding diathesis	2	33.3	3	50	1	16.7	6	0.67
Metabolic acidosis	3	75	1	25	0	0	4	0.56
Pulmonary edema	2	100	0	0	0	0	2	0.37
Repeated convulsions	0	0	1	100	0	0	1	0.40
Shock	1	100	0	0	0	0	1	0.61

**Table 7. Complications of Malaria According to Age Groups**

Out of 40 anaemic patients, majority (62.5%) belongs to <5 years. Out of 4 hypoglycaemic patients, majority (75%) belongs to < 5 years. Out of 6 cerebral malaria patients, all belongs to <5 years. Out of 13 hepatitis patients, majority (53.8%) belongs to 5-10 years. Out of 4 patients with renal failure, majority (50%) belongs to <5 years. Out of 6 patients with bleeding diathesis, majority (50%) belongs to 5-10 years. Out of 4 patients with metabolic acidosis, majority (75%) belongs to <5 years. One patient had repeated convulsions in the age group of 5-10 years. One patient had shock in the age group of <5 years. Statistical significance was found in cerebral malaria and hepatitis.

Laboratory tests	Smear for MP		RDT	
	Frequency	Percent	Frequency	Percent
PF	86	75.4	82	71.9
PF+PV	8	7.0	13	11.4
PV	20	17.5	19	16.7
Total	114	100	114	100

**Table 8. Laboratory Tests for Diagnosis**

RDT- Rapid Diagnostic Test, MP- Malarial Parasite

In smear for MP, PF is positive in 75.4%, PF+PV in 7% and PV in 17.5% cases. In RDT, PF is positive in 71.9%, PF+PV in 11.4% and PV in 16.7% cases.

Laboratory Investigations	PF		PF+PV		PV		Total	P Value
	n	%	n	%	n	%		
Increased TSB	9	69.2	2	15.4	2	15.4	13	0.45
Decreased RBS	4	66.7	0	0	2	33.3	6	0.49
Abnormal RFT	5	100	0	0	0	0	5	0.42

**Table 9. Profile of Other Laboratory Parameters**

TSB-Total Serum Bilirubin. RBS-Random blood sugar, RFT Renal function of test

Out of 13 patients with increased TSB, majority (69.2%) were PF positive. Out of 6 patients with decreased RBS, majority (66.7%) were PF positive. Out of 5 patients with abnormal RFT, all were PF positive. But the association between them was found to be statistically not significant.

Symptoms	PF		PF+PV		PV		Total	P Value
	n	%	n	%	n	%		
Fever	86	75.4	8	7	20	17.5	114	-
Headache	38	74.5	3	5.9	10	19.6	51	0.81
Myalgia	27	79.4	1	2.9	6	17.6	34	0.53
Vomiting	43	79.6	6	11.1	5	9.3	54	0.03*
Loose stools	19	69.2	1	3.8	6	23.1	26	0.57
Abdominal distension	32	72.7	4	9.1	8	18.2	44	0.55
Jaundice	7	77.8	1	11.1	1	11.1	9	0.79
Bleeding	8	100	0	0	0	0	8	0.24
Pallor	18	85.7	1	4.8	2	9.5	21	0.47
Altered Sensorium	20	83.3	2	8.3	2	8.3	24	0.40
Convulsions	7	100	0	0	0	0	7	0.29
Dark urine	5	100	0	0	0	0	5	0.42
Shortness of Breath	2	100	0	0	0	0	2	0.71

**Table 10. Symptoms in Various Species of Plasmodium**

Patients with bleeding, convulsions, dark urine, shortness of breath are 100% positive for PF. Patients with Pallor and altered sensorium are around 80-90% positive for PF. Patients with fever, headache, myalgia, vomiting, loose stools, abdominal distension, jaundice are around 70-80% positive for PF.

Signs	PF		PF+PV		PV		Total	P Value
	n	%	n	%	n	%		
Pallor	41	78.8	2	3.8	9	17.3	52	0.49
Icterus	9	75	1	8.3	2	16.7	12	0.91
Hepato-splenomegaly	10	83.3	1	8.3	1	8.3	12	0.56
Splenomegaly	68	80	5	5.9	12	14.1	85	0.05*

**Table 11. Signs in Various Species of Plasmodium**

Hepato-splenomegaly is present in 83.3% PF positive cases, splenomegaly is present in 80% PF positive cases, pallor is present in 78.8% PF positive cases and icterus in 75% PF positive cases. Splenomegaly in falciparum and vivax species shows statistical significance.

Complications	PF		PF+PV		PV		Total	P Value
	n	%	n	%	n	%		
Anemia	32	80	3	7.5	5	12.5	40	0.58
Hypoglycemia	3	75	1	25	0	0	4	0.26
Cerebral Malaria	6	100	0	0	0	0	6	0.35
Hepatitis	9	69.2	1	7.7	3	23.1	13	0.84
Renal failure	4	100	0	0	0	0	4	0.50
Bleeding diathesis	6	100	0	0	0	0	6	0.35
Metabolic acidosis	4	100	0	0	0	0	4	0.50
Pulmonary edema	2	100	0	0	0	0	2	0.71
Repeated convulsions	1	100	0	0	0	0	1	0.84
Shock	1	100	0	0	0	0	1	0.84

**Table 12. Complications in Various Species of Plasmodium**

Patients with complications of cerebral Malaria, renal failure, bleeding diathesis, metabolic acidosis, pulmonary oedema, repeated convulsions, shock are 100% positive for PF. Anaemia is present in 80% PF positive cases, hypoglycaemia in 75% PF positive cases and hepatitis in 69.2% PF positive cases.

Haemoglobin category		Smear for MP			Total
		PF	PF+PV	PV	
<5.0 g/dl	n	26	2	4	32
	%	30.2%	25.0%	20.0%	28.1%
5.0-7.0 g/dl	n	13	2	1	16
	%	15.1%	25.0%	5.0%	14.0%
>7.0 - 10.0 g/dl	n	47	4	15	66
	%	54.7%	50.0%	75.0%	57.9%
Total	n	86	8	20	114
	%	100.0%	100.0%	100.0%	100.0%

**Table 13. Association Between Anaemia and Species of Plasmodium**

PF positive have 54.7%, PF+PV positive have 50%, PV positive have 75% of patients with haemoglobin of >7.0-10 g/dl. But the association between them is not statistically significant.

Outcome	Frequency	Percent
Death	2	1.8%
Recovered	111	97.4%
Referral	1	0.9%
Total	114	100%

**Table 14. Distribution of Outcome**

97.4% patients recovered from illness, death occurred in 1.8% patients.

Outcome	Death	n	Age category			Total
			<5 YEARS	5-10 YEARS	11-15 YEARS	
Death		n	1	0	1	2
		%	1.7%	0.0%	6.7%	1.8%
Recovered		n	57	40	14	111
		%	98.3%	97.6%	93.3%	97.4%
Referral		n	0	1	0	1
		%	0.0%	2.4%	0.0%	0.9%
Total		n	58	41	15	114
		%	100.0%	100.0%	100.0%	100.0%

**Table 15. Association Between Outcome and Age Category**

98.3% patients recovered in <5 years age group, 97.6% patients recovered in 5-10 years age group and 93.3% patients recovered in 11-15 age group years. But the association between them was found to be statistically not significant.

**DISCUSSION**

- Majority of the study subjects belong to age group of <5 years (50.9%), followed by age group of 5-10 years (36%) and 11-15 years (13.2%). In a study by Tarakeswara Rao et al,<sup>5</sup> Majority of the study subjects belong to age group of <5 years (47.2%), followed by age group of 5-10 years (29.6%) and 11-15 years (19.4%). In the study by Sathpathy et al<sup>6</sup> 62.8% cases of malaria were above 5 years.
- Majority of the study subjects were boys (64%) followed by girls (36%).

Gender	Murthy GL et al <sup>7</sup>	Talib VH et al <sup>8</sup>	Sathpathy SK et al <sup>6</sup>	Tarakeswara Rao et al <sup>5</sup>	Present Study
Boys	69.6%	66.7%	62.5%	67.6%	64.0%
Girls	31.4%	33.3%	37.5%	32.4%	36.0%

**Table 16. Comparison of Gender in Different Studies**

- All the study subjects presented with fever (100%). Majority of the patients presented with vomiting (47.4%) and headache (44.7%). 38.6% study subjects presented with abdominal distension, 29.8% presented with myalgia, 22.8% presented with loose stools, 21.1% presented with altered sensorium, 18.4% presented with pallor, Jaundice in 7.9%, bleeding in 7.0%, convulsions in 6.1%, dark urine in 4.4% and shortness of breath in 1.8% of the study subjects.

Clinical Features	Mehta SR et al <sup>9</sup>	Murthy GL et al <sup>7</sup>	Talib VH et al <sup>8</sup>	Tarakeswara Rao et al <sup>5</sup>	Present Study
Fever	94.6%	98.10%	97.76%	100%	100%
Headache	33.45%	33.4%	73.81%	-	44.7%
Myalgia	-	-	67.59%	-	29.8%
Vomiting	8.47%	-	54.75%	-	47.4%
Diarrhoea	-	5.64%	-	-	22.8%
Breathlessness	1.17%	0.63% %	-	13.9%	1.8%
Convulsion	-	2.53%	-	18.5%	6.1%
Bleeding	0.7%	4.43%	0.16%	-	7%
Pallor	-	-	-	43.5%	45.6%
Icterus	2.58%	23.41%	-	10.2%	10.5%
Splenomegaly	-	-	29.60%	28.7%	74.6%
Hepatosplenomegaly	-	-	24.58%	25.9%	10.5%

**Table 17. Comparison of Clinical Features in Different Studies**

**Symptoms**

**Fever**

100% of patients had complained of fever. A study by Murthy GL et al<sup>7</sup> showed that fever 77 with chills and rigors in 98.10% of patients which is comparable. Another study by Talib VH et al<sup>8</sup> showed it to be 97.76%.

**Headache**

Headache was present in 44.7% of patients. It was present in 33.4% in study by Murthy GL et al<sup>7</sup> and 33.45% in study by Mehta SR et al.<sup>9</sup>

**Myalgia**

In our study it was seen in 29.8% of patients. The study by Talib VH et al<sup>8</sup> showed it was in 67.59%.

**Vomiting**

In our study it was present in 47.4% of patients. In study by S.R. Mehta SR et al<sup>9</sup> it was 8.47% and study by Talib VH et al<sup>8</sup> it was 57.75%.

**Jaundice**

Yellowish discoloration of eyes was complained by 10.5% of our patients. It was 23.41% in study by Murthy GL et al<sup>7</sup>. High incidence of jaundice was because of the haemolysis caused by malaria parasite.

**Diarrhoea**

22.8% of our patient had diarrhoea. In the study by Murthy GL et al<sup>7</sup> it was 5.64%

**4. Bleeding**

The incidence was 7% in our study. It was 4.43% in the study by Murthy GL et al.<sup>7</sup>

Splenomegaly was present in 63% cases in our study.

This finding is consistent with study by Milind BK et al<sup>10</sup> where splenomegaly was present in 53% of cases. Hepatomegaly was seen in 52% cases in our study. In a study by Milind BK et al<sup>10</sup> hepatomegaly was seen in 47% of cases.

- In smear for MP, PF is positive in 75.4%, PF+PV in 7% and PV in 17.5% cases. In RDT, PF is positive in 71.9%, PF+PV in 11.4% and PV in 16.7% cases. In a study by Verma P et al,<sup>11</sup> Maximum number of patients were of Pf (57.8%); Pv was documented in 13.7% and mixed infection in 27.4% cases.
- Patients with bleeding, convulsions, dark urine, shortness of breath were 100% positive for PF. Patients with Pallor and altered sensorium were around 80-90% positive for PF. Patients with fever, headache, myalgia, vomiting, loose stools, abdominal distension, jaundice were around 70-80% positive for PF.
- Hepato-splenomegaly is present in 83.3% PF positive cases, splenomegaly is present in 80% PF positive cases, Pallor is present in 78.8% PF positive cases and icterus is present in 75% PF positive cases. Splenomegaly shows statistical significance.
- Patients with complications of cerebral Malaria, renal failure, bleeding diathesis, metabolic acidosis, pulmonary oedema, repeated convulsions, shock were 100% positive for PF. Anaemia is present in 80% PF positive cases, hypoglycaemia is present in 75% PF positive cases and hepatitis is present in 69.2% PF positive cases.

Complication	Murthy GL et al <sup>7</sup>	Kochar DK et al <sup>12</sup>	Mohapatra MK <sup>13</sup>	Satpathy et al <sup>6</sup>	Al-Taiar A et al <sup>14</sup>	Mockenhau Pt <sup>15</sup>	Present study
Anaemia	74.68%	26.04%	6.9%	26%	37%	55%	35.08%
Cerebral Malaria	48.1%	10.94%	74.3%	40%	8%	17%	5.26%
Acute Renal Failure	24.68%	6.25%	-	14%	9%	-	3.50%
Hypoglycaemia	8.22%	1.56%	-	13%	8%	17%	3.50%
Hypotension/Shock-	-	10.94%	-	-	-	-	0.87%
Bleeding Diathesis	16.45%	25.52%	-	3.7%	3%	-	5.36%
Pulmonary Oedema	11.39%	2.08%	-	2%	-	-	1.75%

**Table 18. Comparison of Complications in Different Studies**

9. In our study, the most common complication was anaemia (35.08%) followed by hepatitis (11.40%), Bleeding diathesis (5.36%), cerebral malaria (5.26%), hypoglycaemia (3.50%), renal failure (3.50%), metabolic acidosis (3.50%), pulmonary oedema (1.75%), repeated convulsions (0.87%) and shock (0.87%).
- In a study by Murthy GL et al,<sup>7</sup> anaemia (74.6%) and cerebral malaria (48.1%) were the common manifestations.
  - In a study by Kochar et al,<sup>12</sup> anaemia were most common manifestations followed by DIC and cerebral malaria. This shows that the spectrum of common manifestations and complications of malaria vary in different geographical regions depending upon parasitic factor, epidemiological factors and host defence factors.
10. PF positive cases (54.7%), PF+PV positive cases (50%), PV positive cases (75%) are more in patients with haemoglobin of >7.0-10 g/dl. But the association between them was found to be statistically not significant.

Haemoglobin (gm %)	Murthy GL et al <sup>7</sup>	Present Study
Mild (>7-10)	43.67%	57.9%
Moderate (5-7)	21.51%	14%
Severe (<5)	9.49%	28.1%

**Table 19. Comparison of Haemoglobin in Different Studies**

11. 97.4% patients recovered from illness, death occurred in 1.8% patients. The Overall mortality was 1.8% in our study. Out of 2 deaths, one due to falciparum and another due to vivax. 98.3% patients recovered in <5 years age group, 97.6% patients recovered in 5-10 years age group and 93.3% patients recovered in 11-15 age group years. But the association between them was found to be statistically not significant.

	Kochar et al <sup>12</sup>	Sathpathy et al <sup>6</sup>	Al Taiar A et al <sup>14</sup>	Mockenhaupt <sup>15</sup>	Tarakeswara Rao et al <sup>5</sup>	Present Study
Mortality %	10.93%	9.9%	3.2%	11.2%	5.5%	1.8%

**CONCLUSION**

Majority of the subjects in this study were <5 years of age and most were males. All the study subjects presented with fever. Majority of the patients also had vomiting and headache. A third of patients had abdominal distension and myalgias. Less prevalent symptoms were bleeding, convulsions, dark urine and shortness of breath. On examination, majority of the subjects had splenomegaly and pallor. Complications like anaemia, hypoglycaemia, renal failure, cerebral malaria, metabolic acidosis, shock were more prevalent in <5 years age group. Majority were infected with falciparum malaria and also had more complications. Cerebral malaria, renal

failure, bleeding diathesis, metabolic acidosis, pulmonary oedema, repeated convulsions, shock were noted only in falciparum malaria. Mortality was 1.8% in this study. Majority of patients recovered.

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