Original Research Article

Study of malaria and associated co-morbidity in children admitted with fever manifestation in a tertiary care centre

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ABSTRACT

Background: Children under five year of age are highly vulnerable to malaria infection and often face dire consequences such as severe malaria if they are not promptly and adequately treated with anti-malarial medications. Authors set out to evaluate malaria and associated co-morbidity among children admitted with febrile illness in tertiary care center NSCB Medical college Jabalpur, India.

Methods: This prospective and analytic study focused on children admitted with fever in pediatric unit of N.S.C.B. Medical College, Jabalpur, Madhya Pradesh, India. If any co-morbidity present with malaria their manifestation was noted. Association of co-morbidity with malaria was done, and effect of co-morbidity on severity of malaria and outcome of patients was noted.

Results: A total number of 1950 of children suspected to have malaria who were tested by RDT and microscopy (PSMP), out of them 100 children were positive. Mean age calculated was 7.3±4.3 years. Maximum number of severe malaria cases (40.6%) were found in 6 months to <5 years age group. Most common co-morbidity associated with malaria was anemia (53%) followed by pneumonia (36%) hepatitis (26%), diarrhea (24%), enteric fever (15%), septicemia and meningoencephalitis (10%) each, UTI (4%), and AKI (6%), while dengue (3%) and severe acute malnutrition (2%). Out of 69 cases of severe malaria 46.3% cases had two and 34.7% cases had more than two co-morbidities while in 31 cases of uncomplicated malaria 38.7% cases had two co-morbidity and only 3% had more than two co-morbidity.

Conclusions: All RDT positive cases have associated co-morbidity with malaria in our study, more is the co-morbidity is longer were the duration of stay and higher the complications and even mortality.

Keywords: Anemia, Children, Febrile, Malaria, Pneumonia, Prospective

INTRODUCTION

Malaria, infected 500000 and killed over 60000 men in World War II, still continues to be a significant health problem in 21st century. According to the latest WHO estimates, there were 212 million cases of malaria in 2015 and 4,29,000 deaths. The incidence of malaria is estimated to have decreased by 41% globally between 2000 and 2015, and by 21% between 2010 and 2015.Malaria mortality rates are estimated to have declined by 62% globally between 2000 and 2015 and by 29% between 2010 and 2015. In children aged under 5 years, mortality rate estimated to have fallen by 69% between 2000 and 2015 and by 35% between 2010 and 2015.[1] In India, the malaria incidence and deaths due to malaria have reduced significantly in recent years. The API (Annual Parasite Index) has also been declining from 3.29 in 1995 to 0.9 in 2015.[2] About 92% of malaria cases and 97% of deaths due to malaria is reported from North-Eastern states, Chattisgarh, Jharkhand, Madhya Pradesh, Orissa, Andhra Pradesh, Maharashtra, Gujarat, Rajasthan, West Bengal and Karnataka.[3] In general, severity of symptoms and risk of death increase with increasing parasitaemia *P. falciparum* malaria is the most severe

form of malaria, with fatality rates up to 15% in non-immune children with anaemia and severe respiratory distress if appropriate therapy is not promptly instituted. *P. falciparum* is the only Plasmodium species that infects all ages of erythrocytes, it can lead to intense parasitaemia that can reach 60% or more.[4]

The present prospective study was undertaken to assess the malaria, complications of malaria, association with any co-morbidity, and outcome in children admitted with fever manifestation in tertiary care center NSCB Medical college Jabalpur, India.

METHODS

This prospective and analytic study was carried out in the Department of Pediatrics, NSCB Medical College, Jabalpur over a period of 18 months from March 2016 to August 2017. All the admitted children were examined for clinical signs of malaria and tested for malarial antigen using Rapid Diagnostic Kits and peripheral smear for microscopy. The patient included in the study after taking consent from their parents. Information regarding demographic profile was taken.

Complete history was taken enquiring about history of fever, chills and rigors, headache, vomiting, convulsions, oliguria or hematuria, jaundice, or any other complaints, and duration of illness. Thorough clinical examination was done to assess the vitals, pallor, icterus, per abdominal examination to look for organomegaly and other relevant systemic examination was done. Malaria severity was classified as per WHO guideline.

All positive malaria cases examined/tested for various other co-morbidities according the clinical presentation. The patients were tested for complete hemogram, blood sugar, serum electrolytes, renal function tests, liver function tests, Widal test, G6PD, DCT, Cerebrospinal fluid examination. Association of co-morbidity with malaria was done, and effect of co-morbidity on severity of malaria and outcome of patients was noted.

Statistical analysis

The data was recorded in the predesigned proforma and analyzed by using statistical software -SPSS version 20. Association and correlation of qualitative data was tested by chi square test and Fischer exact test, Student- t test was applied in quantitative data. A p value <0.05 was considered significant.

RESULTS

A total of 100 patients who were positive for malaria were included in this study, out of 100 cases, 69 cases had severe malaria while 31 cases had uncomplicated malaria. Out of 100 cases 33% cases (n=33) were in the age group 6 month to <5 years, while 35% (n=35) were between 5 to <10 years and 32 % (n=32) cases were between 10 to 14 years. Mean age was 7.3±4.3 years. Maximum number of severe malaria cases (40.6%) were found in 6 months to <5 years age group. There was slightly higher male preponderance with 58 % (n=58) Males and 42 % (n=42) females. Severity of malaria was equal in both genders.

A total number of 68 (68%) patients belongs to rural areas (63%), rest 37 (37%) were residents of urban areas. Majority 47% (n=47) were having P. falciparum Malaria, 26% (n=26) were having *P. vivax* Malaria and 27% (n=27) were having Mixed (*P. vivax* + *P. falciparum*) infection.

Maximum malaria cases were found in the month of June to October. Most common co-morbidity associated with malaria in our study was anemia which had 53% of cases. Pneumonia (36%) was the second most common co-morbidity, hepatitis was the third most common (26%), and diarrhea was the fourth most common (24%), followed by enteric fever (15%), septicemia and meningoencephalitis have equal distribution (10%), four cases of UTI, and 6 cases of AKI, while 5 had other cases (3 cases of dengue and 2 cases of severe acute malnutrition) (Figure 1).

Table 1: Distribution of co-morbidities (species wise).

Comorbidity	*P. vivax* N=26 (%)	*P. falciparum* N=47 (%)	Mixed N=27 (%)
Anemia	11 (42.3)	28 (59.5)	14 (51.8)
Hepatitis	4 (15.3)	15 (31.9)	7 (25.9)
Pneumonia	8 (30.3)	19 (40.4)	10 (37)
Diarrhoea	7 (26.9)	11 (23.4)	3 (11.1)
Enteric fever	5 (19.2)	5 (10.6)	5 (18.5)
Septicemia	5 (19.2)	2 (4.2)	3 (11.1)
Meningoenchephalitis	4 (15.3)	5 (10.6)	1 (3)
Acute kidney injury	1 (3.8)	3 (6.3)	2 (7)
UTI	1 (3.8)	1 (2.1)	2 (7)
Other	0 (0)	2 (4.2)	3 (11.1)
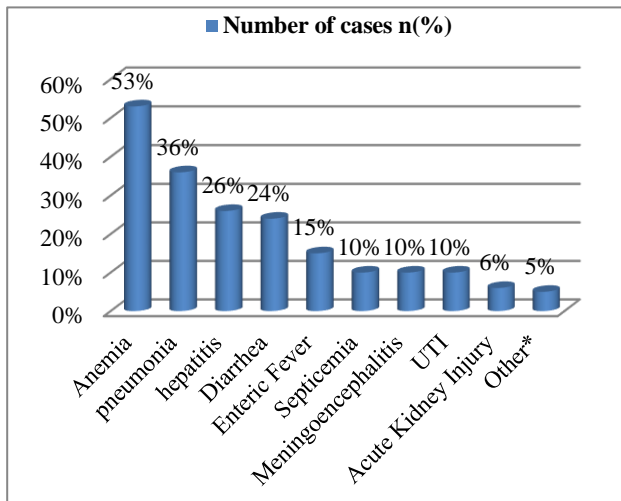
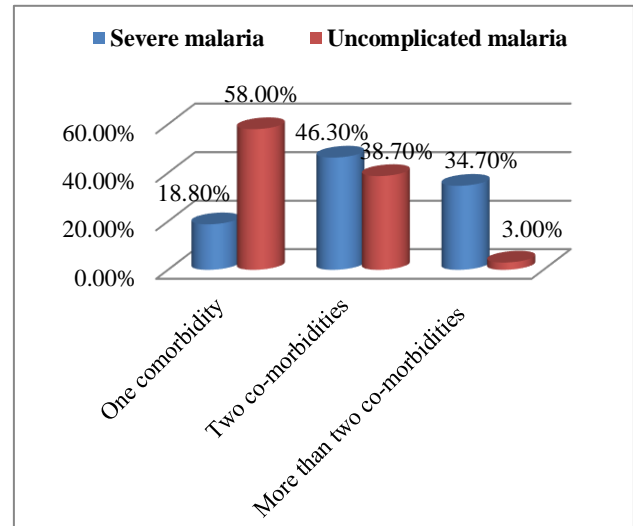**Figure 1: Distribution of co-morbidities in malaria cases.**

In the *P. vivax* group (n=26) anemia (42.3%) was most common co morbidity followed by pneumonia (30.3%), Diarrhea (26.9%), enteric fever (19.2%), and septicemia (19.2%). In *P. falciparum* (n=47) species anemia (59.5%) was more common co-morbidity in followed by pneumonia (40.4%), Hepatitis (31.9%), diarrhea (23.4%) and enteric fever (10.6%). Anemia was most common co-morbidity in both the species. Hepatitis was most commonly associated with *P. falciparum* species. Septicemia was more common in *P. vivax* species. *Plasmodium falciparum* species have more number of co-morbidities compare then *P. vivax* and mixed infection (Table 1). Out of 69 cases of severe malaria the most common co-morbidity was anemia 43(62.3%), followed by hepatitis (34.8%), pneumonia (33.3%), diarrhea (21.7%), and enteric fever (15.9%), Septicemia and meningoencephalitis (13%) each. While among 31 cases of uncomplicated malaria the most common co-morbidity was pneumonia 13 (41.3%) and anemia (32.3%) (Table 2).

Table 2: Severity wise distribution of co-morbidities among THR RDT positive cases.

Co-morbidity	Severe malaria N=69 N (%)	Uncomplicated malaria N=31 N (%)
Anemia	43 (62.3)	10 (32.3)
Pneumonia	23 (33.3)	13 (41.9)
Hepatitis	24 (34.8)	2 (6.5)
Diarrhea	15 (21.7)	9 (29.0)
Enteric fever	11 (15.9)	4 (12.9)
Septicemia	9 (13.0)	1 (3.2)
Meningoencephalitis	9 (13.0)	1 (3.3)
UTI	4 (5.8)	0 (0.0)
Acute kidney injury	4 (5.8)	2 (6.5)
Other	4* (5.8)	1**(3.2)

*Dengue=2, SAM=2, **Dengue=1

In this study out of 69 cases of severe malaria 32 (46.3%) cases and more than two (34.7%) co-morbidities while in uncomplicated malaria 18(58%) cases having only one co-morbidity. There was significant relationship between number of co-morbidity associated with malaria and severity of malaria (p value=<0.001). Severe malaria had more number of co-morbidities (Figure 2).

Figure 2: Distribution of number of co-morbidity according to severity of malaria.

In this study 25 cases had duration of stay up to 7 days, out of them 21 (84%) cases have one co-morbidity and 4 (16%) cases were having 2 co-morbidities.75 cases had duration of stay more than 7 days, out of them 10 (13.3%) cases were one co-morbidity, 40 (53.3%) cases were two co-morbidities and 25 (33.3%) cases were more than two co-morbidities. Those patients who have duration of illness for more than seven days were associated with more number of co-morbidities (p value=<0.001) (Table 3).

Table 3: Effect of number of co-morbidities on duration of stay in hospital.

Co-morbidty (n=Number of co-morbidities)	Duration of stay	
	0-7 days	>7 days
	N=25	N=75
	n (%)	n (%)
1	21 (84)	10 (13.3)
2	4 (9.09)	40 (53.3)
More than 2	0	25 (33.3)
Total	25	75

Out of 9 mortalities in this study there were 9 (100%) patient were died due to severe malaria, out of them 2 (22.2%) patients have two co-morbidity and 7 (77.8%) patients have more than two co-morbidity. In the uncomplicated malaria cases no mortality was found. There was significant relationship of number of co-morbidities with mortality (p value<0.001) (Table 4).

Table 4: Correlation of number of co-morbidities with the mortality of patient.

Severity	One co-morbidity (n=31)	Two co-morbidity (n=44)	More than two co-morbidity (n=25)	Total
Severe malaria n=(69%)	0	2 (22.2)	7 (77.8)	7 (100)
Uncomplicated malaria n (31%)	0	0	0	0
Total n=9(%)	0	2 (22.2)	7 (77.8)	9 (100)

Out of 69 cases of severe malaria 87% patients were discharged, and mortality is 13% in severe malaria cases. All the cases which died were having two or more co-morbidities associated with severe malaria (Figure 1).

DISCUSSION

Total of 100 cases of malaria admitted in Department of Pediatrics (Smt. Jyotsna Devi Patel, Pediatric Centre, N.S.C.B. Medical College, Jabalpur) from March 2016 to August 2017 were included in the study. All the patients presenting with complaints of fever and other features suggestive of malaria were tested for the presence of malarial parasite using RDT kits and microscopic examination. Authors found RDT malaria positive 100 cases out of them 18 cases were microscopy positive.

Demographic and parasitic profile

Malaria affects all ages and both sexes, in present study it is more common in males (n=58, 58%). Male: female ratio is 1.4:1. Desai PD et al conducted a study in tertiary centre in Ahmedabad, Gujarat founds males were more commonly affected (67.89%) than females (32.10%).[5] Male: Female ratio is 2.1:1. Kaushik JS et al, conducted a study on malaria in a tertiary-care in East Delhi,they found that it is more common in males.[6]

Children up to 14 years of age were included in the study. Mean age of presentation is 7.339. Standard deviation calculated is 4.3704. 33% patients (n=33) were in the age group 6mnth to <5 years, 35% (n=35) in the age group of 5 to <10 years and 32% (n=32) in the age group of 10-14 years. This is in accordance with the study done by Gehlawat VK et al, in which there were equal distribution of patients in age group <5 years, 5-10 years and >10 years, with 6 patients in each group.[7] There is only 1 case of malaria seen in infant <1 year of age. The low incidence in infancy is attributed to passive transfer of maternal antibodies through placenta, also to relatively small surface area in infants and neonates and sole milk diet which is rich in para amino benzoic acid (PABA).

In this study majority (63%) of cases belonged to Rural areas. In a study by Gohiya P et al, in GMC Bhopal (MP), 80% cases were admitted from adjacent rural area which explains the patient drainage of tertiary centres in Madhya Pradesh, India.[8] The parasitic profile noted in present study is *P. vivax* in 26% patients (n=26), *P. falciparum* in 47% (n=47) and Mixed infection positive for both vivax and falciparum in 27% patients (n=27), In a study by Kochar DK et al, the proportion of *P. falciparum*, *P. vivax*, and mixed (*P. falciparum* and *P. vivax*) infection is 61.01%, 33.99%, and 4.95%, respectively.[9]

Co-morbidity with malaria

In this study most common co-morbidity associated with malaria was anemia which is seen in 53 (53%) of cases. Pneumonia (36%) is the second most common co-morbidity, hepatitis is the third most common (26%), and diarrhea is the fourth most common (24%), followed by enteric fever (15%), septicemia and meningoencephalitis have equal distribution each have 10 (10%) cases, 4 (4%) cases of UTI, and 6 (6%) cases of AKI, while 5 (5%) had other cases 3 (3%) cases of dengue and 2 (2%) cases of severe acute malnutrition (Figure 1). However there is no known study in India on malaria and associated co-morbidities in children, Orish VN et al, conducted a study in Ghana and they found anemia as the most common co-morbidity in their study and it was present in 64.7% of cases, while anemia is common morbidity in children of developing counties so it can be found most common co-morbid condition with malaria in children.[10] According to National Family Health Survey-4 in Madhya Pradesh 68.9% Children between the age group of 6-59 months are anemic out of them 66.3% from urban and 69.9% from rural areas.[11] Authors found pneumonia was the second most common followed by hepatitis and diarrhea. According to NFHS-4 conducted in M.P. India, Children with fever or symptoms of ARI in the last 2 weeks preceding the survey taken to a health facility is 70.9%, out of them 79.6% from urban and 68.3% from rural areas. (Figure 1).[11]

Malaria with anemia co-morbidity

In our study 53% malaria cases have anemia co-morbidity (Figure 1). Study conducted by Choube A et al, in Rama medical college U.P., India where anemia was present in 35.5% of cases, whereas in another study conducted by Kashikunti in Karnataka India where anemia was found in 69% anemia co-morbidity in malaria cases.[12,13] Authors found the equal distribution of male and female in anemia co-morbidity. Authors found anemia co-morbidity in 62.3% severe malaria cases, and 32.3% in uncomplicated malaria cases, anemia co-morbidity most commonly present with severe malaria

cases in our study (Table 1). Meena HM et al, in Jaipur, India found 69% anemia co-morbidity in their study of severe malaria. This study corresponding to Meena HM et al study.[14]

Malaria with pneumonia co-morbidity

Pneumonia was second most common co-morbid condition after anemia in our study, we found 36 (36%) pneumonia cases with malaria (Figure 1). Few studies done on malaria and pneumonia co-morbidity E Etiaba et al, found most common co-morbidity with malaria was Upper respiratory tract infection (57.7%).[15]

Malaria with hepatitis co-morbidity

Hepatitis is another common co-morbid condition after anemia and pneumonia in our study, we found 26% cases of malaria with hepatitis in this study (Figure 1). Singh R et al, conducted a study in Uttarakhand, India and they found 25% hepatitis cases in there study so this study correspondence to this study another study conducted by Sonwane VB et al, in Mumbai India and they found that hepatic dysfunction is 16% patients in their study.[16,17] Authors found 24 (34.8%) hepatitis as a co-morbidity cases were present with severe malaria, out of these 57.6% (15) cases were co-infected with *P. falciparum* species, while only 4 (15.3%) cases were with vivax species (Table 2). Kochar et al, conducted a study on malaria hepatitis in India and they found hepatic dysfunction is alone a common co-morbidity with malaria in their study.[9] They found 48% severe malaria cases have hepatitis co-morbidity.

Malaria with diarrhoea co-morbidity

Diarrhea was another common co-morbid condition with malaria in this study (Figure 1). Authors found 24 (24%) cases of malaria with diarrhoea in this study. Morris SK et al, found 15% of malaria cases associated with diarrhea.[18] Authors found us of 15 (62.5%) cases were associated with severe malaria, 52.3% (11) cases are co-infected with *P. falciparum* species, while only 7 (33.3%) cases are with *P. vivax* species (Table 1).

Enteric fever

Enteric fever was another common co-morbid condition with malaria in our study. Authors found 15 (15%) cases of malaria with enteric fever in this study (Figure 1), Afoakwah R et al, conducted a study in Ghana which where they found found 17.0% cases positive for typhoid fever, so our study correlates to Afoakwah R et al study.[19]

Co-morbidity and outcome association

Authors found that out of 100 cases of malaria all were associated with co-morbidities out of them 84 (84%) patients were successfully discharged after completion of treatment, 8 (8%) patients went LAMA because, all of them wanted to take their children to private hospital for further treatment) (Table 4).

Mortality was found to be 9% (9 cases) in this study. Authors found that out of 69 cases of severe malaria 87% (60 cases) patients discharged successfully, and mortality rate is 13% (9 cases) in severe malaria cases) (Figure 4). Tripathi R et al, also found 12% mortality in severe malaria cases in their study in Orissa which is comparable to this observation.[20]

Limitation of this study was to there were few studies done in India on malaria and associated co-morbidities, so this study requires further validation.

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