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Study of complex associations between severe malaria and malnutrition in pediatric age group

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ABSTRACT

Background: In India, severe Malaria as well as malnutrition is quite prevalent in children. Till now, relationship between malnutrition and malaria remains inconclusive. Therefore, this study was carried out as an attempt to find relationship between severe malaria and malnutrition in pediatric age group.
Materials and methods: Study design was observational and was conducted in a tertiary care center in Uttar Pradesh. In age group of 6 month–18 years, total of 200 children suffering of severe malaria were included in study. Patients were classified into severe malaria as per WHO guidelines. Diagnosis and grading of malnutrition was done as per WHO guidelines for malnutrition.
Results: In age group of 0.5–5 years, comprising of 64 children with severe malaria, 56(87.5%) were malnourished while 8(12.5%) were well nourished. In age group of 5–18 years comprising of 136 cases of severe malaria, 103 (75.7%) were malnourished while 33 (24.3%) were well nourished. In 0.5–5 years of age group, all three species of malaria were found to be affecting malnourished children in higher percentage as compared to well nourished children.. However, in 5–18 years of age group, cases of P.vivax severe malaria were significantly higher in malnourished children.
Conclusion: This study showed higher percentage of malnourished children as compared to healthy children in cases of severe malaria and P.vivax cases with undernutrition to be significantly higher than other malarial parasites with undernutrition in 5–18 years age group. Therefore, malaria control strategies and nutritional intervention programmes should be consolidated together.

1. Introduction

Malaria and malnutrition co-exist in India and both independently are responsible for large proportion of morbidity and mortality in children.[1] Malaria is endemic in India and many of South East Asia as well as other countries of world. In 2018, an estimated 228 million cases of malaria occurred worldwide, compared to 251 million cases in 2010[2]

As of India, 0.43 million confirmed cases of malaria were reported by NVBDCP in 2018[3]

Children aged below 5 years are the most vulnerable to severe malaria. This age group constitutes 67% of malaria death globally.[4]

As per data of 2018, in less than five age group, wasted and severely wasted children was 49 and 17 million respectively.[5]

Due to heavy burden of both malaria and malnutrition in developing and developed countries, it's very important to understand how these two interact and influence each other. It has been well established that malaria adversely affects weight and height gain in children. However, what impact already existing under nutrition has on malaria is still not well understood and has been subject of controversy since early 1950. Few studies found increased risk of malaria in cases with underlying under nutrition[6–8] While on contrary few studies found protective effect of malnutrition against malaria[9,10,11] . Other studies found no relationship between underlying malnutrition and risk of Malaria.[12] Majority of such studies have been carried out in Africa where P.falciparum is predominant malarial species.

As relation between malnutrition and malaria remains inconclusive and these two morbidities independently as well as with co-existence affect a large proportion of children in India, this study was undertaken.

2. Material and methods

A hospital based observational study was conducted in Pediatric

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ward of a Tertiary care hospital located in Kanpur, India. In age group of 6 months–18 years, 200 cases of severe malaria were included in study by convenient sampling. Written informed consent was taken from parents. Institutional ethical committee approved the study. Severe malaria was defined as per WHO guidelines.[13] Assessment of malnourishment was done by comparing child's weight and height to the standardised age- and sex-specific growth reference charts of WHO for children between 6 and 59 months of age (World Health Organization (WHO) Child Growth Standards 2006).[14] The anthropometric indicators are expressed as a number of standard deviations (SDs) below or above the reference mean or median value, Z-score. Cutoffs of −3 were used to indicate severe malnutrition and values between −2 and −3 were considered to be moderate malnutrition. For children 5–18 years age group, Body Mass Index (BMI) < 5th centile for that age and gender in WHO BMI centiles chart was defined as undernutrition.

Inclusion criteria:

1. 6month −18 years age group children
2. Positive for malaria by peripheral blood smear (PBS) or card test and fulfilling criteria of severe malaria as per WHO guidelines.

Exclusion criteria:

1. Patient who tested negative for malaria on PBS or card test but were empirically treated for malaria on basis of presenting complaints and clinical features.
2. Children with Tuberculosis, HIV, and acute or chronic diarrhoea, any other chronic illness that can cause malnutrition.

3. Diagnosis

Malaria was diagnosed by PBS and RMAT. Diagnosis of malaria and identification of species done by thin and thick blood smears respectively. Whereas, RMAT tests/card tests were based on detection of malarial antigens, Lactate dehydrogenase and histidine rich protein 2. RMAT or peripheral blood smear positive for both P. vivax and P. falciparum were labeled as mixed malarial infections.

4. Data collection and analysis

Data regarding patient clinical presentation, investigations and outcome were recorded. Prevalence of symptoms, signs, severity criteria were studied. Patient's age, gender and anthropometric measurements like weight, height, and weight for height were also recorded. Statistical significance of results was tested by appropriate statistical test like Chi square test/Fisher Exact test.

5. Results

In our study as shown in Table 1, Out of 64 children of severe malaria in 0.5–5 years age group 87.5% had moderate to severe PEM and 12.5% had normal nutritional status. While in 5–18 years of age group, out of total 136 cases of severe malaria, 33(24.2%) had normal nutrition while 103 (75.7%) were undernourished. We observed that percentage of cases with PEM/undernutrition was higher in comparison to children with normal nutritional status.

As shown in Table 2, out of 56 children with undernutrition in 0.5–5 year's age group, number of boys was 30. Whereas, in 5–18 years age group, out of total 159 cases of Undernutrition, 86 were boys. However, in both age group there was no statistically Significant difference in cases of severe malaria with malnutrition on basis of gender (p value = 0.92311, by chi-square).

Further, as shown in Table 3, in 0.5–5 years of age group 40(88.9%) cases of P.vivax, 7 (87.5%) cases of P.falciparum and 9(81.8%) cases of mixed malaria had moderate to severe PEM. Thus all species of malaria were affecting malnourished children more than well nourished children. Not any species of malaria was found to be affecting malnourished children significantly higher than other species (p = 0.404).

As mentioned in Table 4, Out of 136 cases of severe malaria in >5 years age group, 103 (75.7%) were undernourished which included 78 (91.7%) cases of P.vivax, 9 (39.13%) cases of P.falciparum and 16 (57.14%) cases of Mixed malaria. We also found that undernutrition was significantly higher in P.vivax as compared to falciparum and mixed malaria (p = 0.00001).

Table 1
Distribution of cases as per nutritional status in cases of severe malaria.

Age group	Normal nutrition		PEM/Undernutrition	
	No.	%	No.	%
0.5–5 year (n = 64)	8	12.5%	56	87.5%
>5year (n = 136)	33	24.2%	103	75.7%
Total(200)	41	20.5%	159	79.5%

Table 2
Distribution of undernourished children on the basis of gender in cases of severe malaria.

Age group	Cases with undernutrition	Boys	Girls	p value
0.5–5 years (n = 64)	56	30	26	0.923
5–18 years (n = 136)	103	56	47	
Total (200)	159	86	73	

6. Discussion

In our attempt to understand relation between malnutrition and severe malaria in pediatric age group, we found that percentage of malnourished children with severe malaria was higher than well nourished children with severe malaria in both age group of 0.5–5 years and 5–18 years.

Methodological dissimilarities and confounding factors can be responsible for variation in results of studies between malaria and malnutrition in modern era. These confounding factors include socioeconomic status, breastfeeding practices and other infectious diseases.[15]

It has always been known that malnutrition predisposes to various infections. Then it also increases severity of those infections and attenuates body response to medicines. Malnutrition thus increases morbidity and mortality from any infection. On other hand, infection also lead to worsening of nutritional status, this leads to vicious cycle of malnutrition and increased severity of infection. Malnutrition adversely affects cellular as well as humoral immune response of body and complement activation. This suppressed immune response and lymphoid tissues atrophy of malnourished children leads to decreased host defence against malaria and increased susceptibility to occurrence and severity of malaria. [16] Studies have shown decreased anti-malarial immune respondents and specific IgGAb in malnourished children as compared to healthy children.[17]

We further extended our study to find assosciation between malnutrition and type of malarial species. In 0.5–5 years of age group we found that percentage of all species of malaria was higher in malnourished

Table 3
Distribution of cases as per malarial species and nutritional status in 0.5–5 years of age group (n = 64).

Type of malaria	Normal nutrition		PEM (moderate and severe malnutrition)		P value
	No.	%	No.	%	
P.vivax (n = 45)	5	11.1	40	88.9	0.404
P.falciparum (n = 8)	1	12.5	7	87.5	
Mixed malaria (n = 11)	2	18.2	9	81.8	
Total(n = 64)	8	12.5	56	87.5	

Table 4
Distribution of cases as per malarial species and undernutrition in 5–18 years age group.

Type of malaria	Normal nutrition		Undernutrition		P value
	No.	%	No.	%	
P.vivax(n = 85)	7	8.2	78	91.7	0.00001
P.falciparum (n = 23)	14	60.9	9	39.1	
Mixed malaria(n = 28)	12	42.3	16	57.1	
Total(n = 136)	33	24.2	103	75.7	

children as compared to well nourished children. However there was no significant assosciation between malnutrition and type of malarial species. These results are in tune with study done to found assosciation between malaria and malnutrition in 0.5–5 years of age group in Southern Ethiopia.[18]

As larger proportion of cases of malaria were malnourished, our results are also in favour of studies that found children infected with malaria to be at higher risk of malnutrition.[19]

We also analysed association between occurrence of severe malaria in undernourished and well-nourished children of 5–18 years of age group. In our study we found occurrence of P.vivax infections was significantly higher in malnourished children as compared to well-nourished children while P. falciparum and mixed malaria was found in both malnourished and well-nourished children without any statistically significant difference.

Thus, P.vivax infection was significantly higher in malnourished children or P.vivax infection itself had been predisposing to malnutrition. Though effect of malnutrition on risk and severity of malaria remains controversial and contradictory, studies have already shown that malaria predisposes to malnutrition.[20–22]

Only few studies have attempted to establish assosciation between P. vivax and malnutrition after elimination of as much of confounding factors as possible. These studies have found positive assosciation between exposure to P.vivax infection and risk of developing malnutrition.[23,24]

P.vivax infection has been proven to have chronic effect on growth and nutritional status.[25] P vivax is also potent stimulator of pro-inflammatory cytokines and TNF-alpha; these pro-inflammatory mediators are responsible for anorexia and catabolic state thus contributing to malnutrition[26]

P.vivax malaria unlike P.falciparum has unique ability to form hypnozoites in liver and stay in dormant form in body. These dormant hypnozoites then can cause multiple relapses after months of primary infection.[27] In endemic countries like India, these relapses are main cause of malaria than primary infection itself.[28,29] Primaquine is only drug that most effectively targets P.vivax hypnozoites.[30] However, Primaquine is known to cause hemolysis in G-6-P-D deficient individuals.

In individuals with normal G-6-P-D levels and in areas with frequent relapsing P.vivax strains, WHO recommends supervised course of Primaquine at 0.5 mg/kg/day for 14 days.[31] However, because of limited lab facilities and economical constraints G-6-P-D levels are unavailable for most of malaria patients in endemic areas. These countries like India, recommend supervised lower dose of 0.25 mg/kg/day of Primaquine for 14 days. However, because of fear of hemolysis and lack of awareness amongst medical practitioner about crucial role of Primaquine in preventing relapses, even this low dose is not prescribed to malarial patients many a times. As daily supervision is also not feasible in most of health set-ups, patients are discharged on 14 days course of Primaquine. However, very often this course remains incomplete because of poor patient compliance. All these factors lead to persistence of hypnozoites and subsequently multiple malarial relapses in P.vivax infected patients. Multiple episodes of malaria predispose patients to malnutrition.

. Thus our study emphasizes that already existing malnutrition predisposes to increased severity of malaria. Though, there are inconsistent results in studies carried out to observe whether already existing malnutrition can predispose to and increase severity of malaria. Interventional studies have shown that with control of malaria, malnutrition rate in children can be brought down effectively[32]

Many revolutionary steps have been taken since long to control malaria; still control of malaria is far from satisfactory. It's a cause of morbidity and mortality of large proportion of children and globally its sixth leading cause of death in children <5 years[33] especially most vulnerable subpopulation of malnourished children. Hence effective nutritional intervention programme should be consolidated with malaria control programmes.

Limitations of Study: In this study, children were selected conveniently from OPD/Ward of tertiary care hospital of a District from Uttar Pradesh, India. Hence, most of the children were residing in urban slums and belonging to lower socioeconomic class. Therefore, a detailed analysis of assosciation of severity of malaria with malnutrition in relation to sociodemographic.

Variables could not be done. However, study gives insight of relation of malnutrition and severe malaria in different pediatric age groups.

7. Conclusion

Amongst 200 cases of severe malaria, we found higher percentage of children to be malnourished. We did not observe any species of malaria affecting malnourished children in 0.5 – 5years of age group significantly higher than other species. Other interesting observation was that in 5–18 years of age group, P.vivax and mixed malaria was significantly higher than P.falciparum. These results are very important as these indicate that underlying undernutrition in children can be a major obstacle in achieving ambitious goal of malaria elimination. As relationship between malaria and malnutrition is synergistic, nutritional intervention programmes should be integrated with malaria elimination programmes and vice-versa. Better understanding of complex associations between both will help guide much needed interventions to control malaria, curb malnutrition and also optimise antimalarial drug dosing in malnourished children. Further, studies should be done with larger sample size to study effect of P.vivax on nutritional status amongst different age group of children.

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Declaration of competing interest

The authors declare no conflict of interest.

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