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A RETROSPECTIVE STUDY EVALUATING PROCALCITONIN AS AN EARLY BIOMARKER FOR SEVERITY OF PLASMODIUM FALCIPARUM MALARIA

Medicine

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ABSTRACT

Background: Malaria is commonly encountered parasitic infection with varying degrees of severity. Though microscopy is the gold standard for diagnosis, there has been search for surrogate biomarkers for predicting severity. Therefore, the present study was conducted to evaluate the efficacy of procalcitonin as a biomarker. **Method:** The records of 100 patients diagnosed with *Plasmodium falciparum* malaria were included. Demographic details, past and personal history, details of hematological examination and peripheral smear findings were noted. The data was recorded and analysed. **Results:** In the present study, 65% (65 cases) of the cases had severe malaria. There was a male preponderance in the study population. The serum procalcitonin was also significantly raised in cases with severe malaria as compared to the cases with uncomplicated malaria (P value: less than 0.001) and showed significantly strong correlation with ESR, CRP and parasite count (P value: less than 0.001). **Conclusion:** It can be effectively concluded that serum procalcitonin levels are significantly raised in severe malaria as compared to the uncomplicated malaria, making it an effective biomarker for the severity of the disease.

KEYWORDS

Biomarker, erythrocyte sedimentation rate, malaria, procalcitonin, severity.

INTRODUCTION:

Malaria is a disease caused by different species of *Plasmodium*.[1] Of all the species, *Plasmodium falciparum* causes a heterogenous disease with outcome ranging from complete recovery to death. Till date, microscopic smear examination remains the gold standard for diagnosis with the visualization of specific forms of parasite.[2] It requires some degree of expertise which may not be easily available and accessible in a developing country, like ours. Rapid diagnostic tests (RDTs) maybe used for identification of patients with malaria with no information on the severity. Therefore, there has been search for a biomarker which can accurately predict the severity of the disease.

Procalcitonin is one such early biomarker. It is normally secreted by thyroid C cells. It is an amino acid precursor of the hormone calcitonin. It has been shown that the levels of procalcitonin increase in response to inflammation and can be used as a marker of sepsis.[3] The studies assessing the role of procalcitonin in malaria are scarce. Therefore, the present study was conduct to evaluate the efficacy of procalcitonin as a biomarker for *Plasmodium falciparum* malaria.

MATERIALS AND METHOD:

This retrospective study was conducted including records of patients of either gender aged more than 18 years and diagnosed with *Plasmodium falciparum* malaria. Patients with other types of malaria or having any other systemic infection, having documented comorbidities like diabetes, renal failure, liver disease, coronary artery disease, rheumatoid arthritis or any other systemic inflammatory disease and pregnant patients were excluded from the study.

The records of 100 patients admitted with *Plasmodium falciparum* malaria were included in the study. Baseline demographic characteristics were noted for all patients. Detailed present history was noted. The severity of the disease as per WHO definition was noted.[4] The findings of hematological examination and peripheral smear examination were noted. For the type of *Plasmodium species,* the slide was prepared using Giemsa stain and the *Plasmodium falciparum* was confirmed upon observation of classic ring-shaped trophozoite forms. For calculating the parasite count, the parasites were counted in a minimum of 200 leucocytes and the final count was reported considering 8000 leucocytes per microliter (or mm^3) of blood. Erythrocyte sedimentation rate (ESR) was measured by the automated analyser. Serum procalcitonin and CRP levels were measured by the Enzyme Linked Immunosorbent Assay (ELISA) method.

The data was collected from the records and analysed using the SPSS software version 22.0. P values were assessed by Chi square test for qualitative data and Unpaired t test for quantitative data. Correlation was assessed by the Pearson correlation test and strength was interpreted according to the value of Pearson correlation coefficient (r) as very weak correlation (r: less than 0.30), weak correlation (r: 0.31 to 0.50), moderate correlation (r: 0.51 to 0.70) and strong correlation (r: more than 0.71). P value of less than 0.05 was considered as "statistically significant" and indicated by "*" in the Tables.

RESULTS:

In the present study, severe malaria was present in 65 cases (65%). The age distribution of the cases was similar in the cases with uncomplicated malaria and with severe malaria (Table 1).

Table 1: Distribution Of The Demographic And Laboratory Findings In The Study Population

PARAMETER	UNCOMPLICATED MALARIA (n=35)	SEVERE MALARIA (n=65)	P VALUE
Age (in years)	38.02 ± 5.45	37.21 ± 6.81	0.71
Parasite Count (in per mm^3)	2784.17 ± 1167.60	40175.55 ± 5498.64	<0.001*
ESR (in mm/hr)	18.14 ± 3.96	48.29 ± 11.16	<0.001*
CRP (in mg/dL)	17.02 ± 4.43	58.00 ± 6.56	<0.001*
PCT (in ng/mL)	2.96 ± 1.35	14.55 ± 1.46	<0.001*

There was a male preponderance in the study population (73 cases; 73%) with similar distribution in the patients with uncomplicated and severe malaria; P value: 0.642. The parasite levels, ESR and serum level of CRP were significantly higher in cases with severe malaria as compared to uncomplicated malaria (Table 1). The serum level of procalcitonin was also significantly high in severe malaria (Table 1).

There was strongly positive statistically significant correlation of serum procalcitonin level with ESR, CRP and parasite count (Table 2).

Table 2: Correlation Of Laboratory Findings With Procalcitonin

PARAMETER	COEFFICENT (r)	P VALUE
ESR	0.81	<0.001*
CRP	0.92	<0.001*
PARASITE COUNT	0.95	<0.001*

DISCUSSION:

In the present study, it was observed that the parasite count, ESR and CRP were significantly higher in cases with severe malaria than in uncomplicated malaria. The serum procalcitonin level was also

significantly higher in cases with severe malaria as compared to uncomplicated malaria. There was a strongly positive correlation of procalcitonin with ESR, CRP and parasite count.

In the study by Righi E. et al,[5] they included a total of 30 travellers with *Plasmodium falciparum* malaria. They observed a male preponderance in the study population with mean age of 42 ± 13.2 years in cases with complicated malaria and 41 ± 9.9 years in cases with uncomplicated malaria. The age distribution was similar in the two Groups; P value: 0.82. They also observed that CRP and median parasitemia were significantly higher in cases with complicated malaria as compared to the cases with uncomplicated malaria (P values: 0.0005 and 0.0001, respectively). They assessed serum procalcitonin level in the two Groups and observed it to be significantly higher in the cases with complicated malaria; P value: 0.0018. They further noted that procalcitonin and CRP showed significantly positive correlation with parasitemia; P value: less than 0.001. They also noted that higher procalcitonin level was also associated with increased risk of complicated malaria.

In the study by Mbengue B. et al,[6] they included a total of 98 cases of cerebral malaria with *Plasmodium falciparum*. They observed that when the serum procalcitonin level was compared between surviving and fatal cases, the level at Day 0 was significantly higher in the fatal cases at Day 0 (P value: 0.01), Day 1 (P value: less than 0.01) and Day 2 (P value: 0.01). Thus, the serum procalcitonin level at Day 0 was found to be a better marker of fatality in cases with cerebral malaria.

Other studies also found a significantly high serum procalcitonin levels in severe complicated malaria as compared to cases with uncomplicated malaria.[7,8,9] Studies have also found significantly positive correlation between parasitemia and serum procalcitonin level.[7,9,10]

In the meta-analysis by Tripathy R. et al,[11] they also concluded that serum procalcitonin is elevated in cases of malaria with *Plasmodium falciparum*. They also found serum procalcitonin to be a good biomarker for the severity of the disease and multi-organ dysfunction.

Thus, serum procalcitonin level is higher in cases of severe malaria as compared to uncomplicated malaria. Also, in the present study, procalcitonin levels correlated well with other biomarkers of inflammation (ESR and CRP) and of disease severity (parasite count).

Procalcitonin is a biomarker for bacterial infection. Its synthesis is triggered by the inflammatory cytokines[12] and in addition to thyroid C cells, it is also secreted by liver, pancreas, kidney and intestine. During inflammation, it is secreted by the endothelial cells and leucocytes as well.[13] Thus, the increased serum level of procalcitonin in cases of *Plasmodium falciparum* malaria may be due to the underlying inflammation with TNF playing a significant role in its release.[14]

Limitations:

The present single centre study was limited by the availability of records of patients diagnosed with *Plasmodium falciparum* malaria. Hence, the results may not be generalised.

CONCLUSION:

It can be effectively concluded from the present study that serum procalcitonin level is much higher in the cases with severe malaria. It also showed strong correlation with other biomarkers of systemic inflammation. Therefore, procalcitonin may be used as a surrogate biomarker for the severity of *Plasmodium falciparum* malaria, especially in cases where other causes of systemic inflammation can be ruled out. Further large-scale studies are needed to determine the cut-off values for the severity of the disease.

REFERENCES:

1. Mahittikorn A, Masangkay FR, Kotepui KU, Milanez G, Kotepui M. Comparison of Plasmodium ovale curtisi and Plasmodium ovale wallikeri infections by a meta-analysis approach. Sci Rep 2021;11:6409.
2. Mathison BA, Pritt BS. Update on Malaria Diagnostics and Test Utilization. J Clin Microbiol 2017;55:2009-17.
3. Meisner M. Update on procalcitonin measurements. Ann Lab Med 2014;34:263-73.
4. White NJ. Severe malaria. Malar J 2022;6:284.
5. Righi E, Merelli M, Arzese A, Siega P, Scarparo C, Bassetti M. Determination of PCT on admission is a useful tool for the assessment of disease severity in travelers with imported Plasmodium falciparum malaria. Acta Parasitol 2016;61:412-8.
6. Mbengue B, Diatta B, Niang B, Diagne N, Ndiaye M, Marrama L, et al. Differential kinetics of plasma procalcitonin levels in cerebral malaria in urban Senegalese patients according to disease outcome. Microbiol Res 2011;2:80-4.
7. Chiwakata CB, Manegold C, Bönicke L, Waase I, Julch C, Dietrich M. Procalcitonin as a parameter of disease severity and risk of mortality in patients with Plasmodium falciparum malaria. J Infect Dis 2001;183:1161-4.
8. Erdman LK, Dhabangi A, Musoke C, Conroy A, Hawkes M, Higgins S, et al. Combinations of host biomarkers predict mortality among Ugandan children with severe malaria: a retrospective case-control study. PLoS One 2011;25:17440.
9. Hesselink DA, Burgerhart JS, Bosmans-Timmerarends H, Petit P, van Genderen P. Procalcitonin as a biomarker for severe Plasmodium falciparum disease: a critical appraisal of a semi-quantitative point-of-care test in a cohort of travellers with imported malaria. Malar J 2009;8:206.
10. Uzzan B, Izri A, Durand R, Deniau M, Bouchaud O, Perret GY. Serum procalcitonin in uncomplicated falciparum malaria: a preliminary study. Travel Med Infect Dis 2006;4:77-80.
11. Tripathy R, Das BK, Panda AK. Procalcitonin is elevated in severe malaria and is a promising biomarker of severe malaria and multi-organ dysfunction: A cross-sectional study and meta-analysis. Int Immunopharmacol 2023;124:110923.
12. Gregoriano C, Heilmann E, Molitor A, Schuetz P. Role of procalcitonin use in the management of sepsis. J Thorac Dis 2020;12:5-15.
13. Romualdo L, Rojas C, Arenas V, Gamez R, Abellan M, Morales M. Increased concentrations of procalcitonin in patients with paracetamol intoxication. Adv Lab Med 2021;2:287-90.
14. Muller B, Prat C. Markers of acute inflammation in assessing and managing lower respiratory tract infections: focus on procalcitonin. Clinical Microbiology and Infection 2006;12:8-16.