The role of haematological parameters in predicting malaria with special emphasis on neutrophil lymphocyte count ratio and monocyte lymphocyte ratio: A single Institutional experience

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KEY WORDS
Malaria, monocyte lymphocyte ratio, neutrophil lymphocyte count ratio

ABSTRACT

Introduction: Malaria is a mosquito-borne disease which is a major public health problem and a leading cause of morbidity and mortality worldwide. Various haematological parameters have been studied to help predict malaria, such as alteration in the leucocyte count, platelet counts and erythrocyte counts. The neutrophil lymphocyte count ratio (NLCR) was found to have a good predictive value in systemic inflammation, particularly in critical care setting. Aims and Objectives: The present study aims to study the various haematological parameters and ascertain the predictive value of NLCR and MLR in the detection of malaria. Materials and Methods: A prospective cross sectional study was conducted at a tertiary care hospital between the period of August to December, 2014. A total of 200 smear positive malaria patients and a control group of 100 patients who were smear negative for malaria were included. Hemoglobin, Total leucocyte count, Differential leucocyte count, platelet counts and absolute counts were obtained. The NLCR and MLR were obtained from the above data. The data was analysed by statistical tools. Results: A total of 200 smear positive malaria cases were analysed of which, 180 cases were caused by the Plasmodium vivax parasite and 2 cases by Plasmodium Falciparum. Thrombocytopenia and leucopenia were found to have significant association with malaria. In the present study, the NLCR and MLR was not found to have significant association with malaria. Discussion: Although NLCR has been proven to be a useful marker for inflammation in many acute conditions, it is albeit not of much significance in the prediction of malaria. Similarly we have found no significance of MLR in prediction of malaria.

INTRODUCTION

Malaria is a mosquito-borne disease which is a major public health problem and a leading cause of morbidity

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and mortality worldwide.[1] As per the current WHO estimates, around 214 million cases of malaria were reported globally with an estimated 438,000 deaths. Among the endemic countries, India has an estimated burden of 882,000 cases/year.

The diagnosis of malaria posed a challenge particularly in developing countries such as India where there is a need for rapid, cost-effective, and sensitive tests.[2] Various hematological parameters have been studied to help predict malaria, such as alteration in the leukocyte count, platelet counts, and erythrocyte counts.[3] The neutrophil-lymphocyte count ratio (NLCR) was found to have a good predictive value in systemic inflammation, particularly in critical care setting.[3] However, several authors have been of the opinion that sufficient data regarding the predictive value of NLCR have not been available yet.[3] On the other hand, a high monocyte-lymphocyte ratio (MLR) in peripheral blood was found to be a good predictor of an individual’s immune response against Plasmodium falciparum infection.[4] These alterations in the hematological parameters may be useful in alerting the laboratory professional to the possibility of malaria and thus, help in the early detection of the parasite.

The present study aims to study the various hematological parameters and ascertain the predictive value of NLCR and MLR in the detection of malaria.

MATERIALS AND METHODS

A prospective cross-sectional study was conducted at a tertiary care hospital in South India between August 2014 and December 2014. A total of 200 smear-positive malaria cases were analyzed. Of these, 180 cases were caused by Plasmodium vivax parasite and two cases by P. falciparum. Eighteen cases were found to have mixed infection. A control group of 100 smear-negative fever cases was also included in the study.

Between August 2014 and December 2014, a total of 200 smear-positive malaria cases were analyzed. Of these, 180 cases were caused by Plasmodium vivax parasite and two cases by P. falciparum. Eighteen cases were found to have mixed infection. A control group of 100 smear-negative fever cases was also included in the study.

The mean age was 48 years (range = 18–80 years).

Anemia was present in 17.5% of malaria patients (35 cases) but in only 12% of the control group (12 cases). Thrombocytopenia accounted for 57% (114 cases) in malaria patients while it was seen in 26% (26 cases) of the control group. Leukopenia was noted in 11.5% of malaria cases (23 cases) as compared to only 6% (six cases) in the control group. Lymphopenia was present in 55% (111 cases) of all malaria patients and was more commonly encountered in P. vivax as compared to P. falciparum malaria. Neutrophilia was noted in 6.5% (13 cases) and neutropenia was seen in 5% (10 cases) of malaria group. Of these variables, thrombocytopenia showed the strongest association and had the greatest predictive value ($P < 0.001$). The other parameter which showed significant association with malaria as compared to the control group was leukopenia ($P < 0.001$).

In the present study, the NLCR and MLR were not found to have significant association with malaria as shown in Table 1. The $P$ value calculated using Mann–Whitney U-test statistical tool was $P < 0.001$.

In the present study, an Hb value of $<10$ g/dL was considered to be anemia and a platelet count of $<1.5$ lakh/cumm was considered to be thrombocytopenia.

Simultaneously, both thick and thin smears were prepared and stained by Giemsa stain, which were examined by trained microscopists for the detection of Plasmodium parasite and species. Parasite density was calculated and recorded. The data were entered into Microsoft Excel worksheet and analyzed using Mann–Whitney U-test statistical tool. A $P < 0.001$ was considered statistically significant.

DISCUSSION

There is a pressing need for reliable laboratory indicators for the detection of malaria that are cost-effective and rapid, especially in laboratories with an increased workload.[2]
Although NLCR has been proven to be a useful marker for inflammation in many acute conditions, it is albeit not of much significance in the prediction of malaria. This may be attributed to the fact that neutrophilia which is often encountered in bacteremia is infrequently encountered in malaria. In the present study, the neutrophil counts were often in the lower range of normal which when extrapolated onto the NLCR were much lower as opposed to that seen in bacterial sepsis. Similar results were obtained by other researchers. Previous studies have found a high MLR to be a good predictor of an individual’s immune response to \textit{P. falciparum} infection. In contrast, we have found no correlation between the two variables in the present study. These findings were similar to studies by other researchers.

On the other hand, the two hematological parameters which have a striking association with malaria cases are leukopenia and thrombocytopenia.

In the present study, lymphopenia was much higher in the malaria cases as compared to the control group. According to some authors, lymphopenia in infections has been attributed to redistribution, margination, and apoptosis of lymphocytes.

Several studies have suggested that the finding of thrombocytopenia must prompt one to search for malaria. Malaria is often accompanied by mild to moderate thrombocytopenia and hence can be of diagnostic help. The different mechanisms by which thrombocytopenia develops include platelet activation, phagocytosis, and splenic sequestration.

In the underdeveloped areas, particularly when microscopic facilities are suboptimal, thrombocytopenia may help in prediction of malaria and prompt referral to higher centers for further evaluation, thus reducing detrimental delay in diagnosis.

Therefore, in malaria endemic areas, findings of thrombocytopenia and leukopenia in a febrile patient must alert the health-care workers to the possibility of malaria.

Anemia is one of the hematological parameters which has found to be associated with malaria.

In these cases, anemia has been attributed to reduced Hb production and hemolysis. However, in our study, we found no significant association of anemia with malaria cases as compared to the control group. The reason for this could be that the control group taken were hospitalized patients in whom a finding of anemia was common due to underlying chronic conditions.

In the present study, all of the malaria cases were confirmed by microscopic examination of thick and thin smears which is the gold standard for diagnosis of malaria. The automated cell analyzers from which different hematological parameters were obtained was subjected to daily quality controls, thus ensuring precision and accuracy.

### Table 1: Comparison of hematological parameters of control groups and case groups

| Study group | Age (years) | TLC (×10^3/cumm) | ANC (×10^3/cumm) | ALC (×10^3/cumm) | AMC (×10^3/cumm) | Hb (g/dl) | Platelet (×10^3/cumm) |
|-------------|-------------|------------------|------------------|------------------|------------------|-----------|----------------------|
| Control     | Mean        | 48.320           | 9.4840           | 6.5590           | 1.9820           | 0.8260    | 10.4040              | 231.2900 |
|             | SD          | 19.24267         | 5.67028          | 5.52244          | 1.26302          | 1.11868   | 2.98091              | 136.7550 |
|             | Maximum     | 94.00            | 33.00            | 0.20             | 0.10             | 0.10      | 0.50                 | 7.00     |
|             | Minimum     | 11.00            | 3.30             | 31.30            | 8.40             | 11.10     | 18.20                | 718.00   |
| Case        | Mean        | 36.1150          | 6.3410           | 3.9640           | 1.5880           | 0.6890    | 12.1975              | 129.4450 |
|             | SD          | 17.13387         | 3.08850          | 2.98278          | 1.23246          | 0.74150   | 2.65153              | 75.79128 |
|             | Maximum     | 92.00            | 33.00            | 31.20            | 10.30            | 10.00     | 17.60                | 424.00   |
|             | Minimum     | 11.00            | 1.80             | 0.30             | 0.30             | 0.00      | 2.00                 | 17.00    |
| P           |             |                  |                  |                  |                  |           | 0.0001               |          |

SD: Standard deviation, TLC: Total leukocyte count, ANC: Absolute neutrophil count, ALC: Absolute lymphocyte count, AMC: Absolute monocyte count, Hb: Hemoglobin

### Table 2: Comparison of neutrophil-lymphocyte count ratio and monocyte-lymphocyte ratio in control and case groups

| Study group | NLCR | MLR |
|-------------|------|-----|
| Control     | Mean | 5.8250 | 0.6350 |
|             | SD   | 8.36810 | 1.11059 |
|             | Minimum | 0.10 | 0.00 |
|             | Maximum | 62.00 | 10.00 |
| Case        | Mean | 3.9080 | 0.5810 |
|             | SD   | 3.90971 | 0.65120 |
|             | Minimum | 0.10 | 0.00 |
|             | Maximum | 26.00 | 7.10 |
| P           |       | 9.130 | 9.317 |

NLCR: Neutrophil-lymphocyte count ratio, MLR: Monocyte-lymphocyte ratio, SD: Standard deviation
One of the limitations of the study is that we have included febrile patients in the control group who may have different types of infections that may potentially affect the hematological parameters. Although many studies have established the association of various hematological parameters such as platelet counts, total counts, and Hb with malaria, sufficient data on the role of NLCR and MLR in malaria are limited. In this scenario, the present study has tried to throw some light on this limited body of knowledge.

CONCLUSION
In the present study, thrombocytopenia and leucopenia were found to have significant association with malaria. Although NLCR has been proven to be a useful marker for inflammation in many acute conditions, it is albeit not of much significance in the prediction of malaria. Similarly we have found no significance MLR in prediction of malaria.

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Conflicts of interest
There are no conflicts of interest.

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