Monocytes to lymphocytes ratio in peripheral blood and immunoglobulin IgE levels as indicators to Plasmodium falciparum infection in Sudan

Abstract

Background: Malaria infection especially by Plasmodium falciparum species remain the most global threatening life in Africa. The effective immune response to malaria infection, in addition to the effective immunological factors which play a significant role in immune defence reflect in different sorts of infection, such as changes in cellular ratio and the elements quantity according to the immunological challenge still are incompletely understood. In this survey, we examined the ratio of monocytes to lymphocytes beside the levels of total immunoglobulin IgE in both infected patients with Plasmodium falciparum parasite and compared with healthy individual. To search for any correlation on those who had the infection.

Methodology: We obtained 3ml of venous blood samples from both infected patients and control candidates in EDTA containers for immunoglobulin inspection and parasitological tests. A full differential blood count, Immuno-chromatography antigenic test and thin blood films with a microscopic examination had been used to confirm malaria infection. In addition to Electro-chemiluminescence-immunoassay (ECL) had been applied for measuring the total immunoglobulin IgE levels. We entered Data into Microsoft word and analyzed using SPSS (version 20; SPSS Inc., Chicago, IL) software, the correlation to occurrences of malaria infection and between variables calculated using Pearson correlation coefficient. An alpha value of < 0.05 denoted a statistically significant difference in all statistical compares.

Finding: The analysis of the results revealed that the IgE levels were dependent with the incidence of the malaria infection P-value<0.01. Furthermore, the ratio of Monocytes to Lymphocytes (M: L) elevated with the risk of malaria infection (HR=0.30, 95% CI=0.11 to 0.84) and found to be statistically significant P-value <0.05.

Conclusion: The outcome of this work revels that, both the monocytes to lymphocytes (M: L) ratio and the IgE could be used for predication of the malaria infection as well as can used as a good indicator to monitor the density of malaria infection.

Keywords: malaria infection, Plasmodium falciparum, monocytes to lymphocytes ratio (m: l ratio), total immunoglobulin E

Introduction

Plasmodium falciparum malaria is still a major cause of morbidity and mortality in Africa, where the greatest burden of disease is borne by young children; Substantial clinical immunity develops following repeated natural exposure to Plasmodium falciparum such that clinical malaria tends to be less frequent in children over 5years of age and adults. This distinction between immunity to clinical malaria and immunity against Plasmodium falciparum infection per se is further evident in the epidemiological pattern of clinical malaria and asymptomatic parasitemia. The specific host factors underlying susceptibility to clinical malaria despite the ability to sustain asymptomatic Plasmodium falciparum infection is poorly understood. Worldwide, most infections with malaria-causing agents are clinically silent, reflecting the ability of adaptive immune mechanisms to prevent disease. Patients infected with malaria exhibited important changes in most of hematological parameters, including low platelets, white blood cells (WBCs) and lymphocytes counts being the most important predictors of malaria infection. When use these parameters in combination with other clinical and microscopy methods could improve the malaria diagnosis and treatment. Hematological changes are the most common indicators of malaria infection as well as play a significant role in pathology of malaria. These changes involve the major cells types such as RBCs, leucocytes and thrombocytes.

Furthermore, the main role of white blood cells (WBCs) counts and their differential types are basic and essential indicators resulting from infection. Which serve and help to differentiate between different types of infections and serve as a tool in monitoring the patient’s progress during illness, which given the central role of monocyes and lymphocytes in the induction of immune responses, moreover, their frequency in peripheral blood might be expected to reflect the state of an individual’s immune-response to infection. Mechanisms for malaria immunity are highly complex with involvement of several components of immune function, Antibody-dependent mechanisms are presumed to play an important role in protection, with a wide range of antigen specific antibodies as well as polyclonal-antibody production. Structurally different antigens are expressed during each part of the parasite’s life cycle, hence naturally acquired immunity is mostly stage specific. Both antibodies and T cells are required for naturally acquired immunity. Antibodies may block host cell invasion by sporozoites and merozoites; IgE interaction with effectors cells is assumed to play an important although controversial role in protection against parasitic infections. In Plasmodium falciparum infection
induces elevated blood levels of both total immunoglobulin and anti-
plasmodium antibodies belonging to different isotypes. It has been
previously shown that donors living in areas of malaria transmission
develop malaria-specific IgE antibodies that are present at highest
concentrations in patients with severe disease, suggesting a role for
this isotype in malaria pathogenesis. 5,6

Materials and methods

Study design

A cross sectional study was conducted at Dar AL-elaj Specialized
Hospital (D.S.H), Khartoum state, Sudan from March to July 2017.

Study population

Sudanese patients, infected by P. falciparum malaria, the population
categorized according to age group (adult and children less than 14
a years) and gender. The patients with previous history of malaria
infection within last 3 months or how suffering from immunological
disorders were excluded from study.

Sampling and preparation

After obtaining the permission and inform consent from the
treating doctors and each volunteers or patients informed with the aim
of the study. A total of 126 were enrolled during the study period and
3mL venous blood collected from all participants. 76 samples from
admitted patients in (D.S.H) hospital with Plasmodium falciparum
malaria infection and 50 samples from healthy individual’s volunteer
as controls. All laboratory tests were performed within 2hours from
the time of collection.

Parasitological analysis

The immuno-chromatography assay was used for the first
detection of HRP-II of Plasmodium falciparum malaria. thin blood
films were prepared on clean frosted slide, dry, grease free and labeled
and stained using Leishman stain for confirming and determining the
percentage counting of parasitic density Using the formula in count:
Number of infected RBCs Per 1000 RBCs cells *100.

Full WBCs differential count

WBCs count and differential performed by using the full
automated hematological analyzer system. XT-1800i., and the M:
L ratio calculated for each participant. Thin blood film also used to
confirm the ratio and the cell morphology.

Immunoglobulin IgE estimations

All Samples drawn in (EDTA) were centrifuged for 2500 Rounds
per 5 minutes and then separated the plasma in COBAS samples cup
0.5ml. All samples were tested for total Immunoglobulin (IgE) assay
measurement using full automated COBAS e411 and IgE levels were
reported in international units.

Statistical analysis

Statistical analysis was conducted in this study using SPSS
(version 20; SPSS Inc., Chicago, IL) software. Data were expressed
as mean ± standard deviation. Comparisons of continuous variables
made using the Student’s t-test for parametric data. The correlations
between Immunoglobulin E Levels, TWBC and Leucocyte differential
variables calculated using Pearson correlation coefficient. An alpha
value of <0.05 denoted a statistically significant difference in all
statistical compares.

Result

A total of 126 from all study groups analyzed for total IgE. In
stark contrast, however infected patients have the highest level of
total IgE (ranging from 28 to 2105 IU/ml) and this difference highly
statistically significant (P-value <0.001) furthermore M: L ratio (0.49)
found to be a highly statistically significant difference too (P-value
<0.001) (Table 1). In patient with severe malaria the total IgE level
meanwhile, varied from 392.56IU/ml (under 15years) to 369.93 IU/ml
(more than 45years) and this group have a higher level than the other
group 15-29 & 30-44 years old (209.12 & 161.25 respectively). All
these differences were significant (P-value<0.05) Table 2. Reporting
the correlation between the white blood cell count and differential
have negative correlation in spite of monocytes significantly positive
with severity of malaria (P-value<0.05) and the correlation of
immunoglobulin levels with severity of malaria illustrated in (Table
3). Total IgE have a positive correlation with severity of malaria
(P-value<0.001). M/L ratio associated with the risk of clinical malaria
(HR=0.30, 95% CI=0.11 to 0.84) found to be statistically significant
p-value<0.05. The analysis of the results revealed that the IgE levels
Table 4. The relative frequency of monocytes to lymphocytes in
peripheral circulation reflects on the infected individuals’. Show
the considerable an increase in an M/L ratio with the density of the
infection by Plasmodium falciparum (Figure 1). The irregular Climb
in the level of immunoglobulin with the rate of the infection by
Plasmodium falciparum reported in patient groups (Figure 2). Total
IgE levels have been high already in the youngest age group (<15
years), also appeared to be higher in older age patients (>45years).
The apparent decrease in concentrations between 15-44years old and this
difference was statistically significant Figure 3.

Citation: Alfaki DA, Eisa IM, Eibasheir MM, et al. Monocytes to lymphocytes ratio in peripheral blood and immunoglobulin IgE levels as indicators to

Figure 1 Correlation between M/L ratio and severity of malaria.

Figure 2 Correlation between total IgE levels and severity of malaria.
Monocytes to lymphocytes ratio in peripheral blood and immunoglobulin IgE levels as indicators to Plasmodium falciparum infection in Sudan

The study purpose was to find whether if there is any significant correlation, between the specific cellular compounds of the immune system which measured. And total IgE with the infection of malaria by Plasmodium falciparum species. Results revealed that there is slight reduction in total white blood count during the infection when compared against the control group, which is in line with what has been found in antecedent studies. This droop in total might due to the exhaustion in the immunological process to fight out the parasitic invasion. We found that there is light change in WBCS parameter (neutrophil, lymphocytes, monocytes and eosinophils according to each formed with his particular role. To expel the pathogenicity of Plasmodium falciparum, which adapt by wide range of interleukin’s. It was statistically different on the infected patient than controls group (Table 3), and this finding Homogeneously are aligned with similar articles. M: L ratio was found to be highly statistically significant differential with severity of malaria

**Discussion**

The result displayed that there were variation in the levels of total IgE, and it was highest than controls group in difference age categories (Figure 3) and this different was highly statistically significant. Total immunoglobulin IgE elevated to a high concentrations in young children and also the raising was reported in older patients (Table 2). IgE antibodies increased with age, becoming most significantly elevations in children less than 15years of age and in older more than 45-year age. In adult, those with Plasmodium falciparum malaria had significantly higher IgE antibody levels.

**Table 3** Correlation of immunoglobulin E levels, TWBC and leukocyte differential with severity of malaria

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgE</td>
<td>0.49</td>
<td>0.000**</td>
</tr>
<tr>
<td>TWBC</td>
<td>-0.024</td>
<td>0.84</td>
</tr>
<tr>
<td>Neutrophil %</td>
<td>-0.101</td>
<td>0.39</td>
</tr>
<tr>
<td>Lymphocyte %</td>
<td>-0.055</td>
<td>0.64</td>
</tr>
<tr>
<td>Monocyte%</td>
<td>0.237</td>
<td>0.039*</td>
</tr>
<tr>
<td>Eosinophil%</td>
<td>0.209</td>
<td>0.070</td>
</tr>
</tbody>
</table>

P-value<0.05 significant correlation, **P-value< 0.001 strong correlation

**Table 4** Association between ML ratio and total IgE level with severity of malaria

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ML ratio</td>
<td>0.30 (0.11 to 0.84)</td>
</tr>
<tr>
<td>Total IgE</td>
<td>0.99 (0.997 to 0.999)</td>
</tr>
</tbody>
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P-value<0.05 statistically significant association, HR=Hazard ratio

**Conclusion**

Ultimately malaria causing by Plasmodium falciparum parasites has a significant effect to immune system compounds. Admittedly we firmly found that the ratio of monocyte to lymphocyte (M: L) ratio, and total IgE which facilely obtained could contemplate the capability of effectivenss of immune response rate to P. falciparum infection. M/L ratio it might help successfully in severity determination of malaria infection. IgE going to interact effectively to eliminate the pathogenicity of malaria infection.

**Availability of data and materials**

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.
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Funding

No funding was received.

Ethics approval and consent to participate

This study was approved by the Research and Medical Ethics Committee Alzaim Al-Azhari University, Medical record office D, S H Hospital (No. 2017-07-T0021-R003).

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Conflicts of interest

The authors declare that they have no competing interests exist.

References
