Parasitology International 64 (2015) 139–144

Contents lists available at ScienceDirect

Parasitology International

journal homepage: www.elsevier.com/locate/parint

Chemokines responses to *Plasmodium falciparum* malaria and co-infections among rural Cameroonians

Jane Nchangnwi Che [a,b], Onyebiguwa Patrick Goddey Nmorsi [a], Baleguel Pierre Nkot [b], Clement Isaac [a,*], Browne Chukwudi Okonkwo [c]

[a] Tropical Disease Research Unit, Department of Zoology, Ambrose Alli University, Ekpoma, Nigeria
[b] Centre for the Diagnosis and Control of Tropical Disease, Nkolbisson, Yaounde, Cameroon
[c] Department of Internal Medicine, Central Hospital, Agbor, Nigeria

ARTICLE INFO

Article history:
Received 4 August 2014
Received in revised form 10 October 2014
Accepted 6 November 2014
Available online 16 November 2014

Keywords:
Uncomplicated malaria
Chemokines
Co-infections
Symptoms
Cameroon

ABSTRACT

Malaria remains the major cause of disease morbidity and mortality in sub-Saharan Africa with complex immune responses associated with disease outcomes. Symptoms associated with severe malaria have generally shown chemokine upregulation but little is known of responses to uncomplicated malaria. Eight villages in central Cameroon of 1045 volunteers were screened. Among these, malaria-positive individuals with some healthy controls were selected for chemokine analysis using Enzyme-Linked Immunosorbent Assay (ELISA) kits. Depressed serum levels of CXCL5 and raised CCL28 were observed in malarial positives when compared with healthy controls. The mean concentration of CXCL11 was higher in symptomatic than asymptomatic group, while CCL28 was lower in symptomatic individuals. Lower chemokine levels were associated with symptoms of uncomplicated malaria except for CXCL11 which was upregulated among fever-positive group. The mean CXCL5 level was higher in malaria sole infection than co-infections with HIV and *Loa loa*. Also, there was a raised mean level of malaria + HIV co-infection for CXCL9. This study hypothesises a situation where depressed chemokines in the face of clinical presentations could indicate an attempt by the immune system in preventing a progression process from uncomplicated to complicated outcomes with CXCL11 being identified as possible biomarker for malarial fever.

1. Introduction

An estimated two billion people live in areas at risk of malaria with blood stage of the parasite responsible for malaria-associated pathology [1]. In malaria-endemic regions, uncomplicated and severe malaria exists with the former being highly prevalent. Parasite load of more than 100,000 parasites/μL of blood are commonly regarded as indicators of risk of severe malaria in a low-transmission setting [2]. Symptoms of uncomplicated malaria may include fever, althralgia, headache, pallor, liver enlargement (mild hepatomegaly) and spleen enlargement (mild splenomegaly); and any of these could present at any stage of infection. However, since the aforementioned symptoms are non-specific for malaria, WHO recommends that malaria parasite confirmation in blood film through microscopy should be mandatory especially in endemic regions where these symptoms are mostly perceived to be solely caused by malaria and thereby given to arbitrariness and self medication [3]. Most times, among malarial-infected population, symptomatic and asymptomatic individuals are represented with the later largely due to the protective effect of the immune system following a repertoire of infection [4].

Immunity to malaria is dependent on both the innate and adaptive (both cell- and antibody mediated) arms of the immune system [5]. Chemokines are chemotactic cytokines that play important roles in bridging the innate and the adaptive immune system [6]. Being classified into subfamilies, CC, CXC, CX3C and C, chemokines share a significant degree of sequence homology [7] and play key roles in protozoan parasite infections by mediating cell trafficking and immune cells recruitment for the development of protective responses. Generally, during infection, leucocytes could cause a shift from constitutive to inflammatory chemokines with polarisation of $CD4^+$ T cells to T_H1 and T_H2 subsets orchestrated by the upregulation of distinct set of chemokines and their chemokine receptors [8,9]. Typically, T_H1 and T_H2 cells are predominantly characterised by known chemokine receptors' expressions, but the association of T-helper phenotypes in vivo has shown a much more complex profile [10,11].

Results of a study in some human subjects with long periods of non-exposure to *P. falciparum* malaria have shown decrease in cytokines and chemokines profiles [12]. Severe malaria comes with great fatalities and groups of chemokines have been implicated to influence the disease outcomes [13–15]. Current views have proposed that inflammatory responses contribute to the expression of severe malaria through a likely association with parasite density [16,14]. Also, progression from

* Corresponding author.
E-mail address: clementisaac@aauekpoma.edu.ng (C. Isaac).

http://dx.doi.org/10.1016/j.parint.2014.11.003
1383-5769/

uncomplicated to severe malaria is a possibility and the mechanism could be mediated by complex immune responses. Furthermore, in malaria-endemic regions, malaria co-exists with other pathogens in the blood, and this is a factor that could aggravate its pathological conditions. In order to ascertain the importance of chemokines in relation to symptoms of uncomplicated malaria in an effort towards partly understanding the dynamics of progression from mild to possibly documented severe cases, the profiles of some chemokines were determined and their roles were discussed. Also, chemokine reponses to malaria co-infections with HIV and *Loa loa* were highlighted.

2. Materials and methods

2.1. Study area

This study was conducted in November 2012 and samples collected were from rural Cameroon. Eight villages were selected: Koukoum, Minkotmbem, Kaya, Libamba, Bonde, Bondjock, Ngombas and Bakoukoué (Figure 1. These villages are inhabited by the Bakoko-Bassa and Eton ethnic groups and are within the Centre Region of Cameroon, namely Nyong-and-Kelle Division and in Makak Subdivision between coordinates 2° 48′ N–4° 32′ N and 9° 54′ E–13° 30′ E. Also, the villages are located in Nyong valley which has Rain Forest vegetation; and within it, portions of the Nyong River (690 km long) and its tributaries run. The climatic conditions of the area favours mosquito breeding and as such malaria transmission is meso-endemic with highest transmission index during the rainy season. Four climatic seasons characterise this region annually, viz; two dry seasons and two rainy seasons. These seasons are a long rainy season with low intensity from March to June; a short dry season from July to August; a short rainy season with high intensity from September to November and a long dry season from mid-November to February. The majority of the houses seen in this area are mud houses; and many are without door or/and window nettings to prevent mosquitoes and other flying or creeping insects from gaining entry.

2.2. Study population

The human population size of these villages is about two thousand with farming being the major preoccupation. Others are workers in industries including the hydroelectric cooperation. Prior to the mass screening exercise, ethical clearance from the Cameroon National Ethical Committee was obtained; and subsequently, community

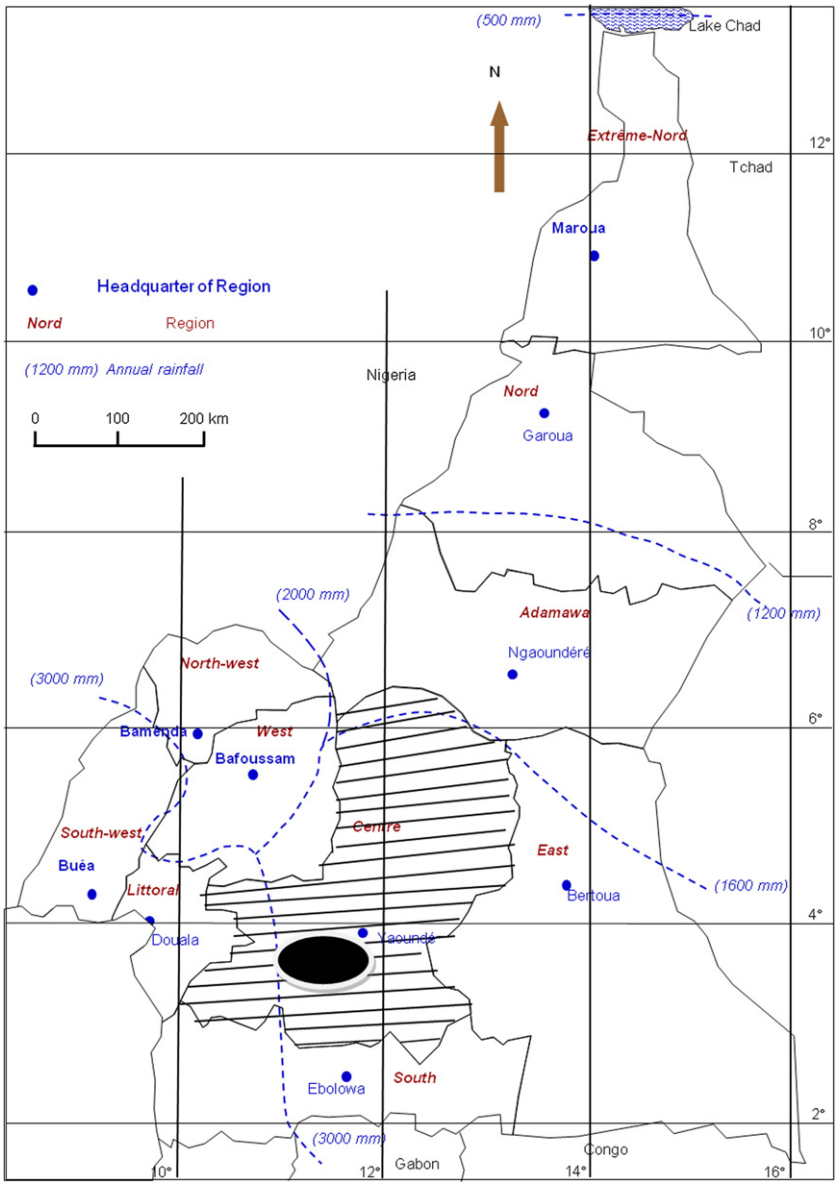

Fig. 1. Map of Cameroon showing study areas (Cellule Cartographie DAT). Legends: Study area. Study Region (the Centre Region).