

Association between Simple Uncomplicated Falciparum Malarial Infection & Acute Severe Asthmatic Attack in Khartoum State 2009

Nagla Abdalghani¹, Tahani Babiker², Amal Hassan³, Mozdalifah Elnaem⁴

^{1,4}Faculty of Applied Sciences, Jazan University, Saudi Arabia

²Faculty of Public and Tropical Medicine, Jazan University, Saudi Arabia

³Faculty of Nursing, Jazan University, Saudi Arabia

* Corresponding author E-mail address: [nagogoraish\[at\]gmail.com](mailto:nagogoraish[at]gmail.com)

Abstract: **Background:** Respiratory symptoms and signs can develop in uncomplicated falciparum malaria in adults' patients, with a reported frequency of 4%–18%; however, in some early studies, the denominator was unclear, accuracy of speciation was not ensured, radiology was often lacking, and secondary bacterial infections were included. In addition, respiratory symptoms and signs are common in uncomplicated plasmodium falciparum malaria, particularly in African children. In these children, there is considerable clinical overlap with the features of pneumonia. Yet; most studies focusing on pulmonary involvement with malarial infection are case reports or included small number of patients. **Method:** A descriptive cross sectional hospital based study it was carried out in the main central hospitals in Khartoum state during the period from June 2008-April 2009; 50 adult patients with acute severe asthmatic attack has been chosen by simple randomization. Data collected through questionnaire by the researcher. The degree of severity of asthma assessed clinically and by measurement of PEFM. All patient investigated by thick & thin films for malaria to find out the degree of parasitemia & to identify the plasmodium species respectively. Data include the different variables age, gender, duration of hospital admission & the signs and the symptoms of severe asthma along with laboratory data support a diagnosis of falciparum malaria with degree of parasitemia analyzed using the suitable statics measurements. **Results:** The result demonstrate that most of the patients were females (68%), their mean age within 40 years; all the patients reside in Khartoum state without any history of travelling to any other endemic states. All patients admitted to Asthma care unit, Blood film for malaria is positive in (24%), who had the lower PEFM mean of 166l/min of their best predicted with higher respiratory rate > 30 cycle/minute with lower oxygen saturations 85%-95% with long duration of (5- 10 days) hospital admission. **Recommendations:** Patients with acute severe asthmatic attack with febrile illness in endemic areas should have prompt investigation of malaria parasites & should receive antimalarial treatment along with standard measurement of bronchial asthma and more study in this topic is highly recommended.

Keywords: Acute severe asthma, Falciparum malaria, Khartoum state, descriptive study

1. Background

Malaria remains a big public ill health problem globally, especially within the tropical and subtropical areas. More than two billion people (36% of the world population) are exposed to the risk of contracting malaria[1, 2]. Each year, malaria directly causes nearly one million deaths and about 500 million clinical cases, of which 2 to 3 million constitute severe and complicated malaria[3, 4]. Recent epidemiologic models, geographical and demographic data suggest that *Plasmodium falciparum* estimates outside Africa, especially in southeast Asia, are 200% higher than reported by the World Health Organization(WHO) — 118.94 million of global estimates of 515 million cases[2, 5]. Malaria, like tuberculosis (TB) has a devastating socioeconomic impact on the affected countries. The term *disability adjusted lifeyears* (DALYs) has been introduced by the WHO, and one lost DALY means one lost year of “healthy life” on account of disease (either through death or illness/disability) 6, 7[6, 7]. It has recently been estimated that in India, the total DALYs lost due to malaria were 1.86 million years [5].

Lung involvement with malarial infection is well recognized for many years; in adults' patients, noncardiogenic pulmonary edema and acute respiratory distress syndrome (ARDS) with normal pulmonary artery occlusion

pressure are grave complications of falciparum malaria, with a high mortality rate. They are also a major cause of death in those adults who present with other manifestations of severe malaria [8, 9–11]. Pulmonary symptoms such as cough with or without expectoration, dyspnea, among others have been described in patients with malaria, [12, 13]. Historically, three clinical types of pulmonary manifestations have been variously described in patients with falciparum malaria, namely *bronchitis*, *pneumonic* and *bronchopneumonia* forms. It has been suggested that malarial pneumonitis is uncommon and these manifestations are probably due to coincident pneumonia, pulmonary edema and perhaps, metabolic acidosis[12, 13]. Altered lung function was common in both patients with uncomplicated falciparum malaria and those with vivax malaria and included obstruction of the small airways, reduced alveolar ventilation, reduced alveolar gas transfer, and increased pulmonary phagocytic cell activity[14].

Observations from other studies and other published reports [12, 13]. suggest that about 5% patients with uncomplicated falciparum malaria and 20% –30% patients with severe and complicated malaria requiring ICU admission may develop ARDS. It should be remembered, however, that different denominators have been used in various publications and meaningful comparison of such data is not possible.

Furthermore, in many of the previously reported studies, the precise definition used for the diagnosis of ARDS is additionally not mentioned.

Despite clinical recognition of pulmonary manifestations in both uncomplicated and severe malaria, there has no definition of disease-related changes in pulmonary function, and underlying mechanisms are not well understood. We, therefore, prospectively examined the clinical manifestation of patients with asthma who admitted to asthma care unit, with association of un-complicated falciparum malaria.

In summary, altered pulmonary physiology in falciparum malaria includes obstructions of the airflow, impaired ventilation; reduce gas transfer and increased pulmonary phagocytic activity [14]. That can lead to respiratory compromise that can lead to exacerbation of severe acute asthma attack.

Malaria remains the most important cause of imported fever and cases requiring ICU admission continue to be associated with a high mortality. While there have been significant advances in our understanding of the management of malaria in the last decade, high-quality data to guide management of imported malaria remain scarce, with most derived from endemic settings or retrospective series. The emergence of artemisinin-based therapy has translated into a significant improvement in outcomes. In endemic countries and is likely to improve outcomes in imported malaria in the future. Despite this advance, the mortality from imported malaria are mains significant; all cases should be discussed with a specialist unit and transfer of the patient considered[15].The objective of this study to study the association between acute severe asthma attack and simple uncomplicated infection of falciparum malaria.

2. Methodology

Study Design:

This is a descriptive cross-sectional hospital based study was carried out in Asthma care unit of the main Elshaab hospital, the central CTM hospital in Khartoum stateso as to identified the relationship between acute severe asthma attack and simple un-complicated infection of falciparum malaria.

Study population and sample collection

All cases presented by clinical manifestation simulate bronchial asthma and admitted in Asthma care unit from June 2008 to April 2009 was study unit, and those were refused to participate in the study were excluded from the study.

Clinical assessments and tests of pulmonary function included respiratory signs and symptoms by were daily reported.

Thick and thin blood sample were collected and transfer to Malaria National program, samples were checked by Malariologist with >10 years' experience samples were examined for species and total malarial parasite count.

Data Analysis:

Data was analyzed by using the statistical package for social sciences programs (SPSS), and then results were presented in tables and figures.

Ethical Consideration:

Ethical approval was obtained from Research Ethics Committee of Sudan Medical Specialization board. Consent written was acquired from hospital and all participants. Confidentiality of all participants was maintained as no names were mentioned in the questionnaires.

3. Results

Table 1: Shows the Socio-demographic characteristic of the patients

Variable	Frequency	Percentage
Gender		
Male	16	32
Female	34	68
Age group		
18-24	8	16
25-35	15	30
36-49	12	24
50-60	10	20
<60	5	10
Residence		
Khartoum	37	74
Outside Khartoum	13	26
Total	50	100

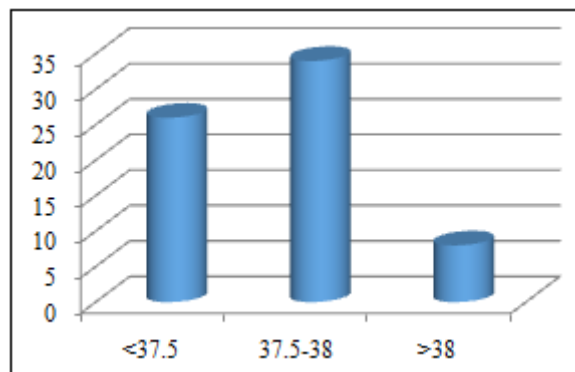


Figure 1: Distribution of patient according to the duration of hospital admission

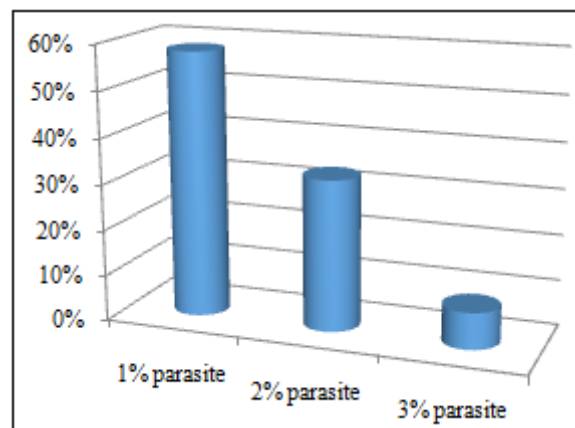


Figure 2: Distribution of patient according to the body Temperature

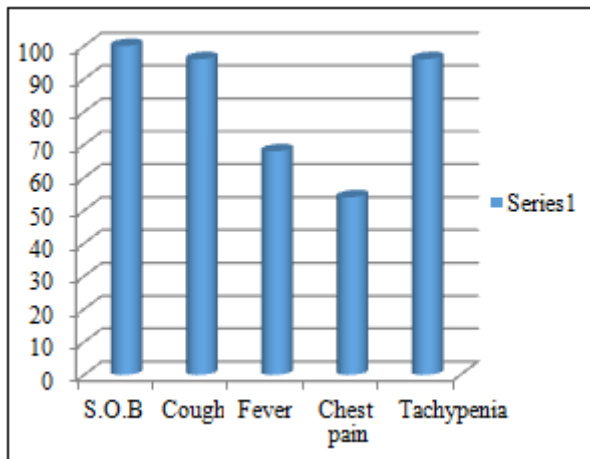


Figure 3: Degree of Parasitemia

Figure 4: Patients symptoms

Table 3: Title: Level of oxygen saturation among study group

Oxygen level	NO	%
<85%	3	6%
85%-95%	28	56%
>95%	19	38%
Total	50	100%

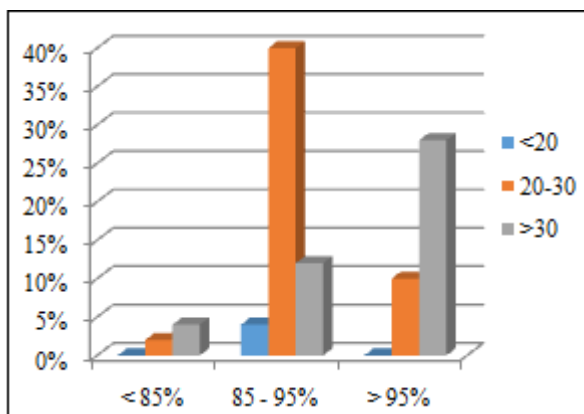


Figure 5: Correlation between respiratory rate & O2saturation

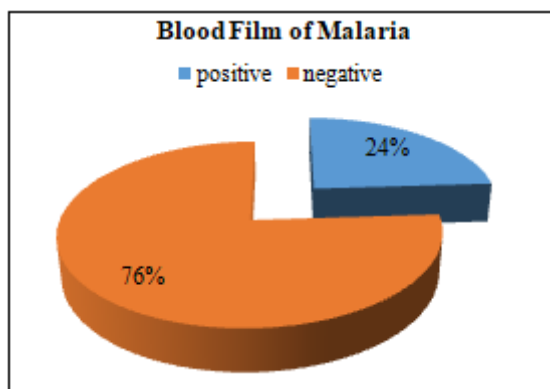


Figure 6: Blood film for falciparum malaria

Table 4: Title BFFM result & Duration of hospital stay amongst study group

Duration of hospital stay	BFFM		Total	%
	Positive	Negative		
< 5 days	3	4	7	14%
5-10 days	7	30	37	74%
>10 days	2	4	6	12%
	12	38	50	100%

Table 5: Title PEFM among positive film for plasmodium falciparum

Patients	PEFR/L/m
1	100
2	110
3	115
4	120
5	125
6	144
7	146
8	165
9	180
10	200
11	210
12	246

4. Results

A total of 50 of patient were interviewed, the result indicates that 68% of patient were female, about 30% of them were in the age group 25–35 years, 74 % of them were residence in Khartoum Sudan capital (Table 1).

The result indicates that 74% were admitted in hospital between 5 to 10days, 34% of the patients have high temperature than the normal values among these patients 24% were positive for Plasmodium Falciparum Malaria by thick blood film and 58% of the patient has low level of parasitemia (Fig 1, 6 & 3).

Shortness of breath is the main clinical presentation; cough is present in 96% of the patients, 68% has fever, 54% presented by chest pain (Fig 4).

Amongst patient who stay in the hospital 5-10 days,18% were positive for Falciparum malaria species (table 4).

High respiratory rate between 20-30cycle/minute in 40% of the with have correspondingly low oxygen saturation between 85%-95%, while patients with respiratory rate >30cycle/minute are4% their oxygen saturation < 85% (Fig 5). With average peak expiratory flow rate amongst all positive for malaria is only 166l/min form the best-predicted values for these patient (table5).

5. Discussion

The current study is the first to link between the acquisition of falciparum malarial infection and exacerbation of acute severe asthmatic attack. As it is well known that simple uncomplicated falciparum malaria can lead to pulmonary affection through different pathophysiological mechanism. The occurrence of lung function impairment in both vivax and falciparum malaria suggests that there are common underlying inflammatory mechanisms, these mechanisms

may be occurring with greater magnitude in severe malaria, where lung injury is a major cause of mortality in non-immune adults [16]. In our study fifty patients admitted to ACU were studied. 68% of them were female, their mean age was 40 years and, compared to Indian study (2000) lung involvement with malarial infection 100-slide positive for malaria their mean age was 29.3 with male predominance in the same study [17].

Twelve of the patients (24%) of them were positive for malaria and plasmodium falciparum is that the only species detected. Compared to an Indian study, where 100 positive patients had the distribution of (53%) were *P. Vivax*, *P. Falciparum* (36%) and mixed infection in (11%), however falciparum species was identified in 25 patients out of 26 who were presented with respiratory manifestation [17]. This was almost like to study conducted in Pediatric Hospital in Los Angeles, during which 9 patients with respiratory manifestations were positive for Falciparum species [18]. Amongst the studied group the main presenting symptom is cough which was present in (96%) Although cough and respiratory symptoms of falciparum malaria have been well recognized in children residing in malaria-endemic areas [19, 20] and in adult returned travelers [14], the present study has demonstrated that cough is also a dominant presenting symptom in adults patients with bronchial asthma with falciparum malaria. Cough occurred with similar frequency in patients with severe malaria and those with uncomplicated malaria and resolved within 2 weeks of treatment. Compared to Los Angeles study it was found in 5 patients [18], while in the Indian study it is found in (77%) [17].

Shortness of breath during this study is found altogether patients; however, it is found in 32% of the patients, within the Indian study 15 [17], this suggesting that asthma patients who contracted falciparum malaria have severe exacerbation of acute asthmatic attack, Chest pain as associated symptoms present in 54 % of studied group, which is almost similar to Indian study 51% [17].

Amongst the studied group, 62% had low O₂ saturation. Perhaps the severity of these symptoms in the studied group in comparison to other studies the inclusion of asthmatic patients in this study. This was supported by one study that discuss the mechanism of lung injury, these mechanisms may be occurring with greater magnitude in severe malaria, In which shows that there is impaired admission values for FEV₁ indicate airflow obstruction in malaria. They are unlikely to reflect consistently poor forced expiratory maneuvers by patients who are ill with malaria, because flows were also reduced in the middle of forced expiration, as assessed by FEF₂₅₋₇₅, which is less effort dependent this study suggest that [16].

Airflow obstruction in both vivax and falciparum malaria suggests that obstruction does not result solely from micro vascular obstruction by parasitized red blood cells in airway vasculature (found only with *P. FALCIPARUM*), but likely results from inflammation of small airways [21, 22, 23]. This support that in this study in these asthmatic patients who were positive for Falciparum malaria the mean PEFR among the study group was 164l/min that because patient with

bronchial asthma has obstructive pathophysiological mechanism.

6. Conclusion

This study concluded that uncomplicated falciparum malarial infection is one of leading factor for acute bronchial asthma exacerbation and it is not related to level of parasitemia.

7. Recommendation

Therefore, bronchial asthma patients who presented with an acute asthmatic attack with febrile illness in endemic areas this should alert the physician for investigating malaria parasite as precipitating factor.

8. Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

9. Conflict of Interest

The author(s) declare no conflict of interest.

References

- [1] Greenwood BM, Fidock DA, Kyle DE, Kappe SH, Alonso PL, Collins FH, *et al.* Malaria: progress, perils, and prospects for eradication. *J Clin Invest* 2008; 118: 1266–76.
- [2] Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature* 2005; 434: 214–7.
- [3] Rowe AK, Rowe SY, Snow RW, Korenromp EL, Schellenberg JR, Stein C, *et al.* The burden of malaria mortality among African children in the year 2000. *Int J Epidemiol* 2006; 35: 691–704.
- [4] Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW. The global distribution and population at risk of malaria: past, present, and future. *Lancet Infect Dis* 2004; 4: 327–36.
- [5] Kumar A, Valecha N, Jain T, Dash AP. Burden of malaria in India: retrospective and prospective view. *Am J Trop Med Hyg* 2007; 77: 69–78.
- [6] Murray CJL. Rethinking DALYs. In: Murray CJL, Lopez AD, editors. *The global burden of disease*. Cambridge: Harvard University Press 1996. p. 1–98.
- [7] Mathers CD, Ezzati M, Lopez AD. Measuring the burden of neglected tropical diseases: the global burden of disease framework. *PLoS Negl Trop Dis* 2007; 1: e114.
- [8] Brooks MH, Kiel FW, Sheehy TW, Barry KG. Acute pulmonary edema in Falciparum malaria. *N Engl J Med* 1968; 279: 732–7.
- [9] Charoenpan P, Indraprasit S, Kiatboonsri S, Suvachittanont O, Tanomsup S. Pulmonary edema in severe falciparum malaria: hemodynamic study and clinicophysiological correlation. *Chest* 1990; 97: 1190–7.

- [10] James MF. Pulmonary damage associated with falciparum malaria: a report of ten cases. *Ann Trop Med Parasitol* 1985;79:123–38.
- [11] Patel V, Khan FA. Pulmonary complications of malaria. *Semin Resp Med* 1991;12:8–17.
- [12] Taylor WR, White NJ. Malaria and the lung. *Clin ChestMed* 2002; 23: 457–68.
- [13] Taylor WR, Cañon V, White NJ. Pulmonary manifestations of malaria: recognition and management. *Treat Respir Med* 2006; 5: 419–28
- [14] Anstey NM, Jacups SP, Cain T, et al. Pulmonary manifestations of uncomplicated falciparum and vivax malaria: cough, small airways obstruction, impaired gas transfer, and increased pulmonary phagocytic activity. *J Infect Dis* 2002; 185:1326–34.
- [15] *British Journal of Anaesthesia* 113 (6): 910–21 (2014) Advance Access publication 19 June 2014. doi:10.1093/bja/aeu157.
- [16] Bates D. *Respiratory function in disease*. 3d ed. Philadelphia: WB Saunders, 1989
- [17] Rajput R, Singh H, Singh S, Menna, Tiwari UC. Pulmonary manifestations in malaria 2000 Oct;98(10):612-4
- [18] Gozal D. The incidence of pulmonary manifestations during Plasmodium falciparum malaria in non-immune subjects. *Trop Med Parasitol* 1992; 43:6–8.
- [19] O'Dempsey TJ, McArdle TF, Laurence BE, Lamont AC, Todd JE, Greenwood BM. Overlap in the clinical features of pneumonia and malaria in African children. *Trans R Soc Trop Med Hyg* 1993;87:662–5.
- [20] Redd SC, Bloland PB, Kazembe PN, Patrick E, Tembenu R, Campbell CC. Usefulness of clinical case-definitions in guiding therapy for African children with malaria or pneumonia. *Lancet* 1992;340:1140–3.
- [21] Applebaum IL, Shrager J. Pneumonitis associated with malaria. *Arch Int Med* 1944;74:155–62.
- [22] Falconer AW, Anderson A. Clinical types of subtertian malaria. *Lancet* 1917;1:607–10.
- [23] Hughes SB, Bomford DM. Clinical features and treatment of malaria in British troops in West Africa. *BMJ* 1944;1:69–73.