



Study Of Serum Malondialdehyde And Uric Acid Levels In Patients With Malaria: Case Control Study

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Abstract

Aim & Objectives: The aim of this study is to estimate the levels of MDA and Serum uric acid in malaria patients and healthy controls.

Materials And Methods: In this study, 25 malaria patients and 25 healthy controls of both gender matching in age and sex were included. The analysis of biochemical parameters was done by using auto analyzer using diagnostic reagent kit.

Results: In the present study Mean of MDA and Serum uric acid was higher in malaria patients than controls (P < 0.001)

Conclusion: Significant changes were observed in MDA and Serum uric acid. They are favorable prognostic biomarkers with high accuracy for predicting the in-hospital mortality in patients with malaria.

Keywords: serum malondialdehyde (MDA), ROS (Reactive Oxygen Species)

Introduction

Malaria is a mosquito-borne infectious disease of humans caused by eukaryotic protists of the genus Plasmodium are responsible for more than 500 million clinical cases of malaria globally each year^[1]. About 1.5 – 3.5 million deaths from malaria have been reported to occur annually and Several studies showed that physicochemical changes in the membrane of the erythrocyte induced by oxidative stress is responsible for membrane lipid peroxidation and increased haemolysis seen in malaria patients^[3,4,5]. Orengo and colleagues showed that after haemolysis, uric acid derived from hypoxanthine accumulated by Plasmodium falciparum-infected erythrocytes is a major

contributor to the inflammatory response triggered in human peripheral blood mononuclear cells (PBMCs)^[6]. The immune system of the body is activated by infections, including malaria, thereby causing the release of reactive oxygen species. The accumulation of organic peroxides and oxidation of membrane lipids place a stress on cellular vitality ultimately leading to destructive effects on the cell. The production of malondialdehyde is used as a biomarker to measure the level of oxidative stress in an organism^[7].

Antioxidants are substances which when present in low concentration compared to the oxidizable substrate, significantly delay or inhibit the oxidation of that substrate^[8]. The physiological role of

antioxidants is to prevent damage to cellular components arising from the activity of chemical reactions involving free radicals seen in oxidative stress. There are three classes of antioxidants namely: primary antioxidants ^[9], secondary antioxidants ^[10, 11]

and tertiary antioxidants ^[12]. All these antioxidants in the body together form the total antioxidant status (TAS) of an individual. Bilirubin is the yellow breakdown product of normal hem catabolism after haemolysis. ^[12]

Figure : 1

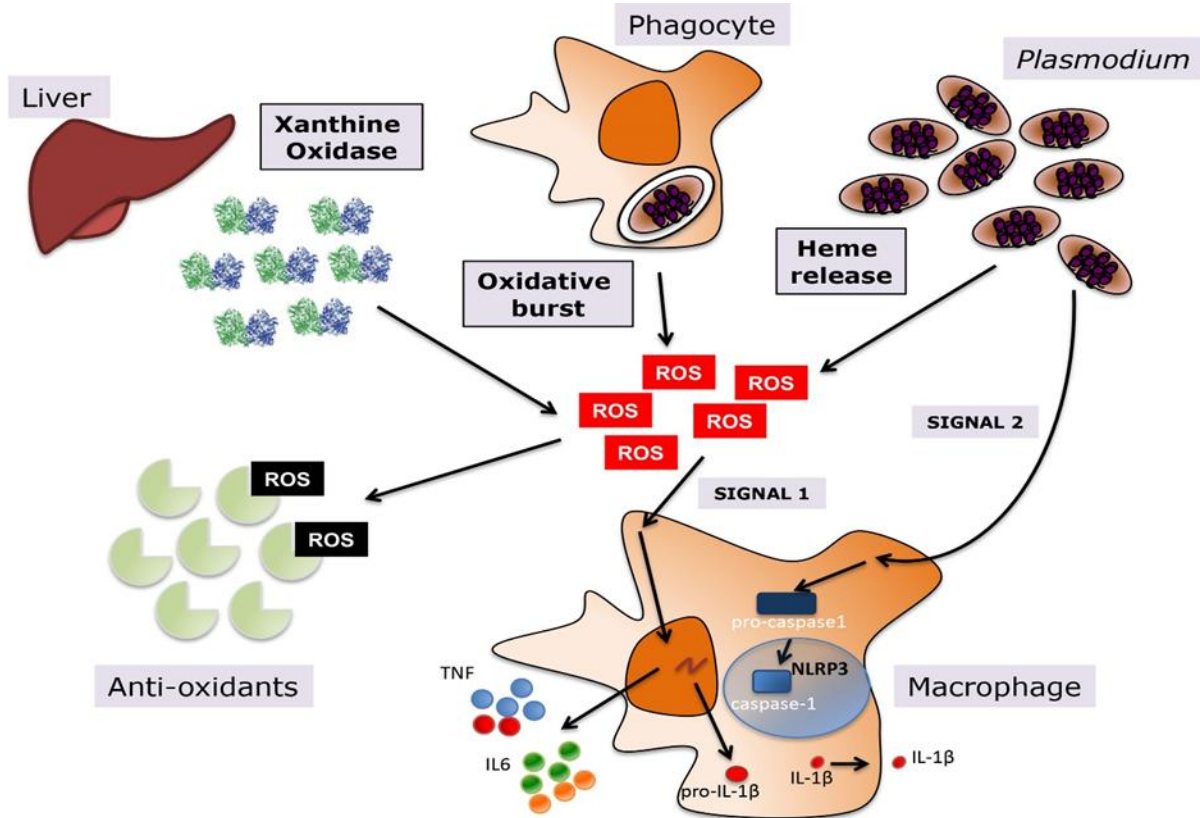


Figure 1 Oxidative stress during Plasmodium infection. Various sources contribute to the oxidative environment during malaria, including up regulation of host enzymes such as XO, the oxidative burst in macrophages upon phagocytosis of infected erythrocytes, and heme release from hemoglobin degradation in host infected erythrocytes. A balance between levels of anti-oxidants in the human host and the generation of ROS determines the levels of oxidative stress. ROS promote inflammation in malaria, leading to the activation of macrophages and the subsequent release of pro-inflammatory cytokines, such as TNF and IL6 among others, but also inflammasome-dependent IL1- β , where ROS provide priming signal 1 and *P. falciparum* the activating signal 2. ^[13]

Therefore this study is designed to determine possible associations and relationships between malaria infection and oxidative stress by assessing changes in uric acid and serum MDA in malaria patients and healthy controls.

Material And Methods

This study was carried out in Department of Biochemistry, Prakash Institute of medical Science and research, Urun-Islampur collaboration with Department of Biochemistry Yogita Dental college and hospital khed. The study includes 25 laboratory diagnosed cases of malaria patients with equal age and sex matched control attending hospital OPD with included in the study often obtaining their informed consent. The study was conducted on with age group

between 20 to 60 years. The analysis of biochemical parameters was done using standard grade reagent chemicals. MDA was estimated using MDA - thiobarbituric acid method, ^[14] uric acid is estimated by phosphotungstic acid method. ^[15]

The exclusion criteria included subjects of any systemic or metabolic disease, liver disease, vascular

diseases, renal artery stenosis, alcoholics, pregnant female and those who were taking any kind of medication last few years. A record was maintained containing current history, diet along with laboratory investigations and previous history of any disease.

Distribution Of Study Subjects:

Group I	N = 25 Malaria patients.
Group II	N= 25 Healthy controls

Collection Of Blood Samples:

Blood was collected from each subject under aseptic conditions by using vacutainers. The blood samples were allowed to clot at room temperature for 20–30 minutes & serum was separated from cells by centrifugation for analysis of biochemical parameters. The analysis of biochemical parameters was done by using standard grade reagents and chemicals. Serum reagent as per the manual provided by the manufacturer.

Results

Table no. 1: The mean value of MDA and Serum Uric acid in malaria patients and controls.

Name Of the Parameters	Malaria Patients (N=25)		Controls (N=25)		Significance
	Mean \pm SD	Std. Error of Mean	Mean \pm SD	Std. Error of Mean	
MDA	9.82 \pm 0.76 ***	0.153	3.46 \pm 1.22	0.244	P =< 0.001
Serum Uric Acid	9.62 \pm 0.97 ***	0.19	4.47 \pm 1.16	0.233	P = <0.001

The statistical method uses to compare data was unpaired' test

*P> 0.05.....Not Significant

**P<0.05.....Significant

***P<0.001.....Highly Significant

There is highly statistically significant difference in means of MDA and Serum uric acid ($P < 0.001$) as compare to controls.

In the present study Mean of Serum MDA and Serum uric acid was higher in malaria patients than controls ($P < 0.001$).

Discussion

Increase of serum MDA level may be due to generation of ROS (Reactive Oxygen Species) during hemoglobin consumption by malaria parasites, which in turn enhance the chain reaction of lipid peroxidation releasing H_2O_2 which accelerate lipid peroxidation again. This indicates the lipid peroxidation is increased in malaria as compared to normal healthy controls. Our study findings were similar with the results found other researchers studies like OB Idonije *et al.* [16] Mohammed Khalid Rashid *et al.* [17] Camila Fabbri *et al.* [18]

Increased levels of serum uric acid show its involvement in pathogenesis, it helps in activation of immune system and release of cytokines. Similar results of increased uric acid levels were also obtained by Gallego Delgado J *et al.* [19] Jamie M *et al.* [20].

Conclusion

In conclusion, this present research Serum MDA and Serum uric acid was higher in malaria patients than controls groups. From our findings, we conclude that the oxidative stress in malaria due to generation of ROS leads to increase MDA levels. Also there are increased uric acid levels due to inflammation. Hence for good healing and recovery from malaria, we need to take good antioxidants in diet during infection.

References

1. R.W Snow, C.A Guerra, A.M Noor, H.Y. Myint, and S.I. Hay, The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature*. 434:2005: 214–217
2. P. Trigg and A.V. Kondrachine, The current global malaria situation. *Malaria*, 4th edition, London, Butterworth Publication (1993) (11-21)
3. I.A. Clark and N.H. Hunt, Evidence of reactive oxygen intermediates causing hemolysis and parasite death in malaria. *Infection and Immunity*. 39, 1983: 1 – 6.
4. I.A. Clark, N.H. Hunt, W.B Cowden, L.E. Maxwell E.J. And Mackie, Radical-mediated damage to parasites and erythrocytes in *Plasmodium vinckei* infected mice after injection of t-butyl hydroxide. *Clinical Experimental Immunol*. 56, 1984: 524-530
5. B.S. Das and N.K. Nanada, Evidence for erythrocyte lipid peroxidation in acute falciparum malaria. *Trans. Roy. Soc. Trop. Med. Hyg.* 93, 1999: 58-62
6. J.M. Orengo, A. Leliwa-Sytek, J. E Evans, B. Evans, D. van de Hoef, M. Nyako, K. Day and A. Rodriguez, Uric acid is a mediator of the *Plasmodium falciparum*-induced inflammatory response. *PLoS ONE*. 4 (4) 2009: e5194
7. K. Moore and L. J. Robert, Measurement of lipid peroxidation. *Free Radical Res.* 28, 1998:659-671
8. Halliwell, B. and Gutteridge, J.M.C. (). The definition and measurement of antioxidants in biological systems. *Free Radic Biomed.* 18,1995: 125-126
9. D.I. Thurnham, (). Antioxidants and prooxidants in malnourished populations. *Proceedings of Nutritional Society*. 49, 1996: 173- 185
10. S.K. Gaby and V.N. Singh, Vitamin C, intake and health; A scientific review (New York, Marcel Dekker,1990) (1033-1044)
11. J.H. Weisburger, Nutritional approach to cancer prevention with emphasis on vitamin antioxidants and Carotenoids. *American Journal of Nutrition*. 53, 1991: 2265-2375
12. N. Miller, C. Rice-Evans and M.J. Davies, A novel method for measuring antioxidant capacity and its application to monitoring the antioxidant status in premature neonates. *Clinical Science*. 84, 1993: 407-412
13. Vasquez M, Zuniga M and Rodriguez A (2021) Oxidative Stress and Pathogenesis in Malaria. *Front. Cell. Infect. Microbiol.* 11:768182. doi: 10.3389/fcimb.2021.768182.
14. Janero DR, Burghardt B. Analysis of cardiac membrane phospholipids peroxidation kinetics as malondialdehyde: unspecificity of thiobarbituric acid-reactivity. *Lipids*. 1988;23:452–8.
15. The phosphotungstic acid method. *Acta Med Scand.* 1937;92:17–38.

16. Idonije OB, Festus O, Okhiai O, Akpamu U. Comparative study of the status of a biomarker of lipid peroxidation (malondialdehyde) in patients with plasmodium falciparum and plasmodium vivax malaria infection. *Asian J Biol Sci.* 2011;4:506–13.
17. Rashid MK. Oxidative stress marker and antioxidant status in falciparum malaria in relation to the intensity of parasitaemia. *Int J Biol Med Res.* 2013;4(3):3469–71.
18. Fabbri C, Mascarenhas-Netto RC, Lalwani P, Melo GC, Magalhães BML. Lipid peroxidation and antioxidant enzymes activity in Plasmodium vivax malaria patients evolving with cholestatic jaundice. *Malar J.* 2013;12:315.
19. Gallego-Delgado J, Ty M, Orengo JM, Hoef D, Rodriguez A. A surprising role for uric acid: the inflammatory malaria response. *Curr Rheumatol Rep.* 2014;16(2):401. doi:10.1007/s11926-013-0401-8.
20. Orengo JM, Leliwa-Sytek A, Evans JE, Evans B, Hoef D. Uric Acid Is a Mediator of the Plasmodium falciparum-Induced Inflammatory Response. *Plos One.* 2009;4(4):e5194.