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Assessment of Haemoglobin Variants in Malaria Infected Individuals Using Haematological Parameters

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Abstract The aim of this study was to determine the effect of haemoglobin variants in *Plasmodium falciparum* infected individuals using haematological parameters. The study was conducted at Federal Teaching Hospital, Ido-Ekiti Nigeria. Two hundred and two blood samples were collected twice from each malaria infected individuals; grouped as pre-treatment and post anti-malaria drug treatment; 4ml of blood sample was collected and dispensed into K_2EDTA vaccutainer bottles for haemoglobin electrophoresis using cellulose acetate electrophoresis as described by Dacie and Lewis, haemoglobin concentration, packed cell volume and red cell indices were analysed using haematology analyser, thick blood film was made and stained with Giemsa's staining technique for malaria parasite detection as described by Monica Cheesbrough. Data obtained was analysed using SPSS version 16. The result of this present study showed that, the mean±SD of red blood cell, haemoglobin concentration, packed cell volume, red cell indices and red cell distribution width of HbAA in pre and post anti-malaria drug treatment were significantly ($P<0.05$) lower compared to HbAS and HbAC in pre and post anti-malaria drug treatment. This present study showed that, HbAS and HbAC suffer less malaria attack with lower incidence of clinical malaria compared to HbAA.

Keywords: *malaria parasite, haemoglobin variants and haematological parameters*

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1. Introduction

Malaria is a serious public health problem in most countries of the tropics. It is a major cause of mortality and morbidity, between 300 and 500 million people suffer acute cases of malaria in 100 developing countries each year, and the majority of the victims are children [1]. In Nigeria about 96 million people are exposed to malaria, and out of these 64 million people get infected and almost 300,000 deaths are being reported annually in the general population, of which over 100,000 deaths are of children [2]. Genetic factors play a key role in determining resistance/susceptibility to infectious disease. Susceptibility of the human host to malaria infection has been reported to be influenced by genetic factors, which could be confounders if not taken into account in the assessment of the efficacy of interventions against malaria. Humans exhibit variable susceptibility to malaria infection; most of the resistance to this infection is either genetic, environmental, based upon previous exposure, or access to therapy. The genetic resistance to malaria infection, particularly *p. falciparum* malaria, associated with the hemoglobinopathies, the mechanisms of genetic resistance to *P. falciparum* malaria at the erythrocytic stage may involve one or more of the following: inhibition of merozoite entry into the red cell [3], impairment in intracellular growth of the parasite, prevention of the erythrocyte lysis that occurs at the end of parasite maturation, which leads to release of merozoites into the blood stream, enhanced phagocytosis of parasite-infected red cells [4]. HbAS is widely known to confer significant protection from severe and uncomplicated malaria [5,6,7,8,9], although underlying mechanisms not precisely defined. Similar protection afforded by haemoglobin C (HbC) was more recently demonstrated although findings are less conclusive. Several innate or immune mechanisms have been hypothesized to explain malaria-protective effects of HbS or HbC [7,8,10,11,12]. Erythrocytes containing HbS or HbC may impede parasite growth and replication relative to normal red cells when subject to low oxygen tensions (Williams, 2011). Protein targets of specific antibodies may be more rapidly exposed in HbS-containing red blood cells [4] resulting in an enhanced immune response to infection [11,13]. It is also possible that unknown innate protective processes may up-regulate the malaria-specific immune response [14] or enhance nonspecific immunity to malaria [15]. Indeed, abnormal haemoglobin may not allow for optimal development of Plasmodium in deep organs where oxygen pressure is reduced. The aim of this study was to determine the effect of haemoglobin genotype variants in *Plasmodium falciparum* malaria infected individuals using haematological parameters.

2. Materials and Methods

2.1. Subjects, Study Design and Sample Collection

This study was conducted at Federal Teaching Hospital, Ido-Ekiti, Ekiti State Nigeria. Subjects were *Plasmodium falciparum* malaria infected adult individuals; presented with signs and symptoms of malaria infection. This was confirmed using malaria rapid kit test and microscopy detection of malaria parasite. Two hundred and two 202 blood samples were collected (4ml) twice from the same malaria infected individuals; grouped as pre-treatment (at presentation) and post anti-malaria drug treatment. One hundred and two 102 blood samples from apparently healthy individuals negative to malaria infection was collected for control; both *Plasmodium falciparum* malaria infected subjects and controls were within the age 15-64 years of both sex. Patient's consent was sort for through an informed consent form; also ethical approval was obtained from the hospital. Structured questionnaire was used to obtained demographic characteristic and other relevant information for the study.

2.2. Methodology

About 4ml of blood sample dispensed into di-potassium ethylenediaminetetracetic acid (K_2EDTA) vaccutainer bottles were used for haemoglobin concentration, packed cell volume and red cell indices analysed using haematology analyser (sysmex automated haematology analyser model kx-21n, manufactured by sysmex co-operation kobe, Japan). Thick blood film was made from EDTA blood sample and stained with Giemsa's staining technique for malaria parasite detection; observed under microscopy using x100 objective lenses, the procedure was described by Monica Cheesbrough [15]. 0.3ml of blood sample was used to prepared hemolysate by centrifuge at 3000g for ten minutes with Hittich universal bench centrifuge, model 1200. Plasma was aspirated off while the precipitate (blood cell layer) was resuspended in equal volume of normal saline (0.85% NaCl) for washing. The washing was repeated three times and finally resuspended in equal volume of normal saline. The red blood cell suspension (40ul) was mixed with equal volume of distilled water to lyse the blood cell. The resulting haemoglobin lysate (the lysate) was used for haemoglobin genotype determination [17]. The method described by Brown was used for haemoglobin electrophoresis. A small quantity of hemolysate of venous blood from each of the subject was placed on a cellulose acetate membrane and carefully introduced into the electrophoretic tank containing tris-EDTA-borate buffer at pH 8.6. Electrophoretic separation was then allowed to operate for 15 to 20 minutes at an electromotive force (e.m.f) of 160v. The results were read immediately. Hemolysate from blood samples of known haemoglobin (AA, AS, AC, SC, CC and SS) were run as controls.

3. Statistical Analysis

Data obtained were analysed for mean and standard deviation; significant test was done by ANOVA. Level of significance was considered as <0.05.

Table 1. MEAN±SD OF HB, PCV AND RBC INDICES ON HAEMOGLOBIN GENOTYPE VARIANTS IN PRE TREATMENT OF MALARIA INFECTED SUJECTS

Groups	RBC $X10^9$/L	Hb g/dL	PCV %	MCV Fl	MCH Pg	MCHC g/dL	RDW %
Hb AA (N=130)	4.30± 0.57	11.31± 1.94	34.06± 5.83	77.75± 6.76	27.33± 3.03	31.43± 1.51	14.82± 2.08
Hb AS (N=54)	4.55± 0.43	12.80± 1.69	38.36± 5.03	80.49± 3.91	28.59± 1.98	32.67± 1.05	13.54± 2.08
Hb AC (N=18)	4.38± 0.33	12.10± 1.31	36.34± 4.06	78.19± 3.02	27.94± 1.66	32.13± 1.10	13.61± 1.56
F (p- value)	4.26 (0.02*)	12.93 (0.00*)	11.96 (0.00*)	4.18 (0.02*)	4.23 (0.02*)	16.23 (0.00*)	2.96 (0.05*)
Hb AA vs Hb AS p-value	0.01*	0.00*	0.00*	0.00*	0.00*	0.00*	0.07
Hb AA vs Hb AC p-value	0.68	0.08	0.11	0.89	0.41	0.06	0.25
Hb AS vs HbAC p-value	0.21	0.18	0.21	0.04*	0.37	0.17	0.99

P<0.05 Significance, P>0.05 no Significant, F (P-value) = mean ± SD of parameters compared using ANOVA.

4. Result

Table 1 show mean ± SD of Hb, PCV and red blood cell indices on Hb genotype variants, in pre anti-malaria drug treatment in *Plasmodium falciparum* malaria infected individuals. The mean ± SD of RBC 4.30 ± 0.57 in Hb genotype AA was significantly (P<0.05) lower compared to 4.55 ± 0.43 and 4.38 ± 0.33 in Hb genotype AS and AC respectively. (F = 4.26, P= 0.02); the mean ± SD of Hb 11.31 ± 1.94 in Hb genotype AA was significantly (P<0.05) lower compared to 12.80 ± 1.69 and 12.10 ± 1.31 in Hb genotype AS and AC respectively (F = 12.93, P=0.00); the mean ± SD of PCV 34.06 ± 5.83 in Hb genotype AA was significantly (P<0.05) lower compared to 38.36±5.03 and 36.34 ±4.06 in Hb genotype AS and AC respectively (F = 11.96, P= 0.00); the mean ± SD of MCV 77.75 ± 6.76 in Hb genotype AA was significantly (P<0.05) lower compared to 80.49± 3.91 and 78.19 ± 3.02 in Hb genotype As and AC respectively (F=4.18; P=0.02); the mean ± SD of MCH 27.33 ± 3.03 in Hb genotype AA was significantly (P<0.05)lower compared to 28.59± 1.98 and 27.94 ± 1.66 in Hb genotype AS and AC respectively (F = 4.23; P =0.02). The mean ± SD of MCHC 31.43 ± 1.51 in Hb genotype AA was significantly (P<0.05) lower compared to 32.67 ± 1.05 and 32.13 ± 1.10 in Hb genotype AS and AC respectively (F = 16.23, P = 0.00);

the mean ± SD of RDW 14. 82 ± 2.08 in Hb genotype AA was significantly (P<0.05) higher compared to 13.54±2.08 and 13.61 ± 1.56 in Hb genotype AS and AC respectively (F = 2.96; P=0.05). Multiple comparison between Hb genotype AA and AS show that; mean ± SD of RBC, Hb, PCV, MCV, MCH and MCHC in Hb genotype AA were significantly (P< 0.05) lower compared to Hb AS, however, mean ± SD of RDW in Hb genotype AA was higher compared to Hb genotype AS; the comparison show no significant difference(P>0.05). Multiple comparison between Hb genotype AA and AC show that; the mean ± SD of RBC, Hb, PCV, MCV, MCH and MCHC in Hb genotype AA were lower compared to Hb genotype AC; however, mean ± SD of RDW in Hb genotype AA was higher compared to Hb genotype AC. The comparison show no significant difference (P>0.05). Multiple comparison between Hb genotype AS and AC show that the mean ±SD of RBC, Hb and PCV in Hb genotype AS were higher compared to Hb genotype AC. The comparison show no significant difference (P>0.05); however, mean ± SD of MCV in Hb genotype AS was significantly (P<0.05) higher compared to Hb genotype AC. The mean ± SD of MCH and MCHC in Hb genotype AS was higher compared to Hb genotype AC, also, mean ± SD of RDW in Hb genotype AS was lower compared to Hb genotype AC. The comparisons show no significant difference (P>0.05).

Table 2. MEAN ± SD OF HB, PCV AND RBC INDICES ON HAEMOGLOBIN GENOTYPE VARIANTS IN POST ANTI MALARIA DRUG TREATMENT IN MALARIA INFECTED SUBJECTS

Groups	RBC $X10^9$/L	Hb g/dL	PCV %	MCV fL	MCH pg	MCHC g/dL	RDW %
Hb AA (N=130)	4.08± 0.56	10.44± 2.25	31.19± 6.61	75.46± 6.54	26.06± 3.07	30.60± 1.48	13.61± 2.05
Hb AS (N=54)	4.32± 0.42	11.90± 1.82	35.79± 5.39	78.35± 4.16	27.09± 2.42	31.79± 1.19	12.86± 2.03
Hb AC (N=18)	4.18± 0.43	11.03± 1.47	33.03± 4.36	76.13± 3.45	26.45± 1.54	31.37± 1.17	12.93± 1.49
F (p-value)	4.09 (0.02*)	9.43 (0.00*)	10.76 (0.00*)	4.77 (0.00*)	2.65 (0.07)	14.67 (0.00*)	3.11 (0.05*)
Hb AA vs Hb AS p-value	0.01*	0.00*	0.00*	0.00*	0.04*	0.00*	0.06
Hb AA vs Hb AC p-value	0.66	0.32	0.28	0.78	0.66	0.05*	0.22
Hb AS vs HbAC p-value	0.48	0.11	0.09	0.08	0.39	0.41	0.99

P<0.05 Significance, P>0.05 no Significant, F (P-value) = mean ± SD of parameters compared using ANOVA.

Table 2 show the mean ± SD Hb, PCV and red blood cell indices on haemoglobin genotype variant in post anti-malaria drug treatment in *Plasmodium falciparum* malaria infected individuals. The mean ± SD of RBC 4.08±0.56 in Hb genotype AA was significantly (P<0.05) lower compared to 4.32 ± 0.42 and 4.18 ± 0.43 in Hb genotype AS and AC respectively (F = 4.09, P = 0.02); the mean ± SD of Hb 10.44 ± 22.25 in Hb genotype AA was significantly (P< 0.05) lower compared to 11.90 ± 1.82 and 11.03 ± 1.47 in Hb genotype As and AC respectively (F = 9.43, P = 0.00); the mean ± SD of PCV 31.19 ± 6.61 in Hb genotype AA was significantly (P<0.05) lower compared to 35.79 ± 5.39 and 33.03 ± 4.36 in Hb genotype AS and AC respectively (F = 10.76, P=0.00); the mean ± SD of MCV 75.46 ±6.54 in Hb genotype AA was significantly (P<0.05) lower compared to 75.46 ± 6.54 in Hb genotype AA was significantly (P< 0.05) lower compared to 78.35 ± 4.16 and 76.13 ± 3.45 in Hb genotype As and AC respectively (F=4.77, P=0.00); the mean ±SD of MCH 26.06 ± 3.07 in Hb genotype AA was lower compared to 27.09 ± 2.42 and 26.45 ± 1.54 in Hb genotype AS and AC respectively. Comparison show no significant difference (P>0.05) (F=2.65, P=0.07); the mean ± SD of MCHC 30.60 ± 1.48 in Hb genotype AA was significantly (P<0.05) lower compared to 31.79 ± 1.19 and 31.37 ± 1.17 in Hb genotype AS and AC respectively (F = 14.07, P=0.00); the mean ± SD of RDW 13.61 ± 2.05 in Hb genotype AA was significantly (P<0.05) higher compared to 12.86 ± 2.03 and 12.93 ± 1.49 in Hb genotype AS and AC respectively (F=3.11, P=0.05). Multiple comparison between Hb genotype AA and AS show that; the mean± SD of RBC, Hb, PCV, MCV, MCH and MCHC in Hb genotype AA were significantly (P<0.05) lower compared Hb genotype AS, however, mean ± SD of RDW in Hb genotype AA was higher compared to Hb genotype AS. The comparison shows no significant difference (P> 0.05). Multiple comparison between Hb genotype AA and AC show that; the mean ± SD of RBC, Hb, PCV, MCV and MCH in Hb genotype AA were lower compared to Hb genotype AC, the comparison show no significant difference (P>0.05). However, mean ± SD of MCHC in Hb genotype AA was significantly (P<0.05 lower compared to Hb genotype AC. Also, mean ± SD of RDW in Hb genotype AA was higher compared to Hb genotype AC, the comparison show no significant difference. Multiple comparison between Hb genotype AS and AC show that; the mean ± SD of RBC, Hb, PCV, MCV, MCH and MCHC in Hb genotype AS were higher compared to Hb genotype AC. The comparison show no significant difference (P>0.05); however, mean ± SD of RDW in Hb genotype AS was lower compared to Hb genotype AC. The comparisons show no significant difference. (P>0.05)

Table 3 show mean ± SD Hb, PCV and red blood cell indices on haemoglobin genotype variant in non-malaria infected individuals control subject. The mean ± SD of RBC 4.80 ± 0.59 in Hb genotype AA was significantly (P< 0.05) higher compared to 4.08 ± 0.42 and 4.48 ± 1.29 in Hb genotype AS and AC respectively. (F = 13.18, P = 0.00); the mean ± SD of Hb 14.12 ± 1.18 in Hb genotype AA was significantly (P<0.05) higher compared to 12.41 ± 0.88 and 12.95 ± 1.06 in Hb genotype AS and AC respectively (F= 19.65, P=0.00); the mean ± SD of PCV 42.45 ± 3.35 in Hb genotype AA was significant (P<0.05) higher compared to 37.41 ± 2.53 and 40.30 ± 5.09 in Hb genotype AS and AC respectively (F=20.34; P=0.00); the

mean ± SD of MCV 82.84 ± 2.41 in Hb genotype AA was higher compared to 81.97 ± 2.91 and 82.80 ± 1.98 in Hb genotype AS and AC respectively. The comparison shows no significant difference. (P>0.05) (F = 0.01; P = 0.99); the mean ± SD of MCH 29.47 ± 0.97 in Hb genotype AA was significantly (P< 0.05) higher compared to 28.68 ± 1.05 and 29. 30 ± 1.20 in Hb genotype AS and AC respectively (F = 5.41, P = 0.01); the mean ± SD of MCHC 32.99 ± 1.37 in Hb genotype AA was significantly (P<0.05) higher compared to 31.94 ± 1.39 and 32.85 ± 0.64 in Hb genotype AS and AC respectively (F = 3.18; p=0.05); the mean ± SD of RDW 13.24 ± 1.47 in Hb genotype AA was lower compared to 13.95 ± 1.17 and 13.25 in Hb genotype AS and AC respectively. The comparisons show no significant difference. (P> 0.05) (F = 2.13, P = 0.12). Multiple comparison between Hb genotype AA and AS show that the mean ± SD of RBC and Hb in Hb genotype AA were significantly (P<0.05) higher compared to Hb genotype AS. Also mean ± SD of PCV and MCV in Hb genotype AA was higher compared to Hb genotype AS. The comparison show no significant difference (P>0.05); however, the mean ± SD of MCH and MCHC in Hb genotype AA were significantly (P< 0.05) higher compared to Hb genotype AS. The mean ± SD of RDW in Hb genotype AA was lower compared to Hb genotype AS. Comparisons show no significant difference (P>0.05). Multiple comparison between Hb genotype AA and AC show that the mean ± SD of RBC, Hb, PCV, MCV, MCH and MCHC in Hb genotype AA were higher compared to Hb genotype AC. However, the mean ± SD of RDW in Hb genotype AA was lower compared to Hb genotype AC. The comparisons show no significant difference (P> 0.05). Multiple comparisons between Hb genotype AS and AC show that the mean ± SD of RBC, HB, PCV, MCV, MCH and MCHC in Hb genotype AS were lower compared to Hb genotype AC. Moreover, the mean ± SD of RDW in Hb genotype AS was higher compared to Hb genotype AC. The comparison show no significant difference (P>0.05).

Table 3. MEAN ±SD OF HB, PCV AND RBC INDICES ON HAEMOGLOBIN GENOTYPE VARIANTS IN NON-MALARIA INFECTED SUBJECTS (CONTROL)

Groups	RBC $X10^9/L$	Hb g/dL	PCV %	MCV fL	MCH pg	MCHC g/dL	RDW %
Hb AA (N=79)	4.80± 0.59	14.12± 1.18	42.45 ± 3.35	82.84± 2.41	29.47± 0.97	32.99± 1.37	13.24± 1.47
Hb AS (N=21)	4.08± 0.42	12.41± 0.88	37.41± 2.53	81.97± 2.91	28.68± 1.05	31.94± 1.39	13.95± 1.17
Hb AC (N=2)	4.48± 1.29	12.95± 1.06	40.30± 5.09	82.80± 1.98	29.30± 1.20	32.85± 0.64	13.25± 0.92
F (p-value)	13.18 (0.00*)	19.65 (0.00*)	20.34 (0.00*)	0.01 (0.99)	5.41 (0.01*)	3.18 (0.05*)	2.13 (0.12)
Hb AA vs Hb AS p-value	0.00*	0.00*	0.52	0.99	0.01*	0.05*	0.06
Hb AA vs Hb AC p-value	0.94	0.52	0.80	0.88	0.99	0.99	1.00
Hb AS vs HbAC p-value	0.91	0.80	0.77	0.86	0.77	0.39	0.67

P<0.05 Significance, P>0.05 no Significant, F (P-value) = mean±SD of parameters compared using ANOVA.

Table 4. FREQEUENCY DISTRIUBUTIUON OF AGE AND SEX ON HAEMOGLOBIN GENOTYPE VARIANTS IN MALARIA INFECTED SUBJECTS

	AGE GROUP					SEX	
Hb Genotype	15-24	25-34	35-44	45-54	55-64	M	F
Hb AA (N=130)	45	41	21	9	14	87	43
Hb AS (N=54)	15	13	11	6	9	32	22
Hb AC (N=18)	8	5	2	2	1	10	8
TOTAL	68	59	34	17	24	129	73

Table 4 Out of the 202 malaria infected patients 129 (63.9%) were males; 87, 32 and 10 in Hb genotype AA, AS and AC respectively while 73 (36.1%) were females; 43, 22 and 8 in Hb genotype AA, AS and AC respectively. Age group 15-24 had highest prevalence of *plasmodium falciparum malaria infection in HbAA*

5. Disscusion

Out of 202 *plasmodium falciparum* malaria patients in this study, 130 were haemoglobin genotype AA, 54 were haemoglobin genotype AS, and 18 were haemoglobin genotype AC, while in control group, 79 were haemoglobin genotype AA, 21 were haemoglobin genotype AS and 02 were haemoglobin genotype AC. Prevalence of haemoglobin genotype AA and haemoglobin genotype AS in this study was similar to the report of Francis and Pete [18], stated that of the four hundred (400) subjects screened for haemoglobin genotype in malaria infected patients, two hundred and sixty-eight (268) (67.0%) were dominant homozygous (HbAA), one hundred and twenty-eight (128) (32.0%) were sickle heterozygous (HbAS), four (4) (1.0%) were recessive homozygous (HbSS), while none of the subjects had HbAC or HbSC genotype, similarly, Edith *et al.*, [19] reported the frequencies of Hb genotypes in *plasmodium falciparum* infected patients as 73.2% AA; 15.0% AC; 8.2% AS; 2.2% CC; 1.1% CS and

0.2% SS. Haematological parameters on Haemoglobin genotype showed Hb AA had significantly lower red blood cell, Hb, and red cell indices compared to Hb AS and AC in pre treatment; there was significant difference in haematological parameters. This present study showed that HbAA had more effect of malaria parasite compared with Hb AS, AC. The result in this present study is similar to the report of Francis and Pete [18], stated that, haemoglobin concentration, packed cell volume (PCV), red blood cell (RBC) and red blood cell indices were significantly lower in HbAA subjects during the progress of malaria when compared with those HbAS is indicative of less severe malaria anaemia in the later groups. Multiple comparisons in pre treatment showed that there is significant difference between Hb AA and Hb AS but there is no significant difference between Hb AA and Hb AC, Hb AS and Hb AC. However, red cell distribution width was observed and significantly higher in Hb AA compared to Hb AS and Hb AC but there is no significant in multiple comparisons among Hb AA, Hb AS and Hb AC. Moreover, in post treatment, there was general significant decreased in mean value of red blood cell, haemoglobin concentration, packed cell volume (PCV), red cell distribution width and red cell indices. Hb AA had more decrease compared to Hb AS and Hb AC; This present study showed the effect of anti-malaria during treatment in clearing malaria parasite within the erythrocyte leading to destruction of parasitized and unparasitized erythrocytes which reflect in haemoglobin degradation and other haematological parameters in this study. Multiple comparison post anti-malaria drug treatment showed significant difference between Hb AA and Hb AS. However, in control subject, haematological parameters were within the normal value, there is no significant difference in most of the parameters, also in multiple comparisons, among Hb AA, Hb AS and Hb AC showed no significant difference in most of the comparison; since control subjects are not infected with malaria parasite. This present study therefore, confirms the genetic resistance of Hb AS and Hb AC to malaria attack and frequent malaria attack in Hb AA. The prevalence of *Plasmodium falciparum* infection in this study was higher in male than in female; this cause could be due to the fact that males expose their bodies more than females when the weather is hot and thus increases their chances of being bitten by the mosquito. Females, on the other hand, are usually not naked and tend to stay indoors, helping out with household chores. This reduces their contact with the mosquito vector. Also, studies have shown that females have better immunity to parasitic diseases and this was attributed to genetic and hormonal factors. Prevalence of malaria infection decrease with advance in age as observed in this study. This may be as a result of gradual acquisition of immunity against malaria infection with increasing age upon repeated infection [20,21,22].

6. Conclusion

The genetic resistance to malaria infection, particularly *p. falciparum* malaria, is associated with hemoglobinopathies. Inheritance of haemoglobin genotype variants (Hb AS and Hb AC) were resistance to malaria infection, therefore suffer less malaria attack compared to normal haemoglobin genotype. AS and AC genotype is associated with lower incidence of clinical malaria relative to AA genotype among the subjects. HbAS is widely known to confer significant protection from severe and uncomplicated malaria. Haemoglobin genotype variants could reduce parasite replication within the red blood cells and enhance splenic clearance in parasitized erythrocytes.

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