*Asian Journal of Immunology*

*4(4): 47-56, 2020; Article no.AJI.65021*

# Distribution of FCR Polymorphism in Children Endemic Population of Burkina and Effect of this Polymorphism on IgG and his Subclass Production

**Mariama Kaba Combasseré-Cherif[1,2*], Fatimata Thiombiano[3], Boubacar Maiga[4], Daniel Amoako-Sakyi[5], Romaric Nebnoma Tiendrébeogo[1], Amagana Dolo[4], Sodiomon B. Sirima[2], Issa Nébié[2] and Marita Troye-Blomberg[6]**

*[1]Unité de Formation et de Recherche en Sciences et Techniques, Université Nazi, Bobo-Dioulasso, Burkina Faso.*
*[2]Groupe de Recherche Action en Santé (GRAS), Ouagadougou, Burkina Faso.*
*[3]Université Ouaga1 Prof Joseph Ki Zerbo, Burkina Faso.*
*[4]University of Sciences, Techniques and Technology of Bamako (USTT-B), Bamako, Mali.*
*[5]Department of Microbiology and Immunology, College of Health and Allied Sciences, School of Medical Sciences, University of Cape Coast, Ghana.*
*[6]Department of Molecular Biosciences, the Wenner Gren Institute, Stockholm University, Sweden.*

***Authors' contributions***

*This work was carried out in collaboration among all authors. Authors MKCC, FT and BM designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors DAS and RNT managed the analyses of the study. Authors AD, SBS, IN and MTB managed the literature searches. All authors read and approved the final manuscript.*

***Article Information***

Editor(s):
(1) Dr. Cynthia Aracely Alvizo Báez, Autonomous University of Nuevo Leon, Mexico.
Reviewers:
(1) Sanjeev V Jakati, Maharashtra University of Health Sciences, India.
(2) Sonali Kar, KIIT, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/65021

***Original Research Article***

***Received 01 December 2020***
***Accepted 03 February 2021***
***Published 09 February 2021***

## ABSTRACT

**Aims:** Malaria is one of disease which caused many deaths every year. Many studies try to understand why since it apparition, malaria is still endemic in certain regions. It appear that some FCR polymorphism may impact on susceptibility to malaria. The present study aimed to determine the distribution of certain FCR polymorphism and their effect on antibodies production.

**Corresponding author: E-mail: cherifkmariama@gmail.com;*

**Study Design:** Two cross-sectional surveys were carried out at Saponé.
**Place and Duration of Study:** Sampling was done at Saponé during low (January 2007) and high (September 2007) malaria transmissions seasons and laboratories activities were done at the department of Molecular Biosciences, the Wenner-Gren Institute, Stockholm University, Sweden.
**Methodology:** During each cross-sectional survey, 5 ml of venous blood in a tube containing EDTA was collected from each child for antibodies assessment by ELISA and FCR genotyping by PCR. Thick and thin blood films were also prepared from finger prick for microscopy diagnosis of malaria.
**Results:** 622 children from Mossi tribes participated in this study**.** Three mutants allele were present in pupation with Frequencies of the mutant alleles of FCGR2C (rs3933769), FCGR3A (rs396991) and FCGR2B (rs1050519) 15.43%, 66.24% and 37.94% respectively. Regarding the SNPs, they are contribute to malaria pathogenesis. Carriers of the mutant allele of FcγRIIB (rs1050519) harboured more parasites than the parasites harboured by non-carriers (*P*=.002). However, the mutant alleles of FCγRIIC (rs3933769) and FCγRIIIA (rs396991) harboured less parasite than wild alleles (*P*=.001) for all of them. SNPs are associated to total IgG responses. The FCγRIIB (rs 1050519) SNP (permutation of G to T) was negatively associated with IgG responses. Children with allele GG (Wild type) produced more antibodies against MSP3 than children with GT (Heterozygous) and TT (Mutant). The difference was statically significant *(P*= 0.05). However the FcRIIB mutation was positively associated with cytophilic IgG production against MSP2B, GLURP R0 and GLURP R2. The difference was statistically significant for MSP2A (*P*<0.001).
**Conclusion:** FCR2b, FCR2c and FCR3a are present in or study population. Malaria antibodies seem to be affected by FCR mutations.

*Keywords: Polymorphism; FCR mutations; malaria; P. falciparum; children.*

## 1. INTRODUCTION

Malaria is one of the disease which caused many deaths every year. Women and children under five years are the most infected. Despite the current efforts to control malaria in the world, the situation has not improved, mainly due to the increasing vector resistance to insecticides [1,2], and resistance to almost all anti-malarial drugs, including some resistance to artemisinin-based combination therapy (ACT). The asexual blood stages of the *P. falciparum* parasite are responsible for the clinical symptoms of malarial infections in Burkina Faso, and people living in areas of high *P. falciparum* endemicity are exposed to repeated malarial infections and gradually develop clinical protection against the disease over a period of several years. The phenomenon called premunition is believed to results from the combination of humoral and cellular component of the immune system which is acquired with age [3-5]. This acquired immunity is strong and incomplete, it is non-sterilizing and depends on many factors such as age, transmission pattern, and duration of exposure and host genetic factors [4,6-9].

This immunity were exploited in vaccine development. The principal immunity which is more elicited is antibodies responses. The level of antibodies play a key role in malaria incidence. IgG contribute to parasite clearance through responses to mérozoïte and sporozoite antigens. Among the different subclasses of IgG, IgG1 and IgG3 are the two cytophilic IgG which contribute to parasite elimination and then to malaria incidence reduction [4]. Many studies have proved that IgG1 and IgG3 are associated with protection against clinical malaria. [10-12]. However, there are several parameters which influence antibody responses and acquisition of immunity against *Plasmodium* such as age, transmission season, exposition and polymorphism of Fc fragment of immunoglobulines.

Fc gamma receptors (FcγRs) for IgG are probably the most extensively studied. There are expressed on a variety of immune cells, including monocytes and other leucocytes. They bind to opsonized pathogens and to activate a variety of cellular immune responses that may culminate in the control of an infection [13]. Thus, FcγRs seem to be an important link between humoral and cellular immune response [13]. Studies on FcγRs polymorphisms and malaria susceptibility have so far focused on the FcγRIIa genotypes, which affect binding of different IgG sub-classes. In FCγRIIa, histamine (H) is replace by arginine (R) in 131 position (H/R131). IFCγRIIa has been associated with levels of antimalarial IgG2 and IgG3 antibodies [9,14]. Several other single

nucleotide polymorphisms (SNPs) in FcγRs (FCγR2b, FCγR2c, FCγR3a and FCγR3b) have been associated with malaria susceptibility but their contribution is unclear [15,16].

The SNP of interest of this study are three SNPs in the FcγRs gene cluster that are have been studied in relation to susceptibility to malaria in Fulani and Dogon ethnic groups in Mali: two intronic SNPs (FCGR2C-rs3933769 and FCGR3Ars396991) and a functional SNP in the FCGR2B rs1050519 [17].

In Burbina Faso, the developing country where malaria is endemic and seasonal, it is clear known that Mossi are more susceptible to malaria than their sympatric ethnic group Fulani [8]. This appear, necessary to investigate more on Mossi population to understand their high susceptibility to malaria compared to their sympatric ethnic group.

The aim of this study was to determine the distribution of these SNPs among Mossi children living in malaria endemic area in Burkina Faso. The study further investigated the association of these SNPs with various clinical, malariometric and immunological indices these children.

## 2. MATERIALS AND METHODS

### 2.1 Study Population

Children from 6 months to 5 years fulfilling the inclusion and the exclusion criteria and attending a cross-sectional surveys were enrolled to the study as previouvely described by Cherif et al. [4]. Data obtained by cross-sectional survey was used to reach study objectives. Children were enrolled for the assessment of Fc polymorphism genes in relation to protection against clinical malaria and antibody responses. Study was carried out at Saponé. The area of the study has been described elsewhere [11]. Saponé is located around 50km from Ouagadougou where malaria transmission is permanent and pick during raining season.

### 2.2 Sample Collection

The study was based on the samples already collected in 2007. Two cross-sectional surveys were carried out during low (January 2007) and high (September 2007) malaria transmissions seasons. During each cross-sectional survey, 5 ml of venous blood in a tube containing EDTA was collected from each child for a complete blood count. The remaining blood was centrifuged and aliquots of plasma were created and stored at −20°C for immunological analysis. Thick and thin blood films were prepared from finger prick for microscopy diagnosis of malaria. Axillary temperature was measured at once. Children with fever, defined as axillary temperature ≥37.5°C or history of fever reported within the last 24 h, had a malaria rapid diagnostic test (RDT) performed. A child with a positive test result was referred to the nearest health center for appropriate treatment of malaria which was given free of charge.

### 2.3 Malaria Diagnosis

Thick and thin blood smears were collected and stained with 6% Giemsa and read by experienced microscopists for microscopic diagnosis of malaria as described elsewhere [18,19] **.** The number of malaria parasites of each species and stage were recorded. Each slide was read twice by two independent technicians and the final result was the average of the two readings. A 100% of qualitative agreement for the diagnosis was required for each slide between readers, and 30% difference for quantitative diagnosis was accepted between the two readers. A third reading was performed in case of significant discrepancy between the two readers. The number of parasites per 1 µl of blood was calculated according to the leukocyte count obtained after the full blood count for each slide collected during the malaria transmission season. A slide was declared negative if no parasite was seen after 200 HPF (High Power Field) were examined.

### 2.4 Antibodies Measurement

The levels of antibodies (IgG and IgG subclasses) to the six malaria-tested antigens were measured using enzyme-linked immunos orbent assays (ELISA), as previously described in the standard operating procedure (SOP) of AMANET [20] with Modifications.

Briefly, 96-well microtitre ELISA plates (Maxisorp Nunc, Denmark) were coated with antigens at 1.0 µg/ml (GLURP R2 and MSP1 hybrid) in 1X PBS (pH 7.04). Coated plates were kept in a refrigerator at 2–8°C overnight. Plates were blocked (PBS with 5% milk powder, 0.1% Tween-20) and incubated at room temperature (RT) in a humidified chamber for 1 h. Plasma samples diluted at 1:200 in serum dilution buffer (PBS with 2.5% milk powder, 0.1% Tween-20 and 0.02% Na-azide) were added in duplicates and incubated 2 h at RT. To control for inter-

assay and day-to-day variations each ELISA plate included a reference curve obtained by a two-fold titration of pool of hyper immune plasma. In addition, each plate included a negative control sample (a pool of plasma sample from Danish blood donors never exposed to malaria), a positive control sample (plasma from clinically semi-immune adults obtained from the Korle-Bu blood bank, Accra) and a buffer blank. The dilutions for the horseradish peroxidase (HRP) conjugated secondary antibodies used in the assays were: goat anti-human IgG (γ) (H10007) (Invitrogen Corporation, CA, USA) (1:80,000) and IgG sub-classes using HRP-conjugated sheep anti-human IgG1 (AP006) (1:5000), IgG2 (AP007) (1:2000), IgG3 (AP008) (1:10,000) and IgG4 (AP009) (1:1000) antibodies (The Binding Site Group Ltd, UK), respectively. These were added at 100 µl/well to respective plates and incubated for 1 h at RT. Plates were washed (PBS with 0.1% Tween-20 and 0.5 M NaCl) four times between consecutive steps. Bound secondary antibodies were quantified using TMB (3, 3, 5, 5-tetramethylbenzidine) substrate (Kem-En-Tec Diagnosis A/S, Taastrup, Denmark) and incubated in the dark for 30 min. Antibody levels, measured as optical density (OD) were determined at 450 nm with a reference at 630 nm, using a Biotek ELx808 microplate reader (Winooski, Vermont 05404-0998 USA). The OD values of the test samples were converted into Arbitrary Units (AU) ADAMSEL b040, Ed Remark© 2009) by means of interpolation from a standard curve on each plate, obtained by using 12 serial dilutions of a pool of positive hyperimmune sera (from CNRFP site). Positive control plasmas were obtained from positive Burkinabè adults over 20 years old, living in malaria hyper-endemic areas and negative controls were Danish (never exposed to malaria) plasma samples from Statens Serum Institute (Copenhagen, Denmark). Samples were re-tested if the coefficient of variation between duplicate absorbance values were higher than 15% and plates were also re-tested if the R2 value of the standard curve was less than 97%. A mean low cut concentration were generated for all the analysis at 0.0028 AU.

## 2.5 Genotyping

DNA was extracted from buffy coat using QIAamp DNA Blood Mini Kit (QIAgen, Inc.) following manufacturer's protocol and stored at −20°C. All SNPs were genotyped using TaqMan® SNP Genotyping Assays following a wet DNA method described elsewhere [21].

In brief, PCR amplification was performed in 25 µl reactions using 2 µl of genomic DNA (10 ng/µl), 12.5 µl of 2× TaqMan Universal PCR Master Mix (No AmpErase UNG), 1.25 µl of 20× working stock of SNP Genotyping Assay, and 9.25 µl of DNA free water. !e PCR was carried out in an Eppendorf Mastercycler (Eppendorf AG, Hamburg, Germany) using a 10-min enzyme activation at 95°C followed by 40 cycles with 92°C for 15 s and 60°C for 1 min. Allelic discrimination was read and analysed by Applied Biosystems 7900HT Fast Real-Time PCR System using two Taq Man® MGB probes for genotype detection.

## 2.6 Statistical Analyses

R Version 4.0.2. software (© 2009-2020 RStudio, PBC) was used for all statistical analyses. The t-test was used to determine differences in the prevalence of P. *falciparum*, mean parasite density and mean level of antibodies produced between children carrying wild alleles and those carrying heterozygous and mutant alleles. The same test was used for association of SNPs with variation of the ratio (cytophilic antibodies ((IgG1+IgG3)/non cytophilic antibodies (IgG2+IgG4)). Statistical tests values of $p<.05$ were considered statistically significant.

# 3. RESULTS AND DISCUSSION

## 3.1 Results

### 3.1.1 Study population characteristiques

The general characteristics of study volunteers are summarized in Table 1. A total of 622 children from Mossi tribes participated in this study. Study participants included males and females no older than 5 years. Mean ages of participants was 2.7 and the sex ratios (F/M) was 1.14. *P. falciparum* prevalence was 55%. In order to determine the genotypes and alleles that are over- or under-represented in the study population, the three SNPs were genotyped in the study population and their distributions compared in Table 1. Frequencies of the mutant alleles of FCGR2C (rs3933769), FCGR3A (rs396991) and FCGR2B (rs1050519) in the entire study population were 15.43%, 66.24% and 37.94% respectively.

### 3.1.2 Association of SNPs with *P. falciparum* infection

To determine the SNPs that may contribute to malaria pathogenesis, the associations of SNPs

with various malariometric was tested. A summary of SNP association with parasite prevalence and density is shown in Table 2. The SNP was associated with parasite prevalence in the entire study population. Carriers of the mutant allele of FcγRIIB (rs1050519) harboured more parasites than the parasites harboured by non-carriers (*P*=.002). However, the mutant alleles of FCγRIIC (rs3933769) and FCγRIIIA (rs396991) harboured less parasite than wild alleles (*P*=.001) for all of them. No statistically difference was seen regarding the trophozoites density when comparing mutant and wild alleles.

### 3.1.3 Effect of Fc polymorphism on antibodies production

#### *3.1.3.1 Association between SNPs total IgG*

The association between SNPs and total IgG responses was tested. Table 3 summarizes the association of SNPs with IgG anti-malaria specific antibodies. All of the SNPs studied were associated with levels of antibody responses in the entire population.

The FCγRIIB (rs 1050519) SNP (permutation of G to T) was negatively associated with IgG responses. Children with allele GG (Wild type) produced more antibodies against MSP3 than children with GT (Heterozygous) and TT (Mutant). The difference was statically significant *(P*= 0.05). However against antigens MSP2A, MSP2B, GLURP R0 and GLURP-R2, patients with allele GT (Heterozygous) and TT (Mutant) produced more statistically significant antibodies than Children with allele GG (Wild type), *P*< .001 for MSP2A, MSP2B and GLURP R2 and *P*=.002 for GLURP R0 (Table 3).

The FCγRIIC (rs 3933769) SNP is characterized by permutation of C to T. Regarding association of mutation in antibodies produced, it saw that children with allele CC (Wild type) produced more antibodies against MSP2A , MSP2B GLURP R0 and GLURP R0 compared to patients with allele CT (Heterozygous) and TT(Mutant) a statistically significant differences *P*< 0.001 for all (Table 3).

Regarding FCγRIIIA (rs 396991) SNP, a mutations occurred by changing A to G, patients with muted allele (AG and GG) produced more antibodies than the patients with non-muted (CC) allele. This increasing of production is observed with MSP2A, MSP2B, GLURP R0 and GLURP-R2 and is statistically significant with P<0.001 for all. However antibodies directed to MSP3 decrease significantly with mutation (p= 0.01).

#### *3.1.3.2 Association between SNPs total IgG subclasses*

The association between SNPs and IgG subclasses responses was tested. Table 4 summarize the association of SNPs with variation of the ratio (cytophilic antibodies ((IgG1+IgG3)/non cytophilic antibodies (IgG2+IgG4)). The ratio of ((IgG1+IgG3)/ (IgG2+IgG4o)) of all tested antigens was superior than one (1) meaning that children included in the study produced more cytophilic antibodies (IgG1 and IgG3) than no cytophilic IgG (IgG2 and IgG4).

The FcRIIB mutation was positively associated with cytophilic IgG production against MSP2B, GLURP R0 and GLURP R2. The difference was statistically significant for MSP2A (*P*<0.001).

**Table 1. Study population characteristiques**

| Characteristiques | Number of children | % |
|---|---|---|
| Mean age (years) | 2.7 | |
| Sex ratio (F/M) | 1.14 | |
| *P. falciparum* prevalence | 337 | 55 |
| FcγRIIB (rs1050519) | 622 | 100 |
| GG (Wild type) | 526 | 84.57 |
| GT(Heterozygous)/TT(Mutant) | 96 | 15.43 |
| FCγRIIC (rs3933769) | 622 | 100 |
| CC (Wild type) | 210 | 33.76 |
| CT(Heterozygous)/TT(Mutant) | 412 | 66.24 |
| FCγRIIIA (rs36991) | 622 | 100 |
| AA (Wild type) | 386 | 62.06 |
| AG(Heterozygous)/GG(Mutant) | 236 | 37.94 |

**Table 2. Association of SNPs with *P. falciparum* infection**

| SNP (gene) | Genotype type | *P. falciparum* prevalence Number (%) | Trophozoites density/ul Mean (CI95%) |
|---|---|---|---|
| FCγRIIB (rs1050519) | GG (Wild type) | 0.54 | 4379,41 |
| | GT(Heterozygous)/TT(Mutant) | 0.6 | 5034,00 |
| P Value | | .002* | .7 |
| FCγRIIC (rs3933769) | CC (Wild type) | 0.61 | 4502,85 |
| | CT(Heterozygous)/TT(Mutant) | 0.52 | 4468,03 |
| P Value | | .001* | .9 |
| FCγRIIIA (rs396991) | AA (Wild type) | 0.58 | 4973,29 |
| | AG(Heterozygous)/GG(Mutant) | 0.5 | 3671,09 |
| P Value | | .001* | .2 |

*Comparison of P. falciparum prevalence and trophozoites density in participates with wild and mutant alleles*
*(Fc RIIB (rs1050519): comparison between GG (Wild type) and GT (Heterozygous)/TT (Mutant)*
*FC RIIC (rs3933769): comparison between CC (Wild type) and CT (Heterozygous)/TT (Mutant)*
*FC RIIIA (rs36991): comparison between AA (Wild type) and AG (Heterozygous)/GG (Mutant)*
** Statistically significant difeerences (p < 0.05)*

**Table 3. Association of SNPs with variation of total IgG**

| SNP (gene) | Genotype (Alleles) | Antibody responses: Mean log10 | | | | |
|---|---|---|---|---|---|---|
| | | MSP3 | MSP2A | MSP2B | GLURP R0 | GLURP R2 |
| FcRIIB (rs1050519) | GG (Wild type) | 21.27 | 77.73 | 141.37 | 30.95 | 139.43 |
| | GT(Heterozygous)/TT(Mutant) | 17.59 | 93.26 | 166.99 | 43.731 | 176.82 |
| P value | | 0.059 | 0.0002* | 0.0008* | 0.0017* | 0.0003* |
| FCRIIC (rs3933769) | CC (Wild type) | 19.65 | 81.62 | 145.19 | 32.92 | 145.28 |
| | CT(Heterozygous)/TT(Mutant) | 22.79 | 75.76 | 139.33 | 32.83 | 136.005 |
| P value | | 0.0265* | 0.0001* | 0.0002* | 0.0004* | 0.0001* |
| FCRIIIA (rs396991) | AA (Wild type) | 20.76 | 75.03 | 145.80 | 31.87 | 141.73 |
| | AG(Heterozygous)/GG(Mutant) | 17.59 | 93.26 | 166.99 | 43.73 | 176.82 |
| P value | | 0.01* | 0.0004* | 0.001* | 0.001* | 0.002* |

*Comparison of antibody levels in participates with wild and mutant alleles*
*Fc RIIB (rs1050519): comparison between GG (Wild type) and GT (Heterozygous)/TT (Mutant)*
*FC RIIC (rs3933769): comparison between CC (Wild type) and CT (Heterozygous)/TT (Mutant)*
*FC RIIIA (rs396991): comparison between AA (Wild type) and AG (Heterozygous)/GG (Mutant)*
** Statistically significant difference (P< 0.05)*

**Table 4. Association of SNPs with variation of total IgG**

| NP (gene) | Genotype type | Antibody responses (IgG1+IgG3)/(IgG2+IgG4): Mean log10 | | | | |
|---|---|---|---|---|---|---|
| | | MSP3 | MSP2A | MSP2B | GLURP R0 | GLURP R2 |
| Fc RIIB (rs1050519) | GG (Wild type) | 2.16 | 6.34 | 7.41 | 3.41 | 3.86 |
| | GT(Heterozygous)/TT(Mutant) | 1.45 | 7.14 | 8.49 | 4.82 | 5.51 |
| P value | | .35 | .00008 | .20 | .17 | .18 |
| FC RIIC (rs3933769) | CC (Wild type) | 2.15 | 6.52 | 7.59 | 3.73 | 4.02 |
| | CT(Heterozygous)/TT(Mutant) | 2.05 | 6.18 | 7.37 | 3.24 | 3.95 |
| P value | | .24 | .00001 | .028 | .14 | .024 |
| FC RIIIA (rs396991) | AA (Wild type) | 2.14 | 6.29 | 7.53 | 3.51 | 3.88 |
| | AG(Heterozygous)/GG(Mutant) | 1.95 | 5.32 | 6.88 | 3.96 | 3.71 |

*Comparison of antibody levels in participates with wild and mutant alleles*
*Fc RIIB (rs1050519): comparison between GG (Wild type) and GT (Heterozygous)/TT (Mutant)*
*FC RIIC (rs3933769): comparison between CC (Wild type) and CT (Heterozygous)/TT (Mutant)*
*FC RIIIA (rs396991): comparison between AA (Wild type) and AG (Heterozygous)/GG (Mutant)*
** Statistically significant difference (P< 0.05)*

The FCRIIC, mutation seem to be negatively associated with cytophilic antibodies production against all the tested antigens. The differences were statiscally significant for MSP2A, MSP2B and GLURP R2 with respectively P<.001, *P*=.028 and *P*=.024.

FcRIII A mutation seem decrease cytophilic antibodies production. Antibodies to MSP2A, MSP2B and GLURP R2 decrease significantly with mutation with respectively P<.003, *P*=.005 and *P*=.001.

## 3.2 Discussion

The confirmed and suggested roles of certain SNPs in protection against malaria and antibodies responses are observed in the present study.

The single nucleotide substitution (SNP) from G to T at cDNA nucleotide position 559 of the FcγRIIIa gene generating two different FcγRIIIa allotypes: one with a valine (V) and one with a phenylalanine (F) at amino acid position 158, known as FcγRIIIA-V158F polymorphism (rs39 6991) [22-24] , the T/T genotype would result in an F/F phenotype (low affinity), T/G in a V/F phenotype, whereas G/G would result in a V/V phenotype (high affinity) (Niken M. Mahaweni). The presence of a valine (V/V or V/F) has been shown to enhance the NK cell's binding affinity to an IgG1 or IgG3 antibody as compared to the presence of a homozygous phenylalanine genotype (F/F), resulting in a higher level of NK cell-mediated ADCC [23-25] . For instance, the homozygous wild genotype of rs396991 was under-represented in HIV infected patients with Kaposi sarcoma [26]. This SNP is also suggested to play a limited role in rheumatoid arthritis, which is an immune-mediated disease [34]. The study done by cherif and al. in 2016 has expanded knowledge by further showing an association between rs396991 mutant allele and higher levels of IgG3 in the Dogon tribe. This is interesting considering the fact this SNP was associated with higher levels of IgG in Hutchison lymphoma patients [27]. The variable distribution of rs396991 among Fulani and Dogon, as well as its association with IgG, could be an indication of a possible role for this SNP in malaria susceptibility. The rs396991 is to be more studied in relation to malaria. Data from this study suggest that this SNP may play a role in malaria pathogenesis and antibody production.

The FcγRIIB (rs 1050519) SNP codes for a threonine instead of isoleucine at position 232 in the transmembrane domain of FcγRIIb. The mutant allele of this SNP is associated with increasing of antibodies production. FcγRIIbT232 is associated with protection against severe malarial infection in animal models Lisa C. Willcocksa et al. [14]. This protection was explained by FcγRIIb deficiency which enhances antibody responses [17], including those to malaria [15], and thus, children with FcγRIIb mutation in this study seen to be less protected to malaria and to develop better humoral immunity against most of the malaria tested antigens. The The FcγRIIC (rs3933769) SNP appeared to influence parasite density in the study population. Study participants with the mutant allele harboured fewer than half the parasites found in their counterparts with the ancestral allele. The FcγRIIC is suggested to play an important role in parasite clearance by effectively bridging humoral and cellular immunity.

Doing ratio Ig Cytophilic/non cytophilic, all the ratio are superior to 1. Mean that all antigens induced more cytophilic antibodies than non cytophilic immunoglobulines. Cytophilic are important in malaria prasites elimination. Some studies as proven that cytophilic antibodies induced protection and reduce the risk of severe malaria [4,10,11]. Having more cytophilic antibodies proven that in endemic area, cytophilic antibodies play a key role in protect against subsequent episode. Exceptionally, in FcRIIb muted patients produced more antibodies than the wild patients. Mutation increase the cytophilic antibodies production. Thus are comparable to results obtained with FCγRIIA mutation which is associated to high level of Ig1 and Ig3 (Amre N, 2009).

Muted allele children of FCRIIB done more malaria than wild allele children; FCRIIB mutation seem to induce susceptibility to malaria. This found is the same to study stained in Kenyan children were FCRIIB polymorphism is associated to protection against severe malaria Lisa C. Willcocksa et al. [14]. However FCγRIIC and FCγRIIIA mutation seem to protect against malaria.

## 4. CONCLUSION

FCR2b, FCR2c and FCR3a are present in or study population. Malaria antibodies seem to be affected by FCR mutations. The FCR2b seem to be the better induced antibodies production. However cytophillic antibodies are the most

induced by theses mutation. FCRIIB is also associated to protection against malaria. However, effect on polymorphism on parasitaemia has not proven.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

The study protocol was approved by the Ethical Committee for Biomedical Research of the Ministry of Health, Burkina Faso. Informed consent was taken from all participants' parents or their guardians in a two-step procedure. First oral community consent was taken prior to the study, where the whole community was informed about the study procedures. Thereafter, an individual consent was obtained from the parent or legal guardian of each child at the time of blood collection. Literate volunteers signed the form and illiterate volunteers applied his or her fingerprints.

## ACKNOWLEDGEMENTS

We would like to thank all the study participants, parents and the Ministry of Health, Burkina Faso. We also thank all the staff of GRAS whose participation was immeasurable to implement this study. Special thanks goes to all PRD College consortium members particularly Prof Diana Boraschi, Prof Carmen Fernandez and Prof Wilfred Mbacham, all of whom facilitated the scientific exchange programme at Stockholm University, Sweden. We are indebted to staff and students of Department of Molecular Bioscience, The Wenner-Gren Institude, Stockholm University for their support. The study was supported by a scientific exchange grant to DAS, MKC and MB under the Poverty Related Diseases-College: International Programme on BioMedicine and Development (Contract/Grant agreement number: 222948) and the Islamic Educational, Scientific and Cultural Organization (ISESCO) for its support to help for research in health biotechnology to MKC.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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