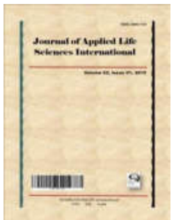

Journal of Applied Life Sciences International

22(1): 1-6, 2019; Article no.JALSI.50841
ISSN: 2394-1103

Association between Non-secretion of ABH Antigens and Sickle Cell Anaemia

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Authors' contributions

This work was carried out in collaboration among all authors. Authors CI and JMO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors OAF and AOA managed the analyses of the study. Author CI managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JALSI/2019/v22i130115
Editor(s):
(1) Dr. Palanisamy Arulselvan, Institute of Bioscience, Universiti Putra Malaysia, Malaysia.
Reviewers:
(1) J. Y. Peter, University of Abuja, Nigeria.
(2) Ugwu, Ngozi Immaculata, Ebonyi State University, Nigeria.
Complete Peer review History: http://www.sdiarticle3.com/review-history/50841

Original Research Article

Received 04 June 2019
Accepted 17 August 2019
Published 24 August 2019

ABSTRACT

Aim: To determine whether non-secretion of ABH blood group antigens was associated with Sickle Cell Anaemia.

Materials and Methods: Haemaglutination inhibition test was carried out on saliva samples from 300 individuals; 100 of whom had haemoglobin (Hb) genotype AA, 100 HbAS, 50 HbAC and 50 HbSS. ABO blood grouping was carried out by standard methods and Haemoglobin genotype test was performed by cellulose acetate electrophoresis technique.

Results: Eighteen percent (18%) of HbAA, 23% of HbAS, 18% of HbAC and 42% of HbSS individuals were non-secretors of ABH antigens ($p = 0.007$). Non-secretion of ABH substances was more associated with HbSS persons than HbAA ($p = 0.002$), HbAS ($p = 0.016$) and HbAC ($p = 0.009$) individuals.

Conclusion: Non-secretion of ABH blood group substances is associated with Sickle Cell Anaemia.

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Keywords: Haemoglobin genotype; ABO blood group; sickle cell anaemia; ABH antigens; Secretor status.

1. INTRODUCTION

In Southwestern Nigeria, in addition to normal haemoglobin A, haemoglobins S and C exist bringing about variants HbAA, HbAS, HbAC, HbSS, HbCC and HbSC among the people in the region [1]. Haemoglobinopathies especially sickle cell anaemia poses a lot of health challenges in Nigeria [2]. Sickle cell anaemia (SCA) is an inherited disorder caused by mutation resulting in replacement of amino-acid glutamic acid with valine at the 6^{th} base position of the beta globin chain. It is a genetic blood disorder characterized by the presence of 2 alleles of the abnormal haemoglobin S (HbSS) in the red cell instead of HbAA with high morbidity and mortality rates [2]. It is recognized by the United Nations as a global public health concern and the World Health Organisation has recommended that by 2020, half of its members should have set up Sickle Cell Anaemia (SCA) control programmes [3]. Worldwide, SCA is estimated to affect 20-25 million people and annually about 300,000 children are born with the disorder [4]; approximately 250,000 of whom are in sub-Saharan Africa [5] with 50-80% of affected children dying before the age of 5 years [6].

The ABO blood group and secretor status of a person are inherited independently. While the ABH (FUT 1) gene codes for the ABO blood group, the secretor (FUT 2) gene interacts with the ABH (FUT 1) gene to determine the secretor status of an individual [7]. Individuals can be homozygous (SeSe) or heterozygous (Sese) secretors or non-secretors (sese). Non-secretion of ABH antigens has been associated with a number of non-communicable diseases and disorders such as autoimmune diseases [8,9], blood clotting and thrombotic diseases [10,11], immunological disorders [12], myocardial infarction [13,14], rheumatic heart disease [15,16], duodenal ulcers [17]. Apart from one study [18] which investigated frequency distribution of secretors and non-secretors in HbAA and HbSS individuals in Zaria, Northwestern Nigeria, we are not aware of any other investigation that has related secretor status with haemoglobin variants. In this study, we hypothesized that secretor status varied significantly with haemoglobin variants and that non-secretion of ABH antigens was associated with sickle cell anaemia.

2. METHODOLOGY

2.1 Study Area and Population

This study was carried out in Osogbo, Southwestern Nigeria. It is the capital of Osun State. Osogbo city seats the Headquarters of both Osogbo Local Government Area (situated at Oke Baale Area of the city) and Olorunda Local Government Area (situated at Igbonna Area of the city). It is some 88 kilometers by road northeast of Ibadan with coordinates Latitude 7.767-7.770°N and Longitude 4.557-4.567°E. A total of 300 participants were screened for this study: 100 HbAA individuals, 100 HbAS, 50 HbAC and 50 HbSS. They were drawn from apparently healthy staff, students and patients of LAUTECH Teaching Hospital visiting the General Out Patient Department for routine examination.

2.2 Collection of Blood Samples

Blood samples were collected for Haemoglobin geneotype test and ABO blood grouping. A sample of 3 ml of venous blood was collected from each participant into ethylenediaminetetraacetic acid (EDTA) bottle. Haemogobin genotype test was performed using cellulose acetate electrophoresis method [1]. In an alkaline pH (8.2-8.6), Hb is a negatively charged molecule and will migrate towards the anode. Different Hbs move at different rates depending on their net charge which is controlled by the amino acid composition of their globin chain. The ABO grouping system is based on agglutination reaction. When a red blood cell carrying an antigen is exposed to its corresponding antibody, they react with each other to form agglutination or clumping. ABO blood group tests were performed by standard techniques [19].

2.3 Collection of Saliva Samples

Saliva samples were collected from participants for the determination of their secretor status; 2 ml of saliva was collected from each participant for determination of secretor status using haemagglutination inhibition test [20]. If the saliva is from a secretor, the soluble blood antigens in it react and neutralize the antibodies in the antiserum. So when red blood cells of appropriate blood group are added to the test mixture of the saliva and antiserum, there will be no free antibody to agglutinate them because the antibodies have already been neutralized by the antigens in the saliva. Therefore the reaction will be negative for agglutination. However, if the saliva is from a non-secretor, there will be no blood group antigens in it and so the antibodies in the antiserum will not be neutralized but free to react with appropriate test cells when added to produced agglutination. Laboratory investigations were carried out on samples collected in the Research Laboratory of the Department of Medical Laboratory Science, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria.

2.4 Data Analysis

The statistical package for social sciences (SPPS version 16) was used for statistical analysis. Differences in proportions or percentages were tested by Chi-square test. A p-value of < 0.05 was considered significant.

3. RESULTS

A total of 300 persons comprising 100 HbAA, 100 HbAS, 50 HbAC and 50 HbSS individuals participated in this study. Table 1 shows the age and sex distributions of the study population. There were no significant differences in the age (p = 0.998) and sex (p = 0.718) distributions among the four groups of haemoglobin variants.

The distributions of the haemoglobin variants of the study participants in relation to secretor status are given in Table 2. Of the 100 individuals with HbAA, 18% were non-secretors; 23%, 18% and 42% of the HbAS, HbAC and HbSS individuals respectively were non-secretors. Non-secretion of ABH antigens varied significantly with haemoglobin variants (χ^2 = 11.99, df = 3, p = 0.007). Further Chi-square tests showed that non-secretion of ABH antigens was more associated with HbSS individuals than HbAA individuals (χ^2 = 9.978, df = 1, p = 0.002), HbAS individuals (χ^2 = 5.805, df = 1, p = 0.016) and HbAC individuals (χ^2 = 6.857, df = 1, p = 0.009). There was no significant variation in secretion of ABH antigens among HbAA, HbAS and HbAC individuals (χ^2 = 0.938, df = 2, p = 0.626). Altogether, non-secretors in the HbSS group (42.0%) were significantly higher than those in the non-SS (HbAA, AS and AC) group (20.0%) (χ^2 = 11.163, df = 1, p < 0.001).

The distributions of the haemoglobin variants of the study participants in relation to ABO blood group are also given in Table 2. Group AB was excluded from the analysis due to its small number across the haemoglobin variants. There was no significant association in the distributions of haemoglobin variants in relation to ABO blood group (χ^2 = 5.69, df = 6, p = 0.458).

The distributions of the non-secretors of the study participants with respect to haemoglobin variants and ABO blood group are given in Table 3. Of the 100 AA individuals, 18 were non-secretors (10 non-group O and 8 group O); of the 100 AS individuals, 23 were non-secretors (14 non-group O and 9 group O); of the 50 AC individuals, 9 were non-secretors (6 non-group O and 3 group O) while 21 of the 50 SS individuals were non-secretors (14 non-group O and 7 group O). Altogether, of the 150 non-O blood group participants, 44 (29.3%) were non-secretors while 27 of the 150 (18.0%) group O participants were non-secretors (χ^2 = 5.332, df = 1, p = 0.021).

4. DISCUSSION

Previous studies in this study area had shown that secretor status was independent of sex [20]. A similar finding was reported in Calabar, South South Nigeria [21]. Similarly, in this study locality, the distribution of ABO blood group and haemoglobin variants had been reported to be sex independent [1,22] which were in line with ABO studies carried out in the same region by other researchers [23,24].

Table 1. Age and sex distributions among the study participants

	Haemoglobin variants					
	HbAA n=100(%)	**HbAS n=100(%)**	**HbAC n=50(%)**	**HbSS n=50(%)**	**Total n=300(%)**	**p-value**
Age group (years)						0.998
16 - 25	32(32.0)	35(35.0)	17(34.0)	15(30.0)	99(33.0)	
26 - 35	28(28.0)	27(27.0)	14(28.0)	15(30.0)	84(28.0)	
≥ 36	40(40.0)	38(38.0)	19(38.0)	20(40.0)	117(39.0)	
Sex						0.718
Male	45(45.0)	48(48.0)	26(52.0)	27(54.0)	146(48.7)	
Female	55(55.0)	52(52.0)	24(48.0)	23(46.0)	154(51.3)	

Table 2. Distribution of the haemoglobin variants of the study participants in relation to secretor status and ABO blood group

	Haemoglobin variants					
	HbAA N=100(%)	**HbAS N=100(%)**	**HbAC N=100(%)**	**HbSS N=100(%)**	**Total 300(%)**	**p-value**
Secretor status						0.007
Secretor	82(82.0)	77(77.0)	41(82.0)	29(58.0)	229(76.3)	
Non-secretor	18(18.0)	23(23.0)	09(18.0)	21(42.0)	71(23.7)	
ABO Blood Group						0.458
A	22(22.0)	23(23.0)	11(22.0)	16(32.0)	72(24.0)	
B	19(19.0)	26(26.0)	13(26.0)	14(28.0)	72(24.0)	
AB	02(2.0)	02(2.0)	01(2.0)	01(2.0)	06(2.0)	
O	57(57.0)	49(49.0)	25(50.0)	19(38.0)	150(50.0)	

Table 3. Distribution of the non-secretors of the study participants with respect to haemoglobin variants and ABO blood group

	Haemoglobin variants				
ABO Blood Group	**HbAA(NS)**	**HbAS(NS)**	**HbAC(NS)**	**HbSS(NS)**	**Total(NS)**
Non-O	43(10)	51(14)	25(06)	31(14)	150(44)
O	57(08)	49(09)	25(03)	19(07)	150(27)
Total	100(18)	100(23)	50(09)	50(21)	300(71)

NS: Non-Secretor

In this study, we tested the hypothesis that non-secretors were more associated with HbSS compared to the other haemoglobin variants. The frequency of non-secretors in SCA (HbSS) individuals was significantly higher than the frequency of non-secretors in the other haemoglobin variants (HbAA, HbAS and HbAC) showing that secretor status varied significantly with haemoglobin variants. A study in Northwestern Nigeria reported a higher frequency of non-secretor in HbSS individuals compared to HbAA individuals [18].

Also in this study, non-secretion of ABH substances was more associated with persons of non-O group compared to those of O group. Previous studies in the study area and elsewhere had reported lower proportion of group O non-secretors compared to non-O group non-secretors [7,20]. Another study in the area showed that malaria was less associated with group O secretors than non-group O secretors [22]. These studies showed that with respect to ABO blood group system, more group O persons were secretors compared to the other groups. The protective effect offered by group O individuals had been linked to higher incidence of secretor compared to non-O group [7].

Non-secretion of ABH antigens has been associated with many non-communicable diseases and disorders [8-17]. Similarly, sickle cell anaemia individuals are known to have several complications including chronic pain, intermittent painful episodes, musculoskeletal problems, stroke, pulmonary hypertension and septicaemia [3,25]. It is not unlikely that the complications exhibited by majority of the persons with sickle cell disorder might largely be due to their inability to secrete ABH substances. Also, the observed association might be linked with the Le^a antigens which are present in greater amounts on the epithelial surface of non-secretors [26]. The positive interaction observed between HbSS and inability to secrete ABH antigens could be suggestive of the fact that the sickle cell gene and the secretor gene might directly or indirectly interact to confer susceptibility on persons with sickle cell anaemia. We opine that the severity of symptoms and complications observed in HbSS patients could be due to their inability to secrete ABH antigens. Further studies can be carried out to confirm or disprove this view.

5. CONCLUSION

Secretor status varies significantly with haemoglohin variants and inability to secrete ABH antigens is associated sickle cell anaemia.

CONSENT AND ETHICAL APPROVAL

Informed consent was obtained from all the participants. Ethical approval for this study was obtained from the Ethical Committee of the

College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Osun State, Nigeria.

ACKNOWLEDGEMENTS

We are indeed very grateful to all the participants involved in this study. We appreciate the important contributions of members of technical staff and thankful to the management of LAUTECH Teaching Hospital for the success of this research study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle3.com/review-history/50841