Saudi Journal of Biomedical Research (SJBR)
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

ISSN 2518-3214 (Print)
ISSN 2518-3222 (Online)

Phenotypic, Allelic and Genotypic Frequencies of ABO and Rhesus Blood Groups, Secretor Status, Phenylthiocarbamide Taste Perception and Haemoglobin Variants in Ore Community, Southwestern Nigeria

C. Igbeneghu[1*], S. A. Adedokun[2,3], A. A. Akindele[3], M. J. Olisekodiaka[4], O. Ojurongbe[2]
[1]Departments of Medical Laboratory Science, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria
[2]Medical Microbiology and Parasitology, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria
[3]Community Medicine, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria
[4]Department of Chemical Pathology, Faculty of Medicine, Nnamdi Azikiwe University, Akwa, Nigeria

Original Research Article

***Corresponding author**
C. Igbeneghu

Article History
Received: 02.02.2018
Accepted: 11.02.2018
Published: 28.02.2018

DOI:
10.21276/sjbr.2018.3.1.3

Abstract: There is dearth of information on the gene frequencies of ABO and Rhesus blood groups, secretor status, PTC taste perception and haemoglobin variants in Osun State, Nigeria and previous studies have been based on heterogeneous population. We wanted to have information on the frequency distributions of these traits in Osun State and among a homogeneous population. A total of 555 individuals comprising 308 male and 247 female indigenes of Ore community participated in this study. Participants' blood samples were typed for ABO, Rhesus blood groups and haemoglobin genotype, saliva samples were analysed for ABH secretory status and PTC taste perception was determined using PTC strips. The frequencies of O, A, B and AB individuals were 41.6%, 30.8%, 21.6% and 6.0% respectively, those of Rh positive and Rh negative were 89.9% and 10.1%, those of secretors and non-secretors were 69.2% and 30.8% respectively while those of tasters and non-tasters were 56.6% and 43.4% respectively. The observed ABO blood group, Rhesus factor, secretor status, PTC taste perception distributions did not differ significantly ($p = 0.986$, $p = 0.943$, $p = 0.926$, $p = 0.864$ respectively) from those expected under the Hardy-Weinberg equilibrium. The allelic frequencies for ABO were p(A) 0.205, p(B) 0.149 p(r) 0.645, those for Rhesus factor were D(0.682) and d(0.318), those for secretion and non-secretion were Se (0.445) and se(0.555) respectively while those of tasting and non-tasting were T(0.341) and t(0.659) respectively. Four haemoglobin genotypes in the order AA (68.6%) > AS (26.7%) > AC (3.8%) > SS (0.9%) were observed with allelic frequencies A(0.839), S(0.142) and C(0.019). This study has provided information on the frequency distributions of the studied genetic indices in Osun State. The information provided herein can be used to give medical and genetic counsel to the people of the State.

Keywords: ABO and Rhesus Blood groups; Secretor status; Phenylthiocarbamide; Haemoglobin variants; Gene frequencies.

INTRODUCTION

A number of genetic traits have been used to explain genetic differences among human population and to study susceptibility or otherwise to certain diseases/disorders. For instance, in ABO blood group system, individuals are classified into A, B, AB and O blood types and differences have been reported among these groups in relation to susceptibility to a number of diseases/disorders [1-5]. For example, non-group O blood groups have been reported to be more associated with cancers than blood group O [6, 7].

The gene coding for the ABO blood group lies on chromosome 9q34 [8]. However, a separate gene (FUT 2) interacts with the ABO gene to determine the ability to secrete ABO antigens into body fluids and tissue [9]. In the genetics of the ABH secretion, an individual can either be a secretor or a non-secretor and this is independent of the ABO blood type. Non-secretors are more associated with infectious and non-infectious diseases compared to secretors. For instance, non-secretors have been significantly associated with influenza, meningitis, pneumonia [10, 11], candidiasis [12], malaria [5], recurrent urinary tract infections [13], autoimmune diseases [14], myocardial infarction [15],

rheumatic heart disease [16], thrombotic diseases [17], diabetes [18] while secretors have only been associated with some viral infections [19-22].

The Rhesus (Rh) blood group system is a complex consisting of several blood group antigens; the most important of which is antigen D commonly referred to as Rh factor. Like the ABO blood group, the Rhesus blood group has been associated with a number of diseases [23, 24] with Rh negative individuals being more susceptible than their Rh positive counterparts [23].

Haemoglobin is the oxygen carrying component of the red blood cell. In Southwestern Nigeria, in addition to normal haemoglobin A, haemoglobins S and C where valine and lysine are substituted respectively for glutamic acid in the 6^{th} position of the beta chain exist, bringing about variants AA, AS, AC, SS, CC and SC among the people in the region [25, 26]. Many studies have associated HbAS and HbAC with resistance to severe and mild falciparum malaria [27-29]. Haemoglobinopathies especially sickle cell anaemia poses a lot of health challenges in Nigeria [30, 31]. Individuals with HbSS are easily susceptible to malaria [32] while HbCC variant is known to protect against malaria [27].

Phenylthiocarbamide (PTC) taste sensitivity has been used as a tool to trace family lineages and population migration patterns and it was previously used in paternity testing before the advent of DNA markers [33]. It has been correlated with a number of dietary preferences and human health [34, 35]. Also, it has been correlated with the ability to taste other naturally occurring bitter substances in cruciferous vegetables [36]. Tasters (TT or Tt) are those who taste PTC while non-tasters (tt) cannot taste it. Bitter taste perception occurs through bitter taste receptors located on the surface of taste cells of the tongue [37] and is thought to be an adaptive feature in mammals to avoid the ingestion of naturally toxic substances [38]. The ability to taste PTC or otherwise has been related to some diseases or disorders. Several studies have reported association or lack of association between PTC taste perception and different diseases/disorders [39-44].

In Nigeria, we are not aware of any study on the frequency distributions and gene frequencies of these genetic indices among the inhabitants of Osun State in Southwestern Nigeria. Also, previous studies carried out on this subject matter were largely based on heterogeneous populations. In this study, we examined the frequency distributions and gene frequencies of these genetic indices among some indigenes of Ore, a rural community in Osun State, Southwestern Nigeria.

MATERIALS AND METHODS

This study was carried out among the indigenes of Ore community, Southwestern Nigeria. A total of 555 individuals (308 males and 247 females) from about 2000 indigenes of Ore community between ages 5 years and 80 years old participated in this study. Questionnaires were administered to each participant to obtain relevant information. The consent of the parents and guardians of the children was obtained. The permission of the community leaders and school authority was obtained before the commencement of the study. Ethical approval for this study was obtained from the Ethical Committee of the Ministry of Health, Osogbo, Osun State.

Five (5) ml of venous blood was collected from each participant into ethylenediaminetetraacetic acid (EDTA) bottle. ABO and Rh blood group antigens tests were performed by standard tile techniques along with standard controls [45]. They were performed on saline washed red cells using commercially prepared monoclonal anti-A, anti-B and anti-D according to the manufacturer's instructions (Biotech Laboratories, U.K). Haemoglobin genotype test was performed using the cellulose acetate electrophoresis technique [45]. In addition, 5 ml of saliva was collected from each participant for determination of secretor status. Secretor and non-secretor phenotypes were identified using the haemagglutination inhibition test as described elsewhere [46]. Phenylthiocarbamide (PTC) taste perception was determined using PTC strips (0.0143 mg of PTC /strip) (Carolina Biological Supply Company, North Carolina, USA). Briefly, each participant was given a PTC taste strip and a filter paper (as control) and was asked to put each on their tongue and allow to be soaked in their saliva before describing their perception to each strip. Taste description of each participant was recorded. Laboratory investigations were carried out in the Research Laboratory, Department of Biomedical Sciences, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria.

Chi-square test was used to compare differences between percentages/proportions and to compare observed and expected frequencies. Allelic and genotypic frequencies were calculated using Hardy-Weinberg equation. A p-value of < 0.05 was considered to be significant.

RESULTS

The distributions of phenotypic, allelic and genotypic frequencies of ABO blood groups among the study population are given in Table 1. The overall frequencies of O, A, B and AB individuals were 41.6%, 30.8%, 21.6% and 6.0% respectively. There was no statistically significant difference in the distributions of ABO blood groups between the male and female participants ($\chi^2 = 0.355$; df = 3; p = 0.949). The allelic frequencies p (A), q (B), r (O) for the males and

females were 0.209, 0.143, 0.647 and 0.200, 0.156, 0.643 respectively while the overall allelic frequencies were 0.205, 0.149 and 0.645 respectively. The overall genotypic frequencies occurred in the following order: OO > AO > BO > AB > AA > BB (0.416 > 0.264 > 0.192 > 0.060 > 0.042 > 0.022 respectively).

Table-2 shows the distributions of phenotypic, allelic and genotypic frequencies of Rh blood groups among the study population. The overall frequencies of Rh positive and Rh negative were 89.9% and 10.1% respectively. The frequency distribution of Rh positive and Rh negative among the study population was not dependent on sex (χ^2 = 0.001; df = 1; p = 0.982). The allelic frequencies for Rh negative males and females were 0.317 and 0.318 respectively while the overall allelic frequencies for Rh positive (D) and Rh negative (d) were 0.682 and 0.318 respectively. The overall genotypic frequencies were 0.465, 0.434 and 0.101 for DD, Dd and dd respectively.

The results of the secretor status of the study population are given in Table-3. The overall frequencies of secretors and non-secretors were 69.2% and 30.8% respectively. The frequencies of male (69.5%) and female (68.8%) secretors were not significantly different (χ^2 = 0.028; df = 1; p = 0.868). The allelic frequencies for non-secretor males and females were 0.552 and 0.558 and the overall non-secretor allelic frequency was 0.555. The overall genotypic frequencies for SeSe, Sese and sese were 0.198, 0.494 and 0.308 respectively.

The phenotypic, allelic and genotypic frequency distributions of PTC taste perception among the study population are given in Table-4. Overall, the frequencies of tasters and non-tasters were 56.6% and 43.4% respectively. There were more female tasters (60.3%) than male tasters (53.6%) but the difference was not statistically significant (χ^2 = 2.544; df = 1; p = 0.11). The non-tasting allelic (t) frequencies for males and females were 0.681 and 0.630 respectively while the overall non-tasting allelic frequency was 0.659. The overall genotypic frequencies were: TT = 0.116, Tt = 0.450 and tt = 0.434.

The observed and expected frequencies for ABO and Rh blood groups, secretor status and PTC taste perception are given in Table 5. The observed and expected frequencies for the ABO blood group, O (41.6%, 42.2%), A (30.8%, 30.1%), B (21.6%, 21.8%) AB (33.0%, 33.0%) (χ^2 = 0.143; df = 3; p = 0.986), Rh positive (89.9%, 90.0%) and Rh negative (10.1%, 10.0%) (χ^2 = 0.005; df = 1; p = 0.943), secretors (69.2%, 69.0%) and non-secretor (30.8%, 31.0%) (χ^2= 0.008; df = 1; p = 0.926) and tasters (56.5%, 56.9%) and non-tasters (43.4%, 43.1%) (χ^2 = 0.005; df = 1; p = 0.943) did not vary significantly under the Hardy-Weinberg equilibrium.

The allelic and genotypic frequencies of the haemoglobin types among the study population are given in Table 6. Three different haemoglobins: HbA, HbS and HbC were observed which occurred in 4 genotypic combinations in the order AA > AS > AC > SS (68.6% > 26.7% > 3.8% > 0.9%). The distribution of haemoglobin variants in male and female participants did not vary significantly (χ^2 = 1.469; df = 3; p = 0.689). The overall allelic frequencies for A, S and C were 0.839, 0.142 and 0.019 respectively.

Table-1: Distribution of Phenotypic, Allelic and Genotypic Frequencies of ABO Blood Group among the Study Participants in Ore, Nigeria

Sex	No Exam.	[a]Phenotypic Frequency				Allelic frequency		
		O(%)	A(%)	B(%)	AB(%)	p	q	r
Male	308	129(41.9)	97(31.5)	64(20.8)	18(5.8)	0.209	0.143	0.647
Female	247	102(41.3)	74(30.0)	56(22.7)	15(6.1)	0.200	0.156	0.643
Total	555	231(41.6)	171(30.8)	120(21.6)	33(6.0)	0.205	0.149	0.645

Sex	No Exam.	Genotypic Frequency					
		OO	AA	AO	BB	BO	AB
Male	308	0.419	0.044	0.270	0.021	0.186	0.058
Female	247	0.413	0.041	0.257	0.024	0.200	0.061
Total	555	0.416	0.042	0.264	0.022	0.192	0.060

[a]χ^2 = 0.355; df = 3; p = 0.949

Table-2: Distribution of Phenotypic, Allelic and Genotypic Frequencies of Rhesus Blood Group among the Study Participants in Ore, Nigeria

Sex	No Exam.	[a]Phenotypic Frequency(%)		Allelic Frequency		Genotypic Frequency		
		Rh Positive	Rh Negative	D	d	DD	Dd	dd
Male	308	277(89.9)	31(10.1)	0.683	0.317	0.466	0.433	0.101
Female	247	222(89.9)	25(10.1)	0.682	0.318	0.465	0.434	0.101
Total	555	499(89.9)	56(10.1)	0.682	0.318	0.465	0.434	0.101

[a]χ^2 = 0.001; df = 1; p = 0.982

Table-3: Distribution of Phenotypic, Allelic and Genotypic Frequencies of Secretors and Non-secretors among the Study Participants in Ore, Nigeria

Sex	No Exam.	[a]Phenotypic Frequency (%)		Allelic Frequency		Genotypic Frequency		
		Secretor	Non-secretor	Se	se	SeSe	Sese	sese
Male	308	214(69.5)	94(30.5)	0.448	0.552	0.200	0.495	0.305
Female	247	170(68.8)	77(31.2)	0.442	0.558	0.195	0.493	0.312
Total	555	384(69.2)	171(30.8)	0.445	0.555	0.198	0.494	0.308
[a]χ^2 = 0.028; df = 1; p = 0.86								

Table-4: Distribution of Phenotypic, Allelic and Genotypic Frequencies of Phenylthiocarbamide Tasters and Non-tasters among the Study Participants in Ore, Nigeria

Sex	No Exam.	[a]Phenotypic Frequency (%)		Allelic Frequency		Genotypic Frequency		
		Taster	Non-taster	T	t	TT	Tt	tt
Male	308	165(53.6)	143(46.4)	0.319	0.681	0.102	0.434	0.464
Female	247	149(60.3)	98(39.7)	0.370	0.630	0.137	0.466	0.397
Total	555	314(56.6)	241(43.8)	0.341	0.659	0.116	0.450	0.434
[a]χ^2 = 2.544; df = 1; p = 0.11								

Table-5: Observed and Expected Frequencies of ABO and Rhesus Blood Groups, Secretor Status and Phenylthiocarbamide Taste Perception among the Study Participants in Ore, Nigeria

Variable	Observed No	Observed Freq/%	Expected No	Expected Freq/%	P
ABO group					0.986
O	231	41.6	234	42.2	
A	171	30.8	167	30.1	
B	120	21.6	121	21.8	
AB	33	6.0	33	6.0	
Total	555	100.0	555	100.0	
Rhesus group					0.943
Rh Positive	499	89.9	500	90.0	
Rh Negative	56	10.1	56	10.0	
Total	555	100.0	556	100.0	
Secretor Status					0.926
Secretor	384	69.2	383	69.0	
Non-secretor	171	30.8	172	31.0	
Total	555	100.0	555	100.0	
PTC Tasting					0.864
Taster	314	56.6	316	56.9	
Non-taster	241	43.4	239	43.1	
Total	555	100.0	555	100.0	

Table-6: Distribution of Allelic and Genotypic Frequencies of Haemoglobin Variants among the Study Participants in Ore, Nigeria

Sex	No Exam	Genotypic Frequency (%)				Allelic Frequency		
		AA	AS	AC	SS	A	S	C
Male	308	214(69.5)	82(26.6)	9(2.9)	3(1.0)	0.842	0.143	0.015
Female	247	167(67.6)	66(26.7)	12(4.9)	2(0.8)	0.834	0.142	0.024
Total	555	381(68.9)	148(26.7)	21(3.8)	5(0.9)	0.839	0.142	0.019

[a]χ^2 = 1.469; df = 3; p = 0.689

DISCUSSION

This study investigated the phenotypic, allelic and genotypic frequencies of ABO and Rh blood groups, secretor status, PTC taste perception and haemoglobin variants of indigenes of Ore community, Southwestern Nigeria. The distributions of genetic indices are known to vary from one race to another and from one geographical region to another. In this study, the phenotypic distribution of ABO blood group was in the order O > A > B > AB (41.6%, 30.8%, 21.6% and 6.0% respectively). This is in line with the reports of similar studies carried out across the country [4, 25, 47-50] and elsewhere in Africa [51-55], Asia [56], Middle East [9, 57-59], Europe [60, 61], North America [62, 63] with the exception of North-western Nigeria where the order O > B > A > AB has been reported [47, 50, 64, 65]. Generally, the O group is reported to be the most common in many given populations across the

world with the exception of some parts of India [66] and Pakistan [67] where group B is reported as the most frequent and in Nepal [62] and Jordan [68] where group A is the most common.

The ABO blood group allelic frequencies order of r(O) > p(A) > q(B) observed in this study is in agreement with the values observed in many previous studies in Nigeria [4, 47, 69] and this signifies that the r (O) allele is the most common in Nigeria followed by p (A) allele. The ABO blood group distribution in this study did not differ from the expected distribution under the Hardy-Weinberg equilibrium. This is not the case with some previous studies [4, 25, 49, 70] carried out among heterogenous populations in Nigeria where the observed distributions differed significantly from those expected under the Hardy-Weinberg equilibrium. Nevertheless, the observation concurs with that of Alimba *et al.*, [71] who reported no difference among a heterogenous population in Lagos, Southwestern Nigeria. That group O is the most common in the present study which is in line with previous studies is an advantage considering its role in conferring resistance against some common infectious diseases. For instance, group O is known to protect against severe malaria [72], *S. mansoni* infections [73-75] and severe form of urogenital schistosomiasis [75, 76].

In this study, the frequencies of 89.9% (comprising 46.6% DD and 43.3% Dd) and 10.1% observed for Rh positive and Rh negative respectively were in agreement with the expected under the Hardy-Weinberg equilibrium. This is line with other previous studies in Nigeria which revealed that Rh positive individuals were more than Rh negative; nevertheless, the Rh negative value reported in this study was slightly higher than those of previous studies across the country where a range of 3% to 7.5% had been reported [4, 25, 47-49, 77]. This slight difference observed might be due to the homogenous nature of our study participants compared to the other studies which involved participants from different ethnic or racial groups. Elsewhere in Asia, Europe and North America, studies on Rh blood group have shown Rh negative range from 0 to 17% [58, 61, 78, 79]. Knowledge of Rh blood group system is used to prevent complications arising from Rh incompatibility between a mother and her foetus which is likely when a Rh negative (dd) mother marries a Rh positive (Dd) man. With 10.1% of the females examined being Rh negative, intending couples in this locality need to seek the advice of genetic counsellors so as to prevent cases of haemolytic disease of the Newborn.

Secretors were more than non-secretors in this study and this is in line with previous studies on prevalence of secretor status in Nigeria [46, 80]. But there was no significant difference between the frequencies of female and male secretors. The phenotypic frequency of non-secretors in this study was 31% and the allelic frequency was 0.56. In Osogbo, a city in Southwestern Nigeria, Igbeneghu *et al*., [23] reported a prevalence of 22% non-secretors. Elsewhere, Jaff [9] reported 24%, Akhter *et al*., [81] reported 40% and Saboor *et al*., [82] 36% and 20% reported among the Caucasians [45]. The low frequency of non-secretors in this study area is good for the population since non-secretors are known to be at a potential health disadvantage compared to secretors [46]. Also, previous studies carried out in the same region and elsewhere have shown that secretors varied significantly with ABO [9, 46, 80] with a higher proportion of group O secretors than any other group. Group O secretors has been associated with resistance to incidence and severity of chronic disorders such as tumours and malignancies including cancer of the stomach and colon [9, 83] and since a larger number of O individuals are secretors compared to the non-O groups, there would be low incidence and severity of such disorders in this locality.

Similarly, tasters were more than non-tasters which is in line with previous studies in Nigeria [71, 84, 85] and even across the world about 30% of the population is non-tasters [43, 44]. There was no significant difference between the frequencies of female and male tasters. The phenotypic and allelic frequencies of 43.4% and 0.66 observed for non-tasting in this study were higher than those of previous studies in the same region. Alimba *et al*., [71] reported 29.4% and 0.54 respectively and Bakare *et al*., [85] reported 25.6% and 0.49 respectively in Southwestern Nigeria. The differences observed could be associated with differences in the nature of the populations studied. These previous studies were carried out among mixed populations while the present study was among a homogenous population. Also, the different methods of the PTC tasting employed in these studies could partly be responsible for the differences observed. Elsewhere, phenotypic and allelic frequencies range from 24.5% to 71.5% and 0.09 to 0.89 respectively had been reported [35, 86]. Owing to the high frequency of non-tasting allele reported in this study, the population might likely be more prone to disorders/diseases that are associated with inability to taste PTC.

The data presented in this study showed that the four most common haemoglobin variants in Southwestern Nigeria were observed in the following order: AA (68.6%) > AS (26.7%) > AC (3.8%) > SS (0.9%). It is in agreement with the reports of a range of 55-75% AA for Africans and about 25% of the population of sub-Saharan Africa as sickle cell trait [87, 88]. Three haemoglobins, Hb A, Hb S and Hb C with allelic frequencies 0.842, 0.143 and 0.015 respectively were observed. These allelic frequencies are similar to those previously reported by Bakare *et al*., [25] (0.81, 0.14 and 0.04) and Alimba *et al*., [71] (0.877, 0.111 and 0.012) in the same region. In view of the prevalence of sickle cell trait (26.7%) and sickle cell anaemia (0.9%)

reported in this study, premarital haemoglobin counselling would certainly play a vital role in the control of haemoglobinopathies in this community. Couples who are both HbAS have one-fourth chance of producing a baby with HbSS for every pregnancy. With four out of every five sickle-cell anaemia cases occurring in sub-Saharan Africa [30] and Nigeria harbouring the highest number of carriers and sufferers of the disorder with about 2% of newborns being affected by sickle cell anaemia annually and about 95% of the children with the disorder dying before the age of 10 years [30, 31] there is the need for the policy makers to take necessary measures without further delay to control this scourge.

CONCLUSION

This study presents the phenotypic, allelic and genotypic frequencies of ABO and Rh blood groups, secretor status, PTC taste perception and haemoglobin variants in a homogenous population in Southwestern Nigeria. Our result is a reflection of the general distribution of these genetic features in Southwestern Nigeria. The slight variations observed compared to the previous studies could be adduced to differences in the nature of population studied. Knowledge of the information regarding these genetic indices in each community is useful for medical diagnosis and genetic counselling.

ACKNOWLEDGEMENTS

We appreciate the valuable contributions and support of the community leaders and most especially the volunteers who participated in this study.

REFERENCES

1. Panda, A. K., Panda, S. K., Sahu, A. N., Tripathy, R., Ravindran, B., & Das, B. K. (2011). Association of ABO blood group with severe falciparum malaria in adults: case control study and meta-analysis. *Malaria journal*, *10*(1), 309.
2. Pelzer, U., Klein, F., Bahra, M., Sinn, M., Dörken, B., Neuhaus, P., ... & Riess, H. (2013). Blood group determinates incidence for pancreatic cancer in Germany. *Frontiers in physiology*, *4*, 118.
3. Sode, B. F., Allin, K. H., Dahl, M., Gyntelberg, F., & Nordestgaard, B. G. (2013). Risk of venous thromboembolism and myocardial infarction associated with factor V Leiden and prothrombin mutations and blood type. *Canadian Medical Association Journal*, cmaj-121636.
4. Anifowoshe, A. T., Oyeyemi, B. F., Iyiola, O. A., Ahmed, I. O., Akinseye, K. M., & Akinsowon, A. J. (2015). Gene Frequencies of ABO and Rh (D) Blood Group Alleles in Minna, North-Central, Nigeria. *Niger J Pure Appl Sci*, *28*, 2644-57.
5. Igbeneghu, C., Olisekodiaka, M. J., Okanlawon, B. M., Onuegbu, J. A., & Odaibo, A. B. (2015). Non-secretors of ABH antigens are susceptible to falciparum malaria. *SJAMS. 2015a*, *3*, 1838-1841.
6. Wolpin, B. M., Chan, A. T., Hartge, P., Chanock, S. J., Kraft, P., Hunter, D. J., ... & Fuchs, C. S. (2009). ABO blood group and the risk of pancreatic cancer. *Journal of the National Cancer Institute*, *101*(6), 424-431.
7. Greer, J. B., Yazer, M. H., Raval, J. S., Barmada, M. M., Brand, R. E., & Whitcomb, D. C. (2010). Significant association between ABO blood group and pancreatic cancer. *World journal of gastroenterology: WJG*, *16*(44), 5588.
8. Dean, L. (2005). *Blood groups and red cell antigens*. National Center for Biotechnology Information.
9. Jaff, M. S. (2010). Higher frequency of secretor phenotype in O blood group–its benefits in prevention and/or treatment of some diseases. *International journal of nanomedicine*, *5*, 901.
10. Blackwell, C. C., Jonsdottir, K., Hanson, M. F., & Weir, D. M. (1986). Non-secretion of ABO blood group antigens predisposing to infection by Haemophilus influenzae. *The Lancet*, *328*(8508), 687.
11. Blackwell, C. C., Jonsdottir, K., Hanson, M. F., & Weir, D. M. (1986). Non-secretion of ABO blood group antigens predisposing to infection by Haemophilus influenzae. *The Lancet*, *328*(8508), 687.
12. Thom, S. M., Blackwell, C. C., MacCallum, C. J., Weir, D. M., Brettle, R. P., Kinane, D. F., & Wray, D. (1989). Non-secretion of blood group antigens and susceptibility to infection by Candida species. *FEMS microbiology immunology*, *1*(6-7), 401-405.
13. May, S. J., Blackwell, C. C., Brettle, R. P., MacCallum, C. J., & Weir, D. M. (1989). Non-secretion of ABO blood group antigens: a host factor predisposing to recurrent urinary tract infections and renal scarring. *FEMS microbiology immunology*, *1*(6-7), 383-388.
14. Shinebaum, R. (1989). ABO blood group and secretor status in the spondyloarthropathies. *FEMS Microbiology Letters*, *47*(6-7), 389-396.
15. Ellison, R. C., Zhang, Y., Myers, R. H., Swanson, J. L., Higgins, M., & Eckfeldt, J. (1999). Lewis blood group phenotype as an independent risk factor for coronary heart disease (the NHLBI Family Heart Study)∗. *American Journal of Cardiology*, *83*(3), 345-348.
16. Jhinghan, B., Mehra, N. K., Reddy, K. S., Taneja, V., Vaidya, M. C., & Bhatia, M. L. (1986). HLA, blood groups and secretor status in patients with established rheumatic fever and rheumatic heart disease. *HLA*, *27*(3), 172-178.
17. Orstavik, K. H. (1990). Genetics of plasma concentration of von Willebrand factor. *Folia haematologica (Leipzig, Germany: 1928)*, *117*(4), 527-531.

18. Patrick, A. W., & Collier, A. (1989). An infectious aetiology of insulin-dependent diabetes mellitus? Role of the secretor status. *FEMS Microbiology Letters*, *47*(6-7), 411-416.
19. Raza, M. W., Blackwell, C. C., Molyneaux, P., James, V. S., Ogilvie, M. M., Inglis, J. M., & Weir, D. M. (1991). Association between secretor status and respiratory viral illness. *Bmj*, *303*(6806), 815-818.
20. Ali, S., Niang, M. A. F., N'doye, I., Critchlow, C. W., Hawes, S. E., Hill, A. V., & Kiviat, N. B. (2000). Secretor polymorphism and human immunodeficiency virus infection in Senegalese women. *The Journal of infectious diseases*, *181*(2), 737-739.
21. Thorven, M., Grahn, A., Hedlund, K. O., Johansson, H., Wahlfrid, C., Larson, G., & Svensson, L. (2005). A homozygous nonsense mutation (428G→ A) in the human secretor (FUT2) gene provides resistance to symptomatic norovirus (GGII) infections. *Journal of virology*, *79*(24), 15351-15355.
22. Kindberg, E., Hejdeman, B., Bratt, G., Wahren, B., Lindblom, B., Hinkula, J., & Svensson, L. (2006). A nonsense mutation (428G→ A) in the fucosyltransferase FUT2 gene affects the progression of HIV-1 infection. *Aids*, *20*(5), 685-689.
23. Flegr, J., Hoffmann, R., & Dammann, M. (2015). Worse health status and higher incidence of health disorders in Rhesus negative subjects. *PloS one*, *10*(10), e0141362.
24. Flegr, J. (2016). Heterozygote advantage probably maintains Rhesus factor blood group polymorphism: Ecological regression study. *PloS one*, *11*(1), e0147955.
25. Bakare, A. A., Azeez, M. A., & Agbolade, J. O. (2006). Gene frequencies of ABO and rhesus blood groups and haemoglobin variants in Ogbomoso, South–West Nigeria. *African Journal of Biotechnology*, *5*(3), 224-229.
26. Igbeneghu, C., Olisekodiaka, M. J., Akinola, F. F. S., & Odaibo, A. B. (2015). Impact of Haemoglobin Variants AS and AC on Asymptomatic Falciparum Malaria among Adults in Iwo, Southwestern Nigeria. *Scholars Journal of Applied Medical Sciences*, *3*(1A), 17-20.
27. Modiano, D., Luoni, G., Sirima, B. S., Simporé, J., Verra, F., Konaté, A., ... & D'urbano, L. (2001). Haemoglobin C protects against clinical Plasmodium falciparum malaria. *Nature*, *414*(6861), 305.
28. Danquah, I., Ziniel, P., Eggelte, T. A., Ehrhardt, S., & Mockenhaupt, F. P. (2010). Influence of haemoglobins S and C on predominantly asymptomatic Plasmodium infections in northern Ghana. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *104*(11), 713-719.
29. Kreuels, B., Kreuzberg, C., Kobbe, R., Ayim-Akonor, M., Apiah-Thompson, P., Thompson, B., ... & May, J. (2010). Differing effects of HbS and HbC traits on uncomplicated falciparum malaria, anemia, and child growth. *Blood*, *115*(22), 4551-4558.
30. World Health Organization. (2005). Sickle-cell anaemia: Report by the Secretariat. In *Sickle-cell anaemia: report by the Secretariat*.
31. [31] WHO. (20130. Sickle cell disease prevention and control. http://www.afro.who.int/en/nigeria/nigeriapublications/1775-sickle cell disease.html
32. Weatherall, D. J., & Clegg, J. B. (2001). Inherited haemoglobin disorders: an increasing global health problem. *Bulletin of the World Health Organization*, *79*, 704-712.
33. Mattes, R. D. (2004). 6-n-Propylthiouracil Taster Status. *Genetic variation in taste s e ns it ivity*, 229.
34. Wooding, S., Kim, U. K., Bamshad, M. J., Larsen, J., Jorde, L. B., & Drayna, D. (2004). Natural selection and molecular evolution in PTC, a bitter-taste receptor gene. *The American Journal of Human Genetics*, *74*(4), 637-646.
35. Kim, U. K., & Drayna, D. (2005). Genetics of individual differences in bitter taste perception: lessons from the PTC gene. *Clinical genetics*, *67*(4), 275-280.
36. Tepper, B. J., Koelliker, Y., Zhao, L., Ullrich, N. V., Lanzara, C., d'Adamo, P., ... & Gasparini, P. (2008). Variation in the Bitter-taste Receptor Gene TAS2R38, and Adiposity in a Genetically Isolated Population in Southern Italy. *Obesity*, *16*(10), 2289-2295.
37. Adler, E., Hoon, M. A., Mueller, K. L., Chandrashekar, J., Ryba, N. J., & Zuker, C. S. (2000). A novel family of mammalian taste receptors. *Cell*, *100*(6), 693-702.
38. Ueda, T., Ugawa, S., Yamamura, H., Imaizumi, Y., & Shimada, S. (2003). Functional interaction between T2R taste receptors and G-protein α subunits expressed in taste receptor cells. *Journal of Neuroscience*, *23*(19), 7376-7380.
39. Facchini, F., Abbati, A., & Campagnoni, S. (1990). Possible relations between sensitivity to phenylthiocarbamide and goiter. *Human biology*, 545-552.
40. Ali, S. G. M., Khan, A. A., Mahtab, H., Khan, A. R., & Muhibullah, M. (1994). Association of phenylthiocarbamide taste sensitivity with diabetes mellitus in Bangladesh. *Human heredity*, *44*(1), 14-17.
41. Pal, S. K., Sharma, K., Pathak, A., Sawhney, I. M., & Prabhakar, S. (2004). Possible relationship between phenylthiocarbamide taste sensitivity and epilepsy. *Neurology India*, *52*(2), 206.
42. Rupesh, S., & Nayak, U. A. (2006). Genetic sensitivity to the bitter taste of 6-n propylthiouracil: a new risk determinant for dental caries in

children. *Journal of Indian Society of Pedodontics and Preventive Dentistry*, *24*(2), 63.

43. Guo, S. W., & Reed, D. R. (2001). The genetics of phenylthiocarbamide perception. *Annals of human biology*, *28*(2), 111-142.
44. Shivaprasad, H. S., Chaithra, P. T., Kavitha, P., & Malini, S. S. (2012). Role of phenylthiocarbamide as a genetic marker in predicting the predisposition of disease traits in humans. *Journal of natural science, biology, and medicine*, *3*(1), 43.
45. Dacie, J. V., & Lewis, S. M. (1994). Red cell blood-group antigens and antibodies In: Practical Textbook of Haematology.
46. Igbeneghu, C., Olisekodiaka, J. M., Alabi, T., Onuegbu, J. A., Oseni, B. A., & Odaibo, A. B. (2015). ABH secretors status in Osogbo, Southwestern Nigeria. *Ind J Fundament Appl Life Sci. 2015c*, *5*(3), 42-47.
47. Falusi, A. G., Ademowo, O. G., Latunji, C. A., Okeke, A. C., Olatunji, P. O., Onyekwere, T. O., ... & Itata, E. O. (2000). Distribution of ABO and RH genes in Nigeria. *African journal of medicine and medical sciences*, *29*(1), 23-26.
48. Enosolease, M. E., & Bazuaye, G. N. (2008). Distribution of ABO and Rh-D blood groups in the Benin area of Niger-Delta: Implication for regional blood transfusion. *Asian journal of transfusion science*, *2*(1), 3.
49. Iyiola, O. A., Igunnugbemi, O. O., Raheem, U. A., & Anifowoshe, A. T. (2011). Gene frequencies of ABO and Rh (D) blood group alleles in Ilorin, North-Central Nigeria. *World J Biol Res*, *4*(1), 6-14.
50. Anifowoshe, A. T., Owolodun, O. A., Akinseye, K. M., Iyiola, O. A., & Oyeyemi, B. F. (2017). Gene frequencies of ABO and Rh blood groups in Nigeria: A review. *Egyptian Journal of Medical Human Genetics*, *18*(3), 205-210.
51. Khalil, I. A., Phrykian, S., & Farr, A. D. (1989). Blood group distribution in Sudan. *Gene geography: a computerized bulletin on human gene frequencies*, *3*(1), 7-10.
52. Loua, A., Lamah, M. R., Haba, N. Y., & Camara, M. (2007). Frequency of blood groups ABO and rhesus D in the Guinean population. *Transfusion clinique et biologique: journal de la Societe francaise de transfusion sanguine*, *14*(5), 435-439.
53. Hamed, C. T., Bollahi, M. A., Abdelhamid, I., Mahmoud, M., Ba, B., Ghaber, S., ... & Houmeida, A. (2012). Frequencies and ethnic distribution of ABO and Rh (D) blood groups in Mauritania: results of first nationwide study. *International journal of immunogenetics*, *39*(2), 151-154.
54. Benahadi, A., Alami, R., Boulahdid, S., Adouani, B., Laouina, A., Mokhtari, A., ... & Benajiba, M. (2013). Distribution of ABO and Rhesus D blood antigens in Morocco. *The Internet Journal of Biological Anthropology*, *6*(1).
55. Ndoula, S. T., Noubiap, J. J. N., Nansseu, J. R. N., & Wonkam, A. (2014). Phenotypic and allelic distribution of the ABO and Rhesus (D) blood groups in the Cameroonian population. *International journal of immunogenetics*, *41*(3), 206-210.
56. Anees, M., & Mirza, M. S. (2005). Distribution of ABO and Rh blood group alleles in Gujrat region of Punjab, Pakistan. *Proceedings-pakistan academy of sciences*, *42*(4), 233.
57. Al-Bustan, S., El-Zawahri, M., Al-Azmi, D., & Al-Bashir, A. A. (2002). Allele frequencies and molecular genotyping of the ABO blood group system in a Kuwaiti population. *International journal of hematology*, *75*(2), 147.
58. Khattak, I. D., Khan, T. M., Khan, P., Shah, S. M. A., Khattak, S. T., & Ali, A. (2008). Frequency of ABO and Rhesus blood groups in District Swat, Pakistan. *J Ayub Med Coll Abbottabad*, *20*(4), 127-129.
59. Sarhan, M. A., Saleh, K. A., & Bin-Dajem, S. M. (2009). Distribution of ABO blood groups and rhesus factor in Southwest Saudi Arabia. *Saudi medical journal*, *30*(1), 116-119.
60. Tauszik, T. (1995). Heterogeneity in the distribution of ABO blood groups in Hungary. *Gene geography: a computerized bulletin on human gene frequencies*, *9*(2), 169-176.
61. Akbas, F., Aydin, M., & Cenani, A. (2003). AB0 blood subgroup allele frequencies in the Turkish population. *Anthropologischer Anzeiger*, 257-260.
62. Pramanik, T., & Pramanik, S. (2000). Distribution of ABO and Rh blood groups in Nepalese medical students: a report.
63. Garratty, G., Glynn, S. A., & McEntire, R. (2004). ABO and Rh (D) phenotype frequencies of different racial/ethnic groups in the United States. *Transfusion*, *44*(5), 703-706.
64. Chima, O. K., Mohammed, T. B., Aisha, K. G., Alhaji, S. A., Muhammad, B. M., & Kwaru, A. H. (2012). ABO and rhesus blood groups among blood donors in Kano, North-Western Nigeria. *Nigerian Journal of Basic and Clinical Sciences*, *9*(1), 11.
65. Erhabor, O., Isaac, I. Z., Saidu, A., Ahmed, H. M., Abdulrahaman, Y., Festus, A., ... & Adias, T. C. (2013). The distribution of ABO and Rhesus blood groups among residents of Gusau, Zamfara State, North Western Nigeria. *Res Rev J Med Health Sci*, *2*(4), 58-63.
66. Chandra, T., & Gupta, A. (2012). Prevalence of ABO and rhesus blood groups in northern India. *J Blood Disord Transfus*, *3*, 132.
67. Vandana, R. A. I., & KUMAR, P. (2011). Genetic analysis of ABO and Rh blood groups in backward caste population of Uttar Pradesh, India. *Notulae Scientia Biologicae*, *3*(3), 07.
68. Hassawi, D. S. (2007). Allele frequency and molecular genotypes of ABO blood group system in a Jordanian population. *J Med Sci*, *7*(1), 51-8.
69. Omotade, O. O., Adeyemo, A. A., Kayode, C. M., Falade, S. L., & Ikpeme, S. (1999). Gene

frequencies of ABO and Rh (D) blood group alleles in a healthy infant population in Ibadan, Nigeria. *West African journal of medicine*, *18*(4), 294-297.

70. Iyiola, O. A., Igunnugbemi, O. O., & Bello, O. G. (2012). Gene frequencies of ABO and Rh (D) blood group alleles in Lagos, South-West Nigeria. *Egyptian Journal of Medical Human Genetics*, *13*(2), 147-153.
71. [71] Alimba CG, Adekoya KO, Oboh BO; Prevalence and gene frequencies of phenylthiocarbamide (PTC) taste sensitivity, ABO and Rhesus factors (Rh) blood groups and haemoglobin variants among a Nigeria population. Egypt J Med Hum Genet, 2010; 11:153-158.
72. Rowe, J. A., Handel, I. G., Thera, M. A., Deans, A. M., Lyke, K. E., Koné, A., ... & Plowe, C. V. (2007). Blood group O protects against severe Plasmodium falciparum malaria through the mechanism of reduced rosetting. *Proceedings of the National Academy of Sciences*, *104*(44), 17471-17476.
73. Pereira, F. E. L., Bortolini, E. R., Carneiro, J. L. A., SILVA, C. D., & Neves, R. C. (1979). A, B, O blood groups and hepatosplenic form of schistosomiasis mansoni (Symmer's fibrosis). *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *73*(2).
74. Trangle, K. L., Goluska, M. J., O'LEARY, M. J., & Douglas, S. D. (1979). Distribution of blood groups and secretor status in schistosomiasis. *Parasite immunology*, *1*(2), 133-140.
75. Ndamba, J., Gomo, E., Nyazema, N., Makaza, N., & Kaondera, K. C. (1997). Schistosomiasis infection in relation to the ABO blood groups among school children in Zimbabwe. *Acta tropica*, *65*(3), 181-190.
76. Deribew, K., Tekeste, Z., & Petros, B. (2013). Urinary schistosomiasis and malaria associated anemia in Ethiopia. *Asian Pacific journal of tropical biomedicine*, *3*(4), 307-310.
77. Jeremiah, Z. A. (2006). Abnormal haemoglobin variants, ABO and Rh blood groups among student of African descent in Port Harcourt, Nigeria. *African health sciences*, *6*(3), 177-181.
78. Salmon, D., Godelier, M., Halle, L., Lemonnier, P., Lory, J. L., Rouger, P., ... & Salmon, C. (1988). Blood groups in Papua New Guinea Eastern Highlands. *Gene geography: a computerized bulletin on human gene frequencies*, *2*(2-3), 89-98.
79. Anees, M., Jawad, A., & Hashmi, I. (2007). Distribution of ABO and Rh blood group alleles in Mandi Bahauddin district of Punjab, Pakistan. *Proc. Pakistan Acad. Sci*, *44*(4), 289-294.
80. Emeribe, A. O., Igweagu, C. A., & Osim, E. E. (1992). ABH secretor status in saliva of Calabar Municipality residents. *East African medical journal*, *69*(1), 27-30.
81. Akhter, S., Kibria, G. M., Akhter, N. R., Habibullah, M. M., Islam, S. M. K., & Zakariah, M. (2011). ABO and Lewis blood grouping with ABH secretor and non-secretor status: A cross sectional study in Dhaka. *Faridpur Medical College Journal*, *6*(1), 38-40.
82. Saboor, M., Ullah, A., Qamar, K., & Mir, A. (2014). Frequency of ABH secretors and non-secretors: A cross sectional study in Karachi. *Pakistan journal of medical sciences*, *30*(1), 189.
83. O'donnell, J., Boulton, F. E., Manning, R. A., & Laffan, M. A. (2002). Genotype at the secretor blood group locus is a determinant of plasma von Willebrand factor level. *British journal of haematology*, *116*(2), 350-356.
84. Odeigah, P. G. (1994). Smell acuity for acetone and its relationship to taste ability to phenylthiocarbamide in a Nigerian population. *East African medical journal*, *71*(7), 462-466.
85. Bakare, A. A., Agbolade, J. O., Iyiola, O. A., Latunji, C. A., & Alimba, C. G. (2009). Distribution and frequency of phenylthiocarbamide (PTC) taster and non-taster alleles in the Nigerian population. *Zoologist (The)*, *7*(1).
86. Bhalla, V., Roy, S., & Bhatia, K. (1978). Genetic polymorphism in Cis-Himalayan populations. *Indian Anthropologist*, *8*(1), 49-53.
87. Omotade, O. O., Kayode, C. M., Falade, S. L., Ikpeme, S., Adeyemo, A. A., & Akinkugbe, F. M. (1998). Routine screening for sickle cell haemoglobinopathy by electrophoresis in an infant welfare clinic. *West African journal of medicine*, *17*(2), 91-94.
88. Nnaji, G. A., Ezeagwuna, D. A., Nnaji, I. J. F., Osakwe, J. O., Nwigwe, A. C., & Onwurah, O. W. (2013). Prevalence and pattern of sickle cell disease in premarital couples in Southeastern Nigeria. *Nigerian journal of clinical practice*, *16*(3), 309-314.