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1 Distribution of ABO and Rhesus Blood Groups, Haemoglobin Variants, Phenylthiocarbamide Taste Perception and Secretor Status in Urogenital Schistosomiasis

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Abstract: Understanding genetic variations among individuals in relation to an infection is necessary for the effective control of the infection. This study examined the distribution of ABO and Rhesus (Rh) blood groups, haemoglobin genotype, phenylthiocarbamide (PTC) taste perception and secretory status in pupils infected with Schistosoma haematobium in order to determine whether there was any association between any of the genetic markers mentioned above and urogenital schistosomiasis. A total of 285 school children of age 3-14 years old comprising two groups participated in this study. The first group consisted of 132 pupils with urogenital schistosomiasis while the second group consisted of 153 apparently healthy pupils without schistosomiasis. Urine specimens from the study participants were examined for Schistosoma haematobium infection. In addition, their blood samples were typed for ABO, Rh blood groups and examined for haemoglobin genotype, saliva samples were analysed for ABH secretory status and PTC taste perception was determined using PTC strips. Among the individuals infected with S. haematobium, the frequency of Rh positive was significantly higher than that of Rh negative (p=0.009). Severe S. haematobium infection was more associated with group A than group O individuals (p=0.01). This study shows that Rh factor influences the prevalence of S. haematobium infection and that ABO blood group influences its severity.

Key words: Urogenital schistosomiasis • ABO and Rhesus blood groups • Haemoglobin variants • Phenylthiocarbamide taste perception • Secretor status

INTRODUCTION

Blood groups are found on the surface of red blood cells [1]. The two main blood group systems in transfusion practice are the ABO system and the Rhesus (Rh) system. The ABO is the most important blood group system in human blood transfusion because the A and B antigens are highly antigenic and both anti-A and anti-B are readily present in the serum of individuals who lack the corresponding antigen [2]. Persons are classified into groups A, B, AB or O depending on the antigens present on their red blood cells [3, 4].

The ABO blood group and secretor status of individuals are inherited independently. While the ABO blood group is coded for by the ABH (FUT 1) gene, the secretor (FUT 2) gene interacts with FUT 1 gene to
determine the ability to secrete blood group antigens into body fluids and secretions [5]. The secretion of ABH substances is controlled by a pair of alleles with dominant allele Se for secretion and recessive allele se for non-secretion. Individuals can either be secretors (SeSe/Ses) or ABH substances who can release their blood group antigens into their body fluids or non-secretors (Ses) who cannot [6].

The Rh blood group, the second most important blood group system in transfusion, derives its significance from the high immunogenicity of the D antigen commonly referred to as Rhesus factor present on the surface of red blood cell [7]. Persons who have the D antigen are known as Rh positive individuals while those who lack it are referred to as Rh negative [3]. Still on red blood cell, haemoglobin is the oxygen carrying component of erythrocyte and there are different forms of haemoglobin in a human population. 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 6th position of the beta chain exist, bringing about variants AA, AS, AC, SS, CC and SC among the people in the region [8].

Phenylthiocarbamide (PTC) is a crystalline solid which has a bitter taste to persons who possess the dominant gene (TT or Tt) and tasteless to those who lack it (tt). Mutations to the gene TAS2R38 that is responsible for this trait produce polymorphisms which correspond to two major haplotypes: the AVI recessive allele for a non-taster and the PAV dominant allele for a taster [9]. Varying combinations of these haplotypes include PAV/PAV homozygotes who report PTC to taste bitter than PAV/AVI heterozygotes, and AVI/AVI homozygotes who report PTC to be tasteless [9]. In Nigeria, urogenital schistosomiasis caused by Schistosoma haematobium is endemic in many rural and urban communities. Several studies have been carried out bordering on its prevalence and intensity [10-13]. It is one of the most common parasitic infections second only to malaria. Unlike malaria, which has been studied in relation to a number of genetic markers such as ABO blood group [8, 14] Rh blood group [15, 16] PTC [17] and secretor status [18] in Southwestern Nigeria, reports on urogenital schistosomiasis in relation to genetic markers are scanty and only in relation with ABO blood group [19, 20]. In the present study, we tested the null hypothesis of no significant association between urogenital schistosomiasis and each of the genetic markers mentioned above.

MATERIALS AND METHODS

This study was carried out among pupils in primary schools in Ore community. A total of 285 primary school pupils (3-14 years) comprising 132 school children infected with S. haematobium and 153 S. haematobium negative (Controls) school children participated in the 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.

Each child was given a universal bottle for collection of urine between 11:00 hours and 14:00 hours. Urine samples collected were immediately transported to the laboratory for examination. Briefly each urine sample was thoroughly mixed and 10 ml was centrifuged at 1000 g for 3 minutes. The supernatant was decanted and the sediment was examined under the microscope for ova of S. haematobium. The eggs were counted using a tally counter and intensity of infection was recorded. Intensity of infection was classified as light (<50 ova/10 ml urine) and severe or heavy (>50 ova/10 ml urine) [21].

Also, 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 [22]. 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 [22]. 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 [23]. 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. Questionnaires were administered to obtain relevant information. Laboratory investigations were carried out in
the Research Laboratory, Department of Biomedical Sciences, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria.

**Statistical Analysis:** The statistical package for social sciences (SPSS version 14) was used for statistical analysis. Differences between percentages and proportions were tested by Chi-square test and Fisher’s exact test. A p-value of < 0.05 was considered to be significant.

**RESULTS**

The age and sex distributions of the study participants are given in Table 1. Of the 285 study participants, 132 (46.3%) were infected with *S. haematobium* while 153 (54.7%) were negative. No significant difference was observed in the distribution of age between the infected and control groups (p = 0.89). Also, the distributions of sexes in the infected and control groups were not significantly associated (p = 0.21).

The ABO blood group, Rh factor blood group, Haemoglobin variants, PTC taste perception and Secretor status of the study participants are given in Table 2. Of the 132 persons infected with urogenital schistosomiasis, 49 (37.1%) had blood group O, 43 (32.6%) blood group A, 31 (23.5%) blood group B and 9 (6.8%) blood group AB. Similarly, of the 153 controls, 69 (45.1%) had group O, 47 (30.7%) had group A, 27 (17.7%) had group B and 10 (6.5%) had group AB. There was no significant difference in the distribution of O, A, B and AB blood groups between the infected and control groups (p = 0.50). The ABO blood group did not influence presence of *S. haematobium* infection.

With respect to Rh factor blood group, 127 (96.2%) of the 132 infected participants were Rh positive and 5 (3.8%) were Rh negative while 134 (87.6%) and 19 (12.4%) of the 153 controls were Rh positive and Rh negative respectively. There was a significant association between *S. haematobium infection* and Rh factor blood group (p = 0.009). Rhesus positive individuals were more prone to urogenital schistosomiasis than Rh negative individuals.

Also, of the 132 persons infected with urogenital schistosomiasis, 93 (70.5%) had haemoglobin genotype AA, 32 (24.2%) has AS, 6 (4.5%) had AC and 1 (0.8%) had SS. Similarly, of the 153 controls, 106 (69.3%) had haemoglobin genotype AA, 39 (25.5%) had AS, 6 (3.9%) had AC and 2 (1.3%) had SS. No significant difference was observed between infection status and genotype distribution (p = 0.94). The haemoglobin variants of the participants did not influence the distribution of the infection.

In addition, the PTC taste perception of the study participants is given in Table 2. Among the 132 children with *S. haematobium*, 81 (61.4%) were tasters and 51 (38.6%) were non-tasters while 80 (52.3%) and 73 (47.7%) of the 153 controls were tasters and non-tasters respectively. The difference was not significant (p = 0.12).

Furthermore, Table 2 shows the secretor status of the study participants with respect to urogenital schistosomiasis. Among the infected participants, 94 (71.2%) were secretors and 38 (28.8%) were non-secretors while among the controls, 108 (70.6%) and 45 (29.4%) were secretors and non-secretors respectively. There was no significant association between *S. haematobium* infection and secretor status (p = 0.91).
Table 3: Distribution of ABO and Rhesus blood groups, Haemoglobin variant, Phenylthiocarbamide taste perception and Secretor status in relation to Severity of Urogenital Schistosomiasis in Ore, Southwestern Nigeria

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ova group &lt;50/10 ml n=107</th>
<th>Ova group ≥50/10 ml n=25</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO Blood Group</td>
<td></td>
<td></td>
<td>0.01*</td>
</tr>
<tr>
<td>O</td>
<td>45(37.4)</td>
<td>4(16.0)</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>30(32.7)</td>
<td>13(52.0)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>23(21.5)</td>
<td>8(32.0)</td>
<td></td>
</tr>
<tr>
<td>AB</td>
<td>9(8.4)</td>
<td>0(0.0)</td>
<td></td>
</tr>
<tr>
<td>Rh Blood Group</td>
<td></td>
<td></td>
<td>0.29</td>
</tr>
<tr>
<td>Rh Positive</td>
<td>102(95.3)</td>
<td>25(100.0)</td>
<td></td>
</tr>
<tr>
<td>Rh Negative</td>
<td>5(4.7)</td>
<td>0(0.0)</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin Variant</td>
<td></td>
<td></td>
<td>0.47</td>
</tr>
<tr>
<td>AA</td>
<td>73(68.2)</td>
<td>20(80.0)</td>
<td></td>
</tr>
<tr>
<td>AS</td>
<td>27(25.2)</td>
<td>5(20.0)</td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td>6 (5.6)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>SS</td>
<td>1 (1.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>PTC Taste Perception</td>
<td></td>
<td></td>
<td>0.88</td>
</tr>
<tr>
<td>Taster</td>
<td>66(61.7)</td>
<td>15(60.0)</td>
<td></td>
</tr>
<tr>
<td>Non-taster</td>
<td>41(38.3)</td>
<td>10(40.0)</td>
<td></td>
</tr>
<tr>
<td>Secretor Status</td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Secretor</td>
<td>79(73.8)</td>
<td>15(60.0)</td>
<td></td>
</tr>
<tr>
<td>Non-secretor</td>
<td>28(26.2)</td>
<td>10(40.0)</td>
<td></td>
</tr>
</tbody>
</table>

*Significant p<0.05

The distributions of the examined genetic markers of the infected participants in relation to the intensity of *S. haematobium* infection are presented in Table 3. Significant association was observed in relation with ABO blood group (p = 0.01). Further test showed that the difference was between infected group A individuals and their group O counterparts (p = 0.01). Severe form of the infection was more associated with group A individuals compared to group O individuals.

**DISCUSSION**

In this study, we examined the interactions of ABO and Rhesus (Rh) blood groups, haemoglobin genotype, phenylthiocarbamide (PTC) taste perception and secretory status with *Schistosoma haematobium* infection. This study reported an association between *S. haematobium* infection and Rh blood group with Rh positive individuals more prone to urogenital schistosomiasis than Rh negative individuals. This observation suggested that there may be some form of interaction between the Rh factor gene and urogenital schistosomiasis in the study area. This result is different from that of Trangle et al. [24] in Swaziland who reported lack of association between *S. haematobium* infection and Rh blood group. Differences in geographical regions and peoples could be adduced to this disparity. The Rh antigens are part of the protein complex in the red cell membrane linked with the maintenance of the shape of the red blood cell [25]. Since the molecules on the Rh positive red cells are different from those on the Rh negative red cells, Rh positive and Rh negative individuals should exhibit variations in their susceptibility or otherwise to various diseases [26]. The significant level observed between *S. haematobium* infection and Rh blood group in the study might have a significant impact on the host–parasite interactions. Nevertheless, further studies with larger sample size are suggested to further confirm this observation.

We did not observe any association between ABO blood group and prevalence of *S. haematobium* infection in this study. Some previous studies on the association between ABO and *S. haematobium* reports observed lack of relationship between them in terms of prevalence [19, 20 & 24]. However, significant associations had been reported between blood groups A and/or B and susceptibility to *S. mansoni* infections [24, 27-29]. This disparity could be associated with differences between the two species.

Severe form of urogenital schistosomiasis was significantly more associated with group A individuals than group O individuals in the present study which is in agreement with the reports of some other studies [29, 30]. Although the exact mechanism by which ABO blood groups affect severity is not known, higher level of antigens A and/B in non-O group individuals compared to group O individuals could be responsible [30]. In non-O group, the chances are higher than in O group, for
the young schistosomula to adsorb host blood antigens on their surfaces to mask antigenic sites and thereby prevent specific antibodies from binding [30, 31]. This results in their higher chance of survival and development of severe form of the disease.

In this study, the presence and severity of S. haematobium infection did not correlate with secretor status, haemoglobin genotype and PTC taste perception. This signifies that there is no interaction between the genes of each of these traits and the infection. Our observation of lack of relationship between S. haematobium infection and secretor status is an agreement with that of Triangle et al. [24] who reported similar findings among Swaziland children.

CONCLUSIONS

Differences in Rh factor influenced S. haematobium infection suggesting that the Rh factor gene might participate directly or indirectly in conferring susceptibility or otherwise to urogenital schistosomiasis. Also, ABO blood group could be an important genetic factor that plays a vital role in the severity of S. haematobium infection.

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