Association of ABO (H) Secretor Status with Diabetes Mellitus

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Abstract
Aims: The study was carried out to determine whether there is any possible association between ABH secretor status, ABO blood group and diabetes mellitus.

Study design: Prospective study; Experimental and Structured Questionnaires

Place and Duration of Study: This study was conducted in endocrinology clinic of University of Maiduguri Teaching Hospital (UMTH) Maiduguri, Borno State, Nigeria, between March and June 2015.

Methodology: A total of 225 individuals of age 17 - 90 years consisting of 100 confirmed diabetic patients and 125 Non-diabetic individuals (controls) participated in this study. 2 mL of blood and 2 mL of saliva were collected from each participant for ABO blood grouping test and determination of secretor status respectively. Secretors and non-secretors phenotypes were determined by haemagglutination inhibition technique using saliva.

Results: Out of the 100 Diabetic patients, 75(75%) were secretors and 25(25%) were non-secretors while 111 (88.8%) and 14(11.2%) of the 125 Non-diabetic subjects were secretors and non-secretors respectively. Non-secretors were significantly more associated with Diabetes than secretors (X2 = 6.953, df = 1, p = 0.005). ABO blood group was not significantly associated with DM (X2= 1.66, df = 2, p = 0.558). Females are more likely to me non-secretors than males.

Conclusion: The findings in this study suggested that while there was no association between ABO blood groups and Diabetes, secretion of ABH antigens was associated with Diabetes Mellitus. A prospective cohort study of Non-secretors in relation to DM is required to verify whether the increased frequency of diabetes among Non-secretors is by mere chance or is indeed genetic.

Keywords: [ABO blood group, ABH antigens, Secretors, Non-secretors, Diabetes Mellitus].

I. Introduction
Detailed ABO (H) blood group antigens are expressed on cell surfaces and other tissues including body secretions like saliva. Ever since the discovery of these antigens, there have been concerted efforts to discover a possible association between ABO (H) antigens and different disease conditions [1].

The ability to secrete water soluble A, B and H antigens was found to be inherited in a Mendelian manner, genetically independent of genes controlling the expression of ABO blood group antigens on the surfaces of red cells. ABH secretion is controlled by two alleles, Se (dominant) and se (recessive). Individuals possessing the dominant allele either in homozygous or heterozygous situation (SeSe/Sese) are termed as secretors, while homozygous recessive individuals (sese) are termed non-secretors [2].

This ability or inability to secrete ABH blood group substances into body fluid has been linked with susceptibility to a number of pathological conditions [3]. For example, increased H. pylori infection with increased duodenal ulcer and peptic ulcer disease and hyperpepsinogenemia [4], recurrent urinary tract infections [5, 6], neisseria meningococcal disease [7], recurrent idiopathic hyperplastic candida vulvovaginitis and oral candidiasis [8] are reported to be associated with non ABH secretor status. Other disease states associated with non ABH secretors are autoimmune diseases [9] and myocardial infarction [10]. On the other hand, secretors have been reported to be more susceptible to infections caused by norovirus [11], HIV 1 [12], influenza virus, rhinovirus, respiratory syncytial virus and echovirus [13] than non-secretors. In Nigeria, we are not aware of any study on the relationship between ABH secretor status and diabetes mellitus.

Diabetes Mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period of time [14]. Diabetes is due to either pancreas not producing enough insulin or the cells of the body not responding to the insulin produced [15], this gives rise to Type 1 and Type 2 DM respectively. Another type of diabetes is Gestational DM which occurs when pregnant women without a previous history of diabetes develop a high blood glucose level. Diabetes has equal rates in women and men, with Type 2 DM constituting about 90% of the cases [16] which is about 8.3% of the adult population [17].
Diabetes mellitus is a common medical problem having significant morbidity and mortality. It has a genetic predisposition, although environmental factors do play their role in its genetic expression. Like many other inherited traits, ABH secretor status is also genetically pre-determined and therefore may have an association with diabetes mellitus.

Most studies in Nigeria and abroad related ABO blood group with DM, but there remains a paucity of published research on the relationship between ABH secretor status and DM. Thus, not only in Nigeria but worldwide, data is lacking on the association between ABH secretor status and DM and our study was conducted to look at such associations.

II. Material And Methods

2.1 Study Design

This study was conducted between March and June 2015 in University of Maiduguri teaching hospital (UMTH), Maiduguri, Borno state, Nigeria. Questionnaires were given to diabetic patients and control subjects to obtain their medical history and socio-demographic parameters (age, sex, educational status, occupation, diabetes status, history of any diabetic complications and blood group if known and willingness to participate in the study).

2.2 Study Subjects

The study recruited a total of 100 diabetic patients. These patients were already diagnosed to have diabetes, were under treatment and coming for follow up to endocrinology clinic of the UMTH for their management. 125 control subjects were also recruited for this study. Both males and females of ages ranging from 17 to 90 years were recruited.

2.1.1 Collection and Processing of Saliva; Determination of Secretor status:

The volunteers were asked to rinse their mouth thoroughly with distilled water two to three times. Approximately 2 ml of saliva was collected in a dry sterile tube. Saliva tube was kept for 10 minutes in a boiling water bath to denature the salivary enzymes. It was then cooled and centrifuged for 5 minutes at 1000g, then supernatant was collected and diluted with an equal volume of normal saline. Secretor and non-secretor phenotypes were identified using the haemagglutination inhibition technique [18].

2.1.2 Determination of ABO blood group and Estimation of Fasting Plasma Glucose

Following aseptic techniques, two milliliter (2ml) of blood was collected from the cubital vein in all the subjects (diabetics and control) into ethylenediaminetetraacetic acid (EDTA) bottles for determination of ABO blood group of all subjects. And also two milliliter (2ml) from control subjects into Fluoride-oxalate bottles for estimation of fasting plasma glucose.

ABO blood group of all subjects was carried out by standard tile and tube techniques [19]. Fasting plasma glucose for control subjects were estimated using the glucose oxidase (Trinder’s) method [20, 21, 22].

2.2 Study Subjects

Frequency distribution and prevalence of the various parameters were determined. Differences in proportions were determined by Chi-square tests using the SPSS software version 20.0 for windows. A two sided p < 0.05 at 95% confidence interval (CI) was considered statistically significant for the variables.

III. Results

Hundred (100) Diabetic patients (40 males and 60 females) and 125 control (50 males and 75 females) subjects participated in this study. All the control subjects had their fasting blood sugar between 2.7 and 5.6 mmol/L. A total of 75(75%) Diabetic patients and 111(88.8%) control subjects were secretors while 25(25%) Diabetic patients and 14(11.2%) control subjects were non-secretors (Table 1&figure 1).

Among the diabetic patients, 93(93%) of them have Type II DM and only 7(7%) have type I DM. 70 out of the 93 subjects having Type II DM (77.8%) were secretors and 23(24.7%) were Non secretors. While 5 out of the 7 subjects with Type I DM (71.4%) were secretors and only 2(28.6%) were Non secretors (Table 2).

The sex distribution of non-secretors among control subjects showed that 5 (4%) of the Non secretors were males and 9(7.2%) were females while among diabetic patients 7 (7%) of the Non secretors were males and 18 (18%) were females (Table 3).

Blood group O had the highest frequency in both control and diabetic secretors (53.2% and 54.7% respectively). The least blood group frequency in both control and Diabetic secretors was blood group AB (6.3% and 8% respectively). Similarly, blood group O was the most frequent in both control and diabetic Non secretors (64.3% and 48% respectively) followed by blood groups A (21.4% and 16% respectively), B (14.3%
and 28% respectively) and AB (0% and 8% respectively). Thus, blood group AB had the least frequency in both control and diabetic Non secretors. (Table 4) There was no statistically significant association ($X^2 = 1.119$ df = 3 $p=0.773$) between ABO blood group phenotypes and secretor status.

<table>
<thead>
<tr>
<th>Table 1:</th>
<th>Secretor status Distribution of Control and Diabetic subjects</th>
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<tbody>
<tr>
<td>Secretor</td>
<td>All subjects</td>
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<tr>
<td></td>
<td>C (%)</td>
</tr>
<tr>
<td>Secretor</td>
<td>111(88.8)</td>
</tr>
<tr>
<td>Total</td>
<td>125</td>
</tr>
<tr>
<td>Non secretor</td>
<td>14(11.2)</td>
</tr>
<tr>
<td></td>
<td>18(30)</td>
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<tr>
<td>C = Control</td>
<td>DM = Diabetic Subjects</td>
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<th>Table 2:</th>
<th>Type of Diabetes Mellitus and Secretor status</th>
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<tr>
<td>Type</td>
<td>Secretor (%)</td>
</tr>
<tr>
<td>I</td>
<td>5 (71.4)</td>
</tr>
<tr>
<td>II</td>
<td>70 (75.3)</td>
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<td>Total</td>
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<th>Table 3:</th>
<th>Sex distribution and secretor status of Control and Diabetic subjects.</th>
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<tr>
<td>Sex</td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>S (%)</td>
</tr>
<tr>
<td>Male</td>
<td>45 (40.5)</td>
</tr>
<tr>
<td>Total</td>
<td>111</td>
</tr>
<tr>
<td>Female</td>
<td>66 (59.3)</td>
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<tr>
<td>S = Secretor</td>
<td>NS = Non Secretor</td>
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<th>Table 4:</th>
<th>ABO Blood Group and Secretor Status of Controls and Diabetic subjects</th>
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<tbody>
<tr>
<td>Blood group</td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td>S (%)</td>
</tr>
<tr>
<td>O</td>
<td>59 (53.2)</td>
</tr>
<tr>
<td>B</td>
<td>30 (27.0)</td>
</tr>
<tr>
<td>A</td>
<td>15 (13.5)</td>
</tr>
<tr>
<td>AB</td>
<td>7 (6.3)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>111</td>
</tr>
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</table>

IV. Discussion

The frequencies of ABH secretors and non-secretors in the control subject were 88.8% and 11.2% respectively. Whereas, the frequencies of secretors and non-secretors in the diabetic subjects were 75% and 25% respectively. The frequency of ABH secretor status reported in the control subjects in this study is generally higher than what is obtainable worldwide where about 20% are non-secretors [19]. Igbeneghu et al [3] reported a frequency of 75% secretors and 22% non-secretors in Osogbo in South-western Nigeria while Jaff [23] reported a frequency of 76% secretors and 23.9% non-secretors in Iraq. Akhter et al [24] found a frequency of ABH secretor status of 60% and non-secretor of 40% in Dhakar.

In this study, more diabetic patients are non-secretors (25%) as compared to control subjects (11.2%). This is in accordance with the research carried out by Patrick and Collier [25] which states that ABH non secretors, and especially Lewis negative individuals, are at a greater risk of developing diabetes (especially adult onset diabetes); and they might be at a greater risk of developing complications from diabetes.

Even though much remains unclear concerning genetics and other factors involved in the aetiology of DM, it was earlier stated that a recessive gene present in double dose causes DM. However, present studies do
not rule out the possibility of multiple genes rather than a single pair of gene coupled with environmental factors as the major predisposing factors to DM [26].

The FUT2 gene encodes fucosyltransferases that transfer a terminal fucose residue to a pre-existing precursor substance to form a soluble H antigen (type 1 H) in secretor tissues, which serves as a precursor for soluble ABH antigens. Hence, individuals having at least one functional FUT 2 allele, their ABH antigens are not only detected on their cell surfaces, but also in their body fluids including saliva. Non-secretors are homozygous for two inactive FUT 2 alleles (sese) [27]. It is therefore possible that the presence of genes that predispose a person to diabetes may down regulate the expression of FUT2 (secretor) gene and secretor enzymes, leading to the higher percentage of non-secretors in the Diabetic subjects.

The available data on association between the distribution of ABO blood types and Diabetes Mellitus is conflicting, some studies reporting no association while others showed positive association. Rahman [28] reported no significant association between ABO blood types and DM in a study from Bangladesh with a sample size of 2,312 patients and 8,939 controls. Koley [29] also reported no association between DM and ABO blood group types among Madhya Pradesh population in Indian. However, Kamil et al [30] in Malaysia reported a positive association between ABO blood group types and DM with group A and O been more frequent among the controls than the diabetic subjects. Okon et al [31] also reported a positive association between ABO blood types and DM in South-Eastern Nigeria where blood group A and O was found to be more frequent among the diabetics than control subjects.

In this study, the frequencies of ABO blood grouping in the control subjects for groups O, A, B and AB were 54.4%, 14.4%, 25.6% and 5.6% and for the diabetics were 53%, 16%, 23% and 8% respectively. There is no major difference in the ABO blood groups of the controls and diabetic subjects. This is in support of the findings by Rahman [28] but contradicts those of Okon et al [31] and Kamil [30]. This may be due to racial and geographical variations.

In this study, the least blood group frequency for both control and diabetic subject is blood group AB (5.6% and 8% respectively). This result supports the finding that blood group AB is the least frequent among the people of Calabar in southern Nigeria [32] and the reports of Rahman [28] and Akhter et al [24].

This study reveals no significant association between ABO blood group phenotypes and secretor status frequency, which contradicts the findings of Emeribe et al [32] and Jaff [23].

The results in this study also revealed that females are more likely to be non-secretors. In control subjects 9(64.3%) out of the 14 non secretors were females and 5(35.7) were males. In the Diabetic subjects, female non secretors were 72% as compared to 28% of males. This is also different from the findings of Emeribe et al [32] where there was no age or sex correlation with secretor status.

V. Conclusion

This study shows an association between the ability to secrete water soluble ABH antigens in body fluid (e.g. saliva) and DM, with non-secretors more likely to be diabetic and that susceptibility is even higher among females than males. However, the study did not show any association between the ABO blood group system and DM.

Acknowledgements

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Competing Interests

Authors have declared that no competing interests exist.

Ethical Approval

All authors hereby declare that the human study have been examined and approved by the Research and ethics committee of the University of Maiduguri Teaching Hospital (UMTH). The study recruited diabetic patients attending endocrinology clinic in University of Maiduguri Teaching Hospital, Maiduguri and control subjects among healthy staff and students of College of Medical Sciences, University of Maiduguri after detailed explanation on the nature and benefit of the study had been given and both verbal and written consent obtained and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.”

References

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