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Secretor Status and Phenylthiocarbamide (PTC) Taste Perception are Risk Factors for Pulmonary Tuberculosis

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Authors' contributions

This work was carried out in collaboration between all authors. Author CI designed the study, wrote the protocol, managed the bench work and wrote the first draft of the manuscript. Authors BMO and JMO managed the literature searches and analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Aim: To examine whether or not non-secretion of ABH substances and non-tasting of PTC are risk factors exhibiting positive interactions for tuberculosis.
Methodology: A total of 210 individuals comprising 110 tuberculosis patients (test group) and 100 apparently healthy subjects (control group) participated in this study. Secretors and non-secretors were determined among the study participants by haemagglutination inhibition test and Tasters and non-tasters were determined using phenylthiocarbamide (PTC) taste strips (0.0143 mg/strip).
Results: Of the 110 tuberculosis patients, 65 (59.1%) and 45 (40.9%) were secretors and non-secretors respectively while 49 (44.5%) were tasters and 61 (55.5%) were non-tasters. Of the 100 control subjects, 78% and 22% were secretors and non-secretors respectively while 67% and 33% were tasters and non-tasters respectively. Non-secretors of ABH substances were significantly

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more associated with test patients than controls (χ^2 = 8.62, df = 1, p = 0.002). Non-tasters of PTC were significantly more associated with test patients than controls (χ^2=10.68, df=1, p=0.001). When combined, secretors and tasters were significantly lower in the test group than in the control group (χ^2=13.44, df=1, p<0.001) while non-secretors and non-tasters were significantly higher in the test group than in the control group (χ^2=9.77, df=1, p=0.002). Individuals who were both non-secretors and non-tasters were significantly associated with tuberculosis compared to those who were not (OR 3.5; 95% C.I 1.59-7.51).

Conclusion: This study shows that there is a remarkable increased incidence of tuberculosis in individuals who are both unable to secrete ABH substances and taste PTC.

Keywords: ABH substances; secretors; non-secretors; phenylthiocarbamide; tasters; nontasters; tuberculosis.

1. INTRODUCTION

Some individuals secrete ABH substances into body fluids and secretions while others do not. The secretor (FUT 2) gene responsible for the secretion of ABH substances has two alleles, Se (dominant allele) and se (recessive allele). Secretors are SeSe or Sese while non-secretors are sese. The secretor gene interacts with FUT 1 gene to determine the ability to secrete blood group antigens into body fluids and secretions. Secretor status has been associated with a number of infectious diseases. Non-secretors have been reported to be more susceptible to infections caused by bacteria [1-5] and *Plasmodium* spp. [6] while secretors have been reported to be more susceptible to viral infections [7-10].

Like secretor status, phenylthiocarbamide (PTC) taste perception is generally referred to as a simple genetic trait governed by a pair of alleles, dominant T for tasting and recessive t for non-tasting. Persons with genotype TT or Tt are tasters and those with genotype tt are non-tasters. Tasters are individuals who can taste PTC while non-tasters are those who describe it as tasteless. Several studies have reported association or lack of association between PTC taste perception and different diseases [11]. Reports on association between tuberculosis patients and tasting of PTC have been conflicting [12,13]. However, a recent study carried out in Southwest Nigeria, reported non-tasters of PTC to be associated with tuberculosis [14]. There is no any other investigation to our knowledge that has related PTC taste perception with tuberculosis among Nigerian population. Also, we are not aware of any study in Nigeria that has related secretor status with tuberculosis. In this study, we tested the hypothesis that non-tasters and non-secretors exhibited positive interaction for tuberculosis.

2. MATERIALS AND METHODS

2.1 Study Area and Subjects

This study was carried out in Osogbo, Southwestern Nigeria. Osogbo is the State capital city of Osun State. It seats the headquarters of both Osogbo and Olorunda Local Government Areas. It is about 88 km Northeast of Ibadan; it is the trade centre for a farming region. Its inhabitants are mainly members of the Yoruba ethnic group and tuberculosis is quite endemic in Osogbo. The test subjects were drawn from patients attending tuberculosis clinics of the State teaching hospital, Asubiaro, Osogbo while the control subjects were apparently healthy members of staff and students of the hospital. A total of 210 individuals comprising 110 tuberculosis patients and 100 controls of age ≥16 years participated in the study. Test subjects were recruited from new cases of those who tested positive to Ziehl Neelsen technique for *Mycobacterium tuberculosis* at the tuberculosis clinic while the controls were apparently healthy individuals without symptoms or physical findings suggestive of tuberculosis and who were negative to skin tuberculin (mantoux) test. Informed consent was obtained from each participant and ethical approval was obtained from the Ethical Committee of the College of Health Sciences, Ladoke Akintola University of Technology, Osogbo.

2.2 Sample Collection and Investigations

A sample of 2 mL of venous blood was collected from each participant into ethylenediaminetetraacetic acid (EDTA) bottle. ABO blood group antigens tests were performed by standard tube and tile techniques. Controls were set up appropriately. The ABO blood grouping is based

on agglutination of red blood cells by antibody [15]. It was performed on saline washed red cells using commercially prepared monoclonal anti-A, anti-B according to the manufacturer's instructions (Biotech Laboratories, U.K). Also, 2 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 [16].

Phenylthiocarbamide (PTC) taste strips (0.0143 mg of PTC /strip) were obtained from Carolina Biological Supply Company, North Carolina, USA. 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.

2.3 Statistical Analysis

The statistical package for social sciences software package (SPSS) was used for statistical analysis. Differences between percentages and proportions were tested by Chi-square test. Sample means were compared by student's t test. A p-value of < 0.05 was considered to be significant.

3. RESULTS

A total of 110 tuberculosis patients (52 males and 58 females) and 100 controls (50 males and 50 females) of age ≥16 years participated in this study. The sex and age distribution of the study population are given in Table 1. The distributions of males and females in the test and control groups were not significantly different ($\chi^2 = 0.16$, df = 1, p = 0.69). Similarly, there was no significant difference in the distribution of age between the HIV subjects and the control subjects ($\chi^2 = 5.94$, df = 3, p = 0.12).

The distribution of secretor status, ABO blood group and PTC taste perception among the test and control subjects are given in Table 2. Of the 110 tuberculosis patients, 59.1% and 40.9% were secretors and non-secretors respectively while 78% and 22% of the controls were secretor and non-secretors respectively. Non-secretors in the test group (40.9%) were significantly higher than non-secretors in the control group (22.0%) ($\chi^2 = 8.62$, df = 1, p = 0.003, OR 2.45; 95% C.I 1.35-4.46). Therefore, non-secretion of ABH substances was significantly associated with tuberculosis.

Also, while 44.5% and 55.5% of the tuberculosis patients were tasters and non-tasters respectively, 67% and 33% of the controls were tasters and non-tasters respectively. Non-tasters in the test group (55.5%) were significantly higher than non-tasters in the control group ($\chi^2 = 10.68$, df = 1, p = 0.001, OR 2.53; 95% C.I 1.45-4.42). so, inability to taste PTC was significantly associated with tuberculosis. However, ABO blood group distribution among the test and control subjects were comparable ($\chi^2=3.75$, df=3, p=0.31).

The two traits, secretor status and PTC taste perception were considered together and the frequency distributions with respect to sex are given in Table 3. There were four combinations observed: secretors and tasters (Se_T_), secretors and non-tasters (Se_tt), non-secretors and tasters (seseT_) and non-secretors and non-tasters (sese tt). Of the 110 test subjects, 32 were secretors and tasters, 33 were secretors and non-tasters, 17 were non-secretors and tasters, 28 were non-secretors and non-tasters while of the 100 control subjects, 54 were secretors and tasters, 24 were secretors and non-tasters, 13 were non-secretors and tasters, 9 were non-secretors. These combined traits varied significantly between the test and control subjects ($\chi^2=16.90$, df=3, p<0.001). Further Chi-square tests showed that secretors and tasters in the test group were significantly lower than secretors and tasters in the control group ($\chi^2 = 13.44$, df = 1, $p < 0.001$) while non-secretors and non-tasters were significantly higher in the test group than in the control group ($\chi^2 = 9.77$, df = 1, p = 0.002). Of the four groups of combination, non-secretors and non-tasters were the most associated with tuberculosis (OR 3.45; CI 1.59-7.51). A person who was both non-secretor and non-taster was about 3.5 times more likely to have tuberculosis than one who was not. On the other hand, secretors and tasters were the least associated with tuberculosis. Therefore, individuals who were both non-secretors and non-tasters were the most susceptible to tuberculosis while those who were both secretors and tasters were the most resistant.

Table 1. Distribution of the study participants by sex and age

Variable	Test group (%)	Control group (%)	Total	p
Sex[a]				
Female	52 (47.3)	50 (50.0)	102 (73.6)	0.69
Male	58 (52.7)	50 (50.0)	108 (26.4)	
Total	110 (52.5)	100 (47.5)	210 (100.0)	
Age[b] (years)				
16 – 25	24 (21.8)	11 (11.0)	35 (10.6)	0.12
26 – 40	47 (42.7)	49 (49.0)	96 (47.6)	
41 – 60	30 (27.3)	35 (35.0)	65 (37.0)	
> 60	9 (8.2)	5 (5.0)	14 (4.8)	
Total	110 (52.5)	100 (47.5)	210 (100.0)	

[a]χ^2 = 0.16, df = 1, p = 0.69; [b]χ^2 = 5.94, df = 3, p = 0.12

Table 2. Distribution of the test and control subjects by secretor status and Phenylthiocarbamide (PTC) taste perception and ABO blood groups

Subjects	Test group (%)	Control group (%)	Total (%)	p
[c]Secretor status				
Secretor	65 (59.1)	78 (78.0)	143 (68.1)	0.003
Non-secretor	45 (40.9)	22 (22.0)	67 (31.9)	
Total	110 (52.4)	100 (47.6)	210 (100.0)	
[d]Tasting status				
Taster	49 (44.5)	67 (67.0)	116 (55.2)	0.001
Non-taster	61 (55.5)	33 (33.0)	94 (44.8)	
Total	110 (52.4)	100 (47.6)	210 (100.0)	
[e]ABO blood grouping				
A	14 (12.7)	21 (21.0)	35 (16.7)	0.31
B	25 (22.7)	22 (22.0)	47 (22.4)	
AB	07 (6.4)	03 (3.0)	10 (4.8)	
O	64 (58.2)	54 (54.0)	118 (56.2)	
Total	110 (52.4)	100 (47.6)	210 (100.0)	

[c]χ^2 = 8.62, df = 1, p = 0.003; [d]χ^2 = 10.68, df = 1, p = 0.001; [e]χ^2 = 3.57, df = 3, p = 0.31

Table 3. Distribution of combination of secretor status and Phenylthiocarbamide taste perception of among the tuberculosis and control subjects

Character combination	Test group (%)	Control group (%)	Total (%)	p
Se_T_	32 (29.1)	54 (54.0)	86 (41.0)	<0.001
Se_tt	33 (30.0)	24 (22.0)	57 (27.1)	
seseT_	17 (15.4)	13 (13.0)	30 (14.3)	
sesett	28 (25.5)	9 (9.0)	37 (17.6)	
Total	110 (52.4)	100 (47.6)	210 (100.0)	

Se_T_: secretors and tasters; Se_tt: secretors and non-tasters
seseT_: non-secretors and tasters; sesett: non-secretors and non-tasters

4. DISCUSSION

In this study, we found that tuberculosis patients were more likely to be non-secretors than those without tuberculosis. This finding is in line with those of Tyagi et al. [4] and Ankur et al. [5] who reported similar findings. Non-secretors have been associated with a number of other bacterial infections (Blackwell et al. [1]; Blackwell et al. [2]; Sheinfeld et al. [3]). The exact mechanism of susceptibility of non-secretors to bacterial infection is not known but is thought to be linked to differences in cell surface carbohydrates. The presence of specific carbohydrates found in non-secretors but not in secretors may be responsible for the susceptibility of non-secretors (Ali et al. [8]). Also, it has been associated with reduced levels of serum and salivary IgA in non-secretors which suggest abnormality in mucosal protection [17].

Also in this study, we found that tuberculosis patients were more likely to be non-tasters than those without tuberculosis. This finding is at variance with the report of Akesson [13] who found no significant difference between tasters and non-tasters of phenylthiourea with respect to tuberculosis and that of Saldanha [12] who observed discordants results between children and adults and remarked that the thresholds for phenylthiourea could be a reflection of pleiotropic effect of genes. The differences observed by these researchers could be due to the techniques adopted. In this study, we used PTC impregnated taste strips (0.0143 mg of PTC /strip) and eliminated differences that could have been caused by age and sex by ensuring that these variables in the test and control subjects were comparable.

The inability to taste PTC which is significantly associated with tuberculosis suggests that TAS2R38 gene may directly or indirectly participate in conferring susceptibility. The exact mechanism is not known but linkage disequilibrium of the taster locus with other loci that predispose to the disease or the pleiotropic effect of the PTC locus has been suggested [11]. There seemed to be an interaction between the secretor gene and the TAS2R38 gene with non-secretors and non-tasters being most susceptible to tuberculosis and secretors and tasters being least susceptible.

From the results of this study, these genetic markers can be used to identify individuals who are at high risk of tuberculosis so that such easily prone individuals can take appropriate precautionary measures to avoid coming down with the disease.

5. CONCLUSION

We conclude that while non-secretion of ABH substances is associated with tuberculosis just as inability to taste PTC, both non-secretion of ABH antigens and PTC taste blindness interacted positively as risk factors for tuberculosis.

CONSENT

Written informed consent was obtained from each of the participants recruited for this study.

ETHICAL APPROVAL

Ethical approval for this study was obtained from the Ethical Committee of the College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria. Therefore, all procedures were performed in accordance with the ethical standards laid down in the 1964 declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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