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Frequency o f (G428A) Polymorphism within *FUT2* Gene among Symptomatic Asthma Diseases in Sudanese Patients

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Abstract:

Asthma is a chronic lung disease that inflames and narrows the airways. A positive association has recently been reported in adult subjects between O/nonSecretor phenotype and asthma. This study was carried out in at Omdurman teaching hospital aimed to determine the frequency of the (G428A) polymorphism among Sudanese Asthmatic patients and explore if it has a correlation with age and gender or not. A total of 49 patients with Asthmatic were enrolled in this study; blood samples were collected from patients and control in EDTA; genomic DNA was extracted from all samples using salting out method, allele specific PCR used to analyze the samples. The allele specific PCR showed that, 34(69.4%) of the 49 patients were homozygous "GG" while that 13 (26.5%) of the 49 patients were heterozygous (Guanine and Adenine alleles), and just 2 (4.1%) individuals were homozygous "AA". In conclusion, In conclusion, frequency of the FUT2 gene polymorphism among Atmatic patients was significantly high among Male. Large percentage of Sudanese individuals has got a "AA" genotype allele in FUT2 gene; this large percentage could be according to human genomes variations worldwide.

Key words: FUT2 gene, Atmatic diseases, Allele specific PCR, Sudanese

1. INTRODUCTION

Asthma is a chronic lung disease that inflames and narrows the airways. Asthma causes recurring periods of wheezing (a whistling sound when you breathe), chest tightness, shortness of breath, and coughing. The coughing often occurs at night or early in the morning(1).

Asthma affects people of all ages, but it most often starts during childhood. In the United States, more than 25 million people are known to have asthma. About 7 million of these people are children(2).To understand asthma, it helps to know how the airways work. The airways are tubes that carry air into and out of your lungs. People who have asthma have inflamed airways. The inflammation makes the airways swollen and very sensitive. The airways tend to react strongly to certain inhaled substances.When the airways react, the muscles around them tighten. This narrows the airways, causing less air to flow into the lungs. The swelling also can worsen, making the airways even narrower. Cells in the airways might make more mucus than usual. Mucus is a sticky, thick liquid that can further narrow the airways. This chain reaction can result in asthma symptoms. Symptoms can happen each time the airways are inflamed. Sometimes asthma symptoms are mild and go away on their own or after minimal treatment with asthma medicine(3). Other times, symptoms continue to get worse. When symptoms get more intense and/or more symptoms occur, you're having an asthma attack. Asthma attacks also are called flareups or exacerbations. ABH secretors are significantly over represented among patients with influenza viruses A and B, 0.025), rhinoviruses respiratory syncytial virus and echoviruses. Why this increased risk appears in secretors has not been clearly established(2).

The Secretor gene (FUT2) that encodes for a2-alpha-L-fucosyltransferase and the ABO bloodgrouping system that encodes for glycosiltransferases, act in concert to build-up

oligosaccharide structures in exocrine secretion systems, including the respiratory tract [3.4.5].

Specific oligosaccharide epitopes are necessary for recognition of micro-organisms [6]. The product of ABO and Secretor genes seems to influence the adhesion of infectious agents, thus having a modulatory effect on viral and bacterial respiratory infection [5.7].

A combined analysis of ABO blood groups and salivary Secretor phenotypes was recently performed in a cohort of coal miners. Lower lung function and higher prevalence of wheezing and asthma in non-Secretor subjects of blood group O was shown.

Histoblood group antigens, such as the O ("H"), A, and B antigens, form capping structures at the terminal ends of the carbohydrate side chains (glycans) on epithelial mucins. They are formed by stepwise addition of monosaccharide units through the action of a set of glycosyltransferases, including fucosyltransferases (FucTs) [8]. In individuals of blood type O, the addition of fucose to terminal galactose in an a1,2 linkage forms the H antigen in a step catalyzed by a1,2 FucTs encoded by FUT1 (active in erythrocytes) and FUT2 (active in epithelial tissues) genes. Additional modifications to the H antigen depend on an individual's blood type and are controlled by genes at the FUT and ABO loci, which are highly polymorphic and give rise to considerable diversity in the profile of glycans on airway mucins.

Approximately 25% of individuals are homozygous for nonsense mutations in FUT2 [9.10], resulting in the inability to synthesize H antigens at epithelial surfaces and the absence of ABO structures on secreted mucins. These "nonsecretors" represent one of multiple possible mucinglycan phenotypes, including several secretor phenotypes characterized by the display and secretion of H (O), A, or B antigens on epithelial mucins.

The importance of mucins in innate defense in the lung and the fact that blood group antigens on mucins play roles in viral infection in the gastrointestinal tract led us to consider thatABH variation in mucinglycan phenotypes may influence susceptibility to asthma exacerbation. Because of the association between Norwalk virus infection and the secretor phenotype, we hypothesized that O-secretors may be more susceptible to asthma exacerbation [9.10].

2. MATERIAL AND METHODS

This study is a descriptive cross sectional study, conducted in Khartoum state, to determine the frequency of (428 G-A) polymorphism within *FUT2* gene among Athmatic Sudanese patients attending Omdurman teaching hospital during the period of August-May 2016. 49 Samples collected from diagnosed Athmatic patients from different ethnic groups.

EDTA blood sample (3ml) was collected from each, and then DNA was extracted using salting out method. For all samples genotyping was performed using allele specific polymerase chain reaction (PCR-TECHNE TC412, UK). Each PCR tube of 20 µlcontains, 3 µl of genomic DNA, 5 µl of master mix (maximum PCR premix kit (i-taq) iNtRON, Korea), 1 µl of antisense primer (5-GGCTGCCTCTGGCTTAAAG), 1 µl to one of reference allele (5-GCTACCCCTGCTCCTGG) or variant allele (5 CGGCTACCCCTGCTCCTA), and 10 µl of water (distilled water).The amplification process were as follow, denaturation at 95°C for 3 minutes, annealing at 54°C for 1 minute, and extension at 72°Cfor 5 minutes. Then PCR products were placed in electrophoresis. 3 ul of 100 Pb (base pair) DNA ladder was applied with each batch of patient samples. Data was collected by structured questionnaire and analyzed using SPSS software version 21.

This study was approved by Omdurman teaching hospital and faculty of medical laboratory sciences, Alneelain University as well as consent was taken from patients.

RESULT:

Forty-nine asthmatic patients were participated in this study as case study. All participant fall in age ranged 20-60 years.

The allele specific PCR showed that, 2 (4.1%) of the 49 patients were homozygous (the two alleles were Adenine), while that 13 (26.5 %) of the 49 patients were heterozygous (Guanine and Adenine alleles), and 34 (69.4%) individuals were homozygous "GG"

Diagnosis	Frequency	Percent
Homozygous "GG"	34	69.4
Heterozygous	2	4.1
Homozygous "AA"	13	26.5
Total	49	100.0

The Genotyping of the FUT2428 showed an increased (AA) among male comparing to females witch correlate insignificantly with (p.value= 0.407) (Table 2).

Table 2. Distribution of genotyping among gender

Gender	Homozygous "GG"	Heterozygous	Homozygous "AA"	Total
Male	21	2	6	29
Female	13	0	7	20

In Table 3 the genotype in each age group demonstrate that the age does not affect the hetro or homogeneity of the sample.

Table 3. Distribution of genotyping among age

Age	Homozygous "GG"	Heterozygous	Homozygous "AA"
20-29	5	1	3
30-39	15	1	2
40-49	10	0	4

50-59	4	0	3
above 60	0	0	1

In table 4 the genotype in each mutant type demonstrate that the wild type does not affect the hetro or homogeneity of the sample **while mutant type affect the** hetro or homogeneity of the sample

		Result			p.value
		WW	**MM**	**MW**	
Mutant type	**Yes**	0	2	12	0.000
	No	34	0	1	
Wild type	**Yes**	34	0	13	0.493
	No	0	2	0	

DISCSSION

Alpha-2-fucosyltransferases FUT1 (previously termed H) of red cells and vascular endothelium, and FUT2 (previously termed Se) of exocrine secretion system, are structural genes that collaborate with glycosiltransferases. Glycosiltransferases are controlled by the ABO system, to build oligosaccharide structures on the cell surface of erythrocytes and vascular endothelium, as well as in the exocrine secretion system including the respiratory tract 3.

This study conducted to determine the frequency of the FUT2 (428 G-A) polymorphism Sudanese patients with UTI infections, the allele specific PCR results showed that 2 (4.1%) was homozygous, 13 (26.5%) was heterozygous while 34 (69.4%) are normal among Athmaticpatient, these results are support the findings of previous study done by Innes et al which found that having the O-secretor phenotype was associated with a 5.8-fold increase in the odds of being a case (95% confidence interval, 1.7–21.0; P 5 0.006). (11).

Age ranged from 20 above to 60 years, the result showed there was an increase susceptibility of the 428 G-A in the FUT2 gene polymorphism with increasing age but observationally

without statistical correlation, These demonstrate that there was no significant correlation between age of Sudanese's patients and FUT2 gene polymorphism this result disagreed with study carried out by Innes et al [12]who reported that there was significant correlation between gene polymorphism and age.

The present study demonstrated that there were an increased number of males compared to females and correlate insignificantly this result disagreed with Ronchetti et al [13]who reported that the association was more marked in males than in females.

This study also showed that 2 (4.1%) of the 49 patients were homozygous (the two alleles were Adenine), while that 13 (26.5 %) of the 49 patients were heterozygous (Guanine and Adenine alleles), and 34 (69.4%) individuals were homozygous "GG", our findings can be compared with those of D'ADAMO et al[15]

Individuals with secretor phenotype were either homozygous (GG) or heterozygous (GA) while the AA genotype considered non secretor as study done by Soejima et al [16]. The non-sense mutation G428A and the missense mutation A385T are responsible for the vast majority of the non-secretor status in Caucasians, Africans, and Asians, respectively. The distributions of nonsense mutation (428 G-A) in the *FUT2* gene which is the most frequent polymorphism.

In addition, many studies showed the relation between *FUT2* gene polymorphisms and disturbed in ABH secretion in conjunction that lead to large number of diseases.

CONCLUSION

In conclusion, frequency of the FUT2 gene polymorphism among Athmatic Sudanese patients was significantly high among Male. Large percentage of Sudanese individuals has got

a "GA" genotype allele in FUT2 gene; this large percentage could be according to human genomes variations worldwide.

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