International Journal of Scientific Engineering and Research (IJSER)
www.ijser.in
ISSN (Online): 2347-3878, Impact Factor (2015): 3.791

Frequency of (G428A) Polymorphism within *FUT2* Gene among Symptomatic UTI Diseases in Sudanese Patients

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Abstract: ***National Kidney & Urologic Diseases Information Clearinghouse (NKUDIC) reports that UTIs account for over 8 million doctor visits annually disease significantly affects females. Bacteria cause the vast majority of UTIs. Fungi or viruses can also cause UTIs. Symptoms of UTI depend upon what part of the urinary tract is infected; Single- nucleotide polymorphisms (SNPs) play a major role in the understanding of the genetic basis of many complex human diseases. Also, the genetics of human phenotype variation could be understood by knowing the functions of these SNPs. This study was carried out in Omdurman Military hospital aimed to determine the frequency of the (G428A) polymorphism among Sudanese UTI patients and explore if it has a correlation with age and gender or not. A total of 49 patients with UTI 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, 9(18.4%) of the 49 patients were homozygous "AA" while that 30 (61.2%) of the 49 patients were heterozygous (Guanine and Adenine alleles), and just 10 (20.4%) individuals were homozygous "GG". In conclusion, In conclusion, frequency of the FUT2 gene polymorphism among urinary tract infection was significantly high among female. 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.***

Keywords: FUT2 gene, UTI diseases, Allele specific PCR, Sudanese

1. Introduction

Urinary tract infections (UTIs) are symptomatic infections of the urinary tract, mainly caused by the bacterium Escherichia coli. One in two women suffers from a UTI at least once in her life. The young and sexually active are particularly affected, but it is also seen in elderly, postmenopausal women. The like hood of recurrences high Diagnosis is made with regard to typical complaints and the presence of leucocytes and nitrites in the urine [(1)].

A urinary tract infection (UTI) can occur in any part of the urinary tract. Bacteria cause the vast majority of UTIs. Fungi or viruses can also cause UTIs. It is the second most common type of infection in humans. The National Kidney & Urologic Diseases Information Clearinghouse (NKUDIC) reports that UTIs account for over 8 million doctor visits annually [(2)]

A form of synergy also appears to exist between UTI risk, secretor status and the lack of ability to create anti-B is hemagglutinin. Essentially, blood group B and AB and the non-secretor phenotype seem to work together to increase the relative risk of recurrent UTI among these women [(3)]. Evidence also indicates that women and children with renal scarring subsequent to recurrent UTI and pyelonephritis are more likely to be ABH non-secretors [(4, 5)].As many as 55-60% of all ABH non-secretors have been found to develop renal scars, even with the regular use of antibiotic treatment for UTI whereas as few as 16% of ABH secretors will develop similar renal scarring [(6)].

The ABO blood group and secretor status of individuals are inherited independently. The ABH (FUT 1) gene codes for the ABO blood group. The secretor (FUT 2) gene interacts with FUT 1 gene to determine the ability to secrete blood group antigens into body fluids and secretions. A person can either be a secretor (SeSe/Sese) or a non-secretor (sese) of ABH substances. Secretors are persons who put their blood type antigens into their body fluids and secretions while non-secretors do not put their blood type antigens into their body fluids and secretions. Non-secretors are at a potential health disadvantage compared to secretors as an appreciable number of diseases/disorders have been associated with inability to secrete ABH substances. For example, non-secretors had been reported to be more prone to infection caused by *Haemophilusinfluenzae* meningitis and pneumonia (Blackwell *et al.*, 1986b) recurrent urinary tract infections thrombotic and heart disease [(7)].

Single nucleotide polymorphisms (SNPs) are variations of a single base, either between two homologous chromosomes within a single individual, or between two individuals. Genetic polymorphisms are well-recognized sources of individual differences in disease risk and treatment response [(8)]. SNPs are found throughout the genome in exons, introns, intergenic regions, promoters, enhancers, SNP in a promoter can influence gene expression [(9)]etc and thus more likely to contain an allele being more functionally or physiological relevant than other types of polymorphism. There are about 500, 000 SNPs fall in the coding regions of the human genome [(10)]. Among these SNPs, nonsynonymous SNPs (nsSNPs), those cause changes in the amino acid residues. Missense, nonsense and frameshift; are the nsSNPs types. These are likely to be an important factor contributing to the functional diversity of the encoded proteins in the human population. Nonsynonymous SNPs affect the functional roles of proteins in the signal transduction of visual, hormonal, and other stimulants[(11)]. Identification of SNPs responsible for specific phenotypes seems to be a problem, since requiring multiple testing of hundreds or thousands of SNPs in candidate genes.

The aim of the present study was to determine the frequency of the most common polymorphism (428 G-A) within *FUT2* gene among symptomaticUTI Sudanese patients.

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 symptomatic UTI Sudanese patients attending Omdurman Military hospital during the period of August-May 2016. 49 Samples collected from diagnosed UTI 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 µl contains, 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 military hospital and faculty of medical laboratory sciences, Alneelain University as well as consent was taken from patients.

3. Results

The study included 49 UTI patients; 5 (10.2%) of them were males and 44 (89.8%) were females, the age ranged between 20-60 years.

The allele specific PCR showed that, 9 (18.4 %) of the 49 patients were homozygous (the two alleles were Adenine), while that 30 (61.2 %) of the 49 patients were heterozygous (Guanine and Adenine alleles), and just 10 (20.4%) individuals were homozygous "GG" (**Table 1**).

Table 1: The frequency of (G-A 428) FUT2 polymorphism among the study group

Diagnosis	Frequency	Percent
Homozygous "GG"	9	18.4
Heterozygous	30	61.2
Homozygous "AA"	10	20.4
Total	49	100.0

The Genotyping of the FUT2428 showed an increased (AA) among female comparing to males witch correlate insignificantly with (p.value= 0.981) (Table 2).

Table 2: Distribution of genotyping among gender

Gender	Homozygous "GG"	Heterozygous	Homozygous "AA"	Total
Male	0	3	2	5
Female	10	6	28	44

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

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Table 3: Distribution of genotyping among age

Age	Homozygous "GG"	Heterozygous	Homozygous "AA"
20-29	4	0	4
30-39	6	2	17
40-49	0	3	6
50-59	0	3	1
above 60	0	1	2

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	9	30	0.000
	No	10	0	0	
Wild type	Yes	10	1	30	0.122
	No	0	8	0	

4. Discussion

Urinary tract infections (UTIs) are symptomatic infections of the urinary tract, mainly caused by the bacterium Escherichia coli. One in two women suffers from a UTI at least once in her life. The young and sexually active are particularly affected, but it is also seen in elderly, postmenopausal women. The likelihood of recurrence is high.

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 20 (40.8 %) was homozygous, 20 (40.8 %) was heterozygous while 9 (18.4%) are normal among UTI infection patient, these results are support the findings of previous study done by Ferrer-Ademetlla. et al which explained in their study FUT2, a fucosyltransferase responsible for ABO biosynthesis in body fluids. Homozygotes for null variants at this locus present the nonsecretor phenotype (se), because they cannot express ABO antigens in secretions [(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 intermediate 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 Igbeneghu 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 females compared to males and

correlate insignificantly this result agreed with Jaff et al [13] and saboor et al[14].

This study also showed that 9 (18.4 %) were homozygous (the two alleles were Adenine), while that 30 (61.2 %) were heterozygous (Guanine and Adenine alleles), and just 10 (20.4%) individuals were homozygous "GG" among urinary tract infection patient, our findings can be compared with those of (Birrey et al., 2007)[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.

5. Conclusion

In conclusion, frequency of the FUT2 gene polymorphism among urinary tract infection was significantly high among female. 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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