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Relationship of ABO and Lewis Blood Groups in Patients with Urinary Tract Infection

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ABSTRACT

Aims Urinary tract infection is the most common adult bacterial infection worldwide. Antigens of ABO and Lewis blood groups may influence bacterial adherence and lead to an increase in the frequency of urinary tract infections in adults. This study aimed to evaluate the relationship of ABO and Lewis blood groups with urinary tract infections.

Materials & Methods In this experimental study, a blood sample of 80 urinary tract infection patients from AL-Sader Teaching Hospital, Iraq, and 50 healthy persons was used for the determination of ABO and Lewis blood groups by agglutination assay. Urine samples of urinary tract infection patients were cultured and identified based on culture characteristics, gram staining, and biochemical tests.

Findings Urinary tract infection was significantly higher in patients with the O blood group (42.5%) and the Lewis (a-b-) phenotype (38.8%) than in patients with other blood groups and the control group. Escherichia coli was the most common bacterial isolate observed in urinary tract infection patients. Also, E. coli was significantly higher in the UTI patients with the O blood group and the Lewis (a-b-) phenotype.

Conclusion People of the O blood group and the Lewis (a-b-) phenotype are more susceptible to urinary tract infections. *Escherichia coli* is the main cause of urinary tract infections.

Keywords Urinary Tract Infection; *Escherichia coli*; ABO Blood Group; Lewis Blood Group; Secretor Status

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Introduction

Urinary tract infection (UTI) is a major health issue, as it is considered one of the most frequent adult bacterial infections worldwide [1]. Approximately 150-250 million cases a year is the range of UTI global prevalence [2]. It can affect males and females of different ages, with dangerous effects including recurrent infection, kidney damage in young children, and pyelonephritis with sepsis [3]. It is linked to an elevated risk of maternal and neonatal illness and mortality in pregnant women [4]. UTI is caused by both gram-negative and gram-positive bacteria in addition to some fungi, which have different virulence factors for adhesion and colonization [5].

Escherichia coli is responsible for More than 95% of urinary tract infections, the most prevalent infecting bacterium in acute urinary tract infection [6]. Various bacterial attachment mechanisms play a key part in the pathophysiology of UTI [7]. Uropathogenic *E. coli* has different virulence factors that increase its ability to colonize the urogenital tract [8]. Different isolates of *Klebsiella pneumonia*, *Pseudomonas aeruginosae*, *Proteus mirabilis*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, and Pseudomonas *spp.* were also obtained from UTI in different studies [9, 10]. The ABO blood group system identifies the many blood groups in the human population, which are A, B, O, and AB. In contrast, the Rh factor identifies various human blood groups' positive and negative status [11]. Blood group antigens are hereditary biological markers present throughout life and play an important role in transfusion safety, genetics, inheritance patterns, and disease susceptibility [12]. ABO blood group antigens are glycoproteins and glycolipids present on erythrocytes and the mucosal epithelial cells, as well as free antigens in body fluids such as saliva, blood, milk, and intestinal contents [13, 14]. ABO blood group has an association with another blood group known as the Lewis blood group, which has three frequent phenotypes, including Le(a+b-), Le(a-b+), and Le(a-b-) [15]. Lewis blood antigens are found on the surfaces of erythrocytes, kidneys, endothelium, genitourinary, and gastrointestinal epithelium, in addition to being secreted in body fluids [16].

According to secretor status, secretors secrete ABO blood group antigens in bodily fluids like saliva, sweat, tears, and serum. While non-secretors who lack these antigens in bodily fluids [17]. The secretors have Le(a-b+) phenotypes, where they express ABO carbohydrates in exocrine secretions as well as red blood cells. Non-secretors have the Le (a+b-) phenotype and Lewis (a-b-), where they solely express ABO carbohydrates in erythrocytes only [18]. ABO and Lewis blood group antigens have been linked to susceptibility and resistance to infections and infectious diseases in various studies [19]. Many diseases, including duodenal ulcers, urinary tract infections, and diabetes, as well as genetic disorders, are linked to antigens of ABO and Lewis blood types [12, 20]. Bacterial adhesion and the occurrence of urinary tract infection can be altered by the presence of antigens of the ABO blood group on the uroepithelial cell surface [21, 22]. Also, another study revealed the susceptibility of persons with the Lewis Le(a-b-) phenotype to the uropathogenic *Escherichia coli* strain [23]. Certain studies confirmed recurrent UTI infections and an increased incidence of chronic inflammation with ABO non-secretors [24].

The aim of the study was to study the relationship of ABO and Lewis blood groups as well as secretor status with urinary tract infection. Also, to determine the most common species of bacteria among UTI patients and their relation with ABO and Lewis blood groups.

Materials and Methods

In this experimental study, All the patients of AL-Sader Teaching Hospital of Basrah City, Iraq, between 2021 and 2022 ranging from 20 to 80 years old, who were diagnosed with urinary tract infection by the specialist based on their histories, clinical examinations, and laboratory tests were selected for the study. A homogeneous control group was also selected from healthy individuals.

Blood samples were collected from both UTI patients and the control group. The ABO blood groups, as well as Rh blood typing, were determined by using a commercially available ABO kit that includes three types of solution antisera A, B, and Rh (D). To determine the type of ABO blood group, the tested blood reacted with either anti-A or anti-B and anti-Rh antibodies s, and the agglutination process may be seen with the naked eye. A blood drop was mixed with an anti-D solution to establish if the blood type was Rh-positive or Rh-negative. When a reaction occurs, the patient's blood is Rh positive; when no reaction occurs, the patient's blood is Rh negative. Also, the Lewis blood phenotypes were determined by standard agglutination techniques using anti-Le a and anti-Le b according to the manufacturer's instructions (Lorne Laboratories; England). First, erythrocyte suspension (2-3%) was prepared. Then, the anti-Lewis a and anti-Lewis b test tubes were identified, with a drop of each reagent, and the cell suspension was added to each tube and mixed. The sample was centrifuged (Hettich/Germany) for 20 seconds at 1500rpm. The sediment at the end of the tube was gently removed and read directly under the microscope (Olympus/Japan). When the test red blood cells agglutinated, it was considered a positive result and showed the presence of Lewis antigen, either Lea or Leb. However, if no agglutination of the test red cells was considered a negative result, it indicated the absence of Le a or Le b. Individuals with Lewis (a-b+) were classified as secretors, while those

with Lewis (a+b-) and Lewis (a-b-) were classified as non-secretors. Urine samples were also collected from patients with UTIs for bacterial culture. The samples were collected from midstream into sterile tubes and transported to the laboratory within 2 hours. Using a sterile loop, urine samples were inoculated into MacConkey's agar (Merck; Germany) and blood agar (Merck; Germany) media. Plates were then aerobically incubated at 37°C for 24-48 hours. Identification depended on culture characteristics, gram staining, and routine biochemical tests [25, 26].
Data analysis was done using SPSS 20 software, and a Chi-square test with p values computed at the 0.05 significance level was used.

Findings

The mean age of patients was 29.2±5.4 years old, and for the control group was 30.5±6.1 years old. The differences in sex and age distributions between the two groups were insignificant (Table 1).

Table 1. Comparing the frequency (the numbers in parentheses are percentages) of UTI patient group (n=80) and healthy control group (n=50) according to sex and age (Chi-square test)

Parameter	Patients	Control	Total	Statistics
Sex				
Male	30 (37.5)	21 (42)	51 (39.2)	χ^2=2.61;
Female	50 (62.5)	29 (58)	79 (60.8)	p>0.05
Age group				
20-29	21 (26.3)	11 (22)	32 (24.6)	χ^2=2.48;
30-39	31 (38.8)	16 (32)	47 (36.2)	p>0.05
40-49	20 (25)	19 (38)	39 (30)	
≥50	8 (10)	4 (8)	12 (9)	

The O blood group (42.5%) was the most common in the UTI patients, whereas the A blood group (34%) was the most common in the control group (p<0.05). Most of the UTI patients (85%) and control healthy individuals (88%) had Rh^+ phenotype (p>0.05; T. 2).

Table 2. Comparing the frequency (the numbers in parentheses are percentages) of the UTI patient group (n=80) and healthy control group (n=50) according to ABO blood groups and Rh phenotypes (Chi-square test)

Parameter	Patients	Control	Total	Statistics
ABO blood group				
O	34 (42.5)	13 (26)	47 (36.2)	χ^2=6.701;
A	13 (16.3)	17 (34)	30 (23.1)	p<0.05
B	23 (28.8)	15 (30)	38 (29.2)	
AB	10 (12.5)	5 (10)	15 (11.5)	
Rh phenotype				
Rh^+	68 (85)	44 (88)	112 (86.2)	χ^2=0.232;
Rh^-	12 (15)	6 (12)	18 (13.8)	p>0.05

The highest frequency of Lewis phenotype in UTI patients was a-b- (38.8%), while the highest frequency of Lewis phenotype in the control group was a-b+ (52.0%; p<0.05). Most UTI patients were non-secretors (75%), while most control healthy individuals were secretors (25%; Table 3).

Table 3. Comparing the frequency (the numbers in parentheses are percentages) of the UTI patient group (n=80) and healthy control group (n=50) according to Lewis phenotypes and Rh phenotypes (Chi-square test)

Parameter	Patients	Control	Total	Statistics
Lewis phenotype				
a-b+	20 (25)	26 (52)	46 (35.4)	χ^2=9.848;
a+b-	29 (36.3)	11 (22)	40 (30.8)	p<0.05
a-b-	31 (38.8)	13 (26)	44 (33.3)	
Secretor state				
Secretor	20 (25)	26 (52)	46 (35.4)	χ^2=9.811;
Non-secretor	60 (75)	24 (48)	84 (64.6)	p<0.05

The most common bacteria isolated from the urine culture of UTI patients was *E. coli* (37.5%). Gram-negative isolates (66.25%) were higher than gram-positive isolates (33.75%; Table 4).

Table 4. The distribution of gram-negative and gram-positive bacteria among UTI patients

Bacteria type	Pathogens	No. (%)
Gram-negative (n=53)	*Escherichia coli*	30 (37.5)
	Klebsiella *spp.*	14 (17.5)
	Pseudomonas aeruginosa	7 (8.7)
	Proteus mirabilis	2 (2.5)
Gram-positive (n-27)	*Staphylococcus saprophyticus*	12 (15)
	Staphylococcus aureus	11 (13.8)
	Streptococcus faecalis	4 (5)
Total		80 (100)

The most common bacterial isolates were *E. coli*, the highest among patients with O and B blood groups (p<0.05). The most common bacterial isolates were *E. coli*, the highest in patients with Le (a-b-) and Le (a+b-) phenotypes (p<0.05; Table 5).
Gram-negative bacteria had the highest frequency among patients with the O blood group (28.8%). Also, gram-positive bacteria had the highest frequency among patients with the O blood group (28.8%), and the difference was significant (p<0.05). Furthermore, gram-negative bacteria had significantly the highest frequency in Le(a-b-) phenotype patients, and the gram-positive bacteria had significantly the highest frequency in Le(a+b-) phenotype patients (10%; Table 6).

Table 5. Comparing the frequency (the numbers in parentheses are percentages) of the bacterial isolates in the UTI patient group according to ABO blood groups and Lewis phenotypes (Chi-square test)

Bacterial species	ABO blood group				Lewis phenotype		
	O	A	B	AB	a-b+	a+b-	a-b-
***Escherichia coli* (n=30)**	15 (18.8)	6 (7.5)	7 (8.8)	2 (2.5)	9 (11.3)	8 (10)	13 (16.3)
Klebsiella *spp.* (n=14)	6 (7.5)	3 (3.8)	5 (6.3)	0 (0)	4 (5)	5 (6.3)	5 (6.3)
***Staphylococcus saprophyticus* (n=12)**	6 (7.5)	0 (0)	2 (2.5)	4 (5)	1 (1.3)	7 (8.8)	4 (5)
***Staphylococcus aureus* (n=11)**	3 (3.8)	2 (2.5)	4 (5)	2 (2.5)	4 (5)	3 (3.8)	4 (5)
***Pseudomonas aeruginosa* (n=7)**	2 (2.5)	1 (1.3)	4 (5)	0 (0)	2 (2.5)	2 (2.5)	3 (3.8)
***Streptococcus faecalis* (n=4)**	2 (2.5)	1 (1.3)	0 (0)	1 (1.3)	0 (0)	3 (3.8)	1 (1.3)
***Proteus mirabilis* (n=2)**	0 (0)	0 (0)	1 (1.3)	1 (1.3)	0 (0)	1 (1.3)	1 (1.3)
Statistics	χ^2=20.818; p<0.05				χ^2=8.898; p<0.05		

Table 6. Comparing the frequency (the numbers in parentheses are percentages) of the gram-negative and gram-positive bacteria in the UTI patient group according to ABO blood groups and Lewis phenotypes (Chi-square test)

Parameter	Gram-negative	Gram-positive	Statistics
ABO blood group			
O	23 (28.8)	11 (13.8)	χ^2=7.173;
A	10 (12.5)	3 (3.8)	p<0.05
B	17 (21.3)	6 (7.5)	
AB	3 (3.8)	7 (8.8)	
Lewis phenotype			
La-b+	15 (20)	5 (6.3)	χ^2=4.905;
La+b-	16 (26.3)	13 (10)	p<0.05
La-b-	22 (27.5)	9 (17.5)	

Discussion

This study concentrates on the association of urinary tract infection with ABO and Lewis blood types because UTIs are considered a serious issue globally. It also highlights the most common bacterial species related to ABO and Lewis blood types in patients with UTI. According to this study, female patients had a higher rate of UTI than male patients. Also, patients in the 30-39 age group are more infected by UTI than other age groups and with control, but the difference in these results was not statistically significant. The results showed that both sexes were infected with urinary tract infections in all age groups. Similar results have been recorded in other studies, suggesting no difference among patients with urinary tract infections according to sex and age [27, 28]. Other studies revealed that UTI was highest in females as compared with males and showed a high ratio in old age (>45 years) [29]. The reason suggested that the shorter length of the urethra makes females more prone to UTI than males [30]. Results confirmed a relationship between the ABO blood group and UTI. It was observed that the urinary tract infection was significantly the highest ratio (p<0.05) in patients with blood group phenotypes O (42.5%) followed by blood group B (28.8%). This lines with what was found in other studies [31-33]. According to the Rh(D) system, although UTI patients have a higher Rh-positive phenotype than a Rh-negative phenotype, this difference is insignificant. Differences in the ABO blood group antigen expression can promote infection by serving as receptors. The variation of ABO blood group antigens of mucosal glycans can have a role in affecting bacterial adhesion and bacteria-mucus interactions [34]. Also, Amjadi discovered that the carbohydrates of ABO blood antigens work as a receptor for bacteria, facilitating their entry and causing infection [35]. Additionally, results showed a significant relation between Lewis blood groups and urinary tract infection (p<0.05). They revealed that urinary tract infection was significantly highest in patients with Lewis (a-b-) phenotypes (38.8%), followed by other Lewis blood groups phenotypes Le(a+b-) (36.3%) and Le(a-b+) (25%). Also, urinary tract infection was significantly higher among non-secretor patients than among secretor patients. These results agree with other studies that revealed more urinary tract infections among non-secretors than secretors [36, 37]. Sheinfeld *et al.* discovered that women with Lewis (a-b-) and Lewis (a+b-) blood phenotypes have a threefold higher risk of recurrent UTI than Lewis (a-b+) phenotype, implying that epithelial cells in non-secretor individuals have more receptors for bacteria and tend to have an increase in the inflammatory responses than the epithelial cells with secretors [38]. Also, non-secretors' increased recurrent UTI susceptibility has been attributed to the absence of exposure. In these fucosylated sugar residues on bladder and vaginal epithelial cells, the cells may not be protected from *E. coli* binding [39].

Urine culture results showed that *Escherichia coli* (37.5%) was the major bacterial isolate among UTI patients, followed by *Klebsiella pneumonia* (17.5%) compared to other bacterial isolates. The other species of bacteria were less frequent, including *Staphylococcus saprophyticus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus faecalis*, and *Proteus mirabilis*. Also, results revealed gram-negative bacteria are higher than gram-positive bacteria. These findings are consistent with those of other studies that showed that *E. coli* is the major etiological agent in causing urinary tract infections [40, 41]. The predominance of *E. coli* could be attributed to their distinctive features, such as (pili or fimbriae), which aid in adhesion to the uroepithelium and raise infection risks [42]. In addition, other studies discovered that *E. coli* was the most common isolate causing UTI; *Klebsiella pneumonia* was next [43]. Furthermore, many studies reveal that most bacterial isolates in UTI infection are gram-negative than gram-positive bacterial isolates [44]. The most frequent gram-positive bacteria isolated from UTI patients were *Staphylococcus saprophyticus* and Staphylococcus aureus [45, 46]. Many studies showed the other pathogens that followed *E. coli* were (Klebsiella *spp.*, *Enterococcus faecalis*, group B streptococci, *Staphylococcus saprophyticus,* and *Proteus mirabilis*) [44, 47]. In terms of ABO blood types and bacteria species, the data showed that *E. coli* was the most pathogen causing UTI among patients with the O blood group, followed B blood group. Gram-negative bacteria have the highest frequency in patients with O and B blood groups than other blood groups. This agrees with other studies that *E. coli* was the most common pathogen causing UTI among O blood group patients (18.8%) [32]. It also demonstrated that *E. coli* was the most prevalent bacteria discovered in all ABO blood groups of UTI patients [41]. Additionally, according to Lewis's blood phenotypes, the results revealed that *E. coli* had the highest prevalence among UTI patients with Le (a-b-) phenotypes compared to other Lewis phenotypes. Lewis blood groups, as well as ABO blood groups, had a significant connection with urinary tract pathogens (p<0.05). Gram-negative bacteria were more common and had the highest frequency in patients

with Le (a-b-) phenotype than other Lewis phenotypes. These agree with other investigations that have found that the Lewis negative phenotype Le (a-b-) is related to an increased vulnerability to *Escherichia coli* infections [48].

Due to some limitations, this study investigated only one hospital, and it is suggested that some more places and medical centers be examined.

Conclusion

The ABO and Lewis blood types, as well as secretor status, have a great association with susceptibility to urinary tract infection. Urinary tract infection is more prevalent in patients with O blood group and Lewis blood group phenotype Le(a-b-) in addition to secretor status. The most frequent pathogen is *E. coli*.

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