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Full Length Research Paper

Urinary tract infections and blood groups: Do they relate?

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Abstract

The urinary tract is one of the most common places for the occurrence of bacterial infections, especially in women. Urinary infection can be defined as an infection of the urinary tract structures which occurs, generally, as a consequence of the presence or colonization of bacteria, like *Escherichia coli (E.coli)* and other *Enterobacteriaceae.* The aim of this study was to evaluate the relation between urinary tract infections (UTIs) and blood groups. The population of this study consisted of 307 patients (83 men and 224 women) from the District Hospital of Figueira da Foz, E.P.E. (HDFF, E.P.E.) and from the Coimbra Health School (ESTeSC) in Portugal. The AB0 blood groups were determined through a gel-test methodology. The microorganisms identification was made using the VITEK® 2 Compact equipment. In a total of 307 patients, the most common pathogen was *E. coli* with 48.4%, followed by *Klebsiella pneumoniae,* with 17%. Infection by *E. coli* was significantly more common in patients with A blood group phenotypes ($p<0.0005$). A statistically higher risk for developing urinary tract infections in women compared to males ($p<0.001$) was found. The results suggest that *E. coli* was the main pathogen causing urinary tract infections, and we found statistically significant association between A blood group phenotypes and this infection. These results might be useful for describing an individual's risk for a higher predisposition in developing urinary tract infections.

Keywords: Urinary tract infection; blood groups; *Escherichia coli; Klebsiella sp.*

INTRODUCTION

Urinary Tract Infections (UTIs) are of the most common diseases worldwide affecting all age groups, and can be defined as an inflammation of the tubular or parenchymal structures(Souza, 2009; Heilberg and Schor, 2003; Martins *et al.*, 2010). The colonization of the urinary tract may occur due to the ascension of intestinal bacteria from the anus to the urinary opening, causing invasion of the urethra, bladder and ureters, and may even harm kidney function(Moura and Fernandes, 2010). Adult females are the most affected, and this fact is related to mechanical factors, such as the female urethra being shorter and closer to the anus (Heilberg and Schor, 2003; Martins *et al*., 2010; Moura and Fernandes, 2010; Lopes and Tavares, 2005; Costa *et al*., 2010). There are also other factors that may contribute to this high rate of urinary infections, such as sexually active young women, pregnancy, menopause, diabetes and urinary catheters (Souza, 2009; Heilberg and Schor, 2003; Moura and Fernandes). In men, UTI usually appears at older ages and commonly associated with anatomical abnormality or a decrease in the prostatic bactericidal activity (Moura and Fernandes, 2010).

UTIs can be classified according to their anatomical origin, in two groups: inferior or cystitis and superior or pyelonephritis. The main symptoms which help to diagnose and distinguish UTIs are dysuria, pollakiuria, hematuria and suprapubic or lower back pain. Some of the microorganisms involved in UTIs are *Escherichia coli*

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(*E. coli*), *Klebsiella sp.*, *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa* and *Enterococcus faecalis*, which are the main etiological agents(Souza, 2009; Martins *et al*., 2010).

Uropathogenic *E. coli* (UPEC) is the primary agent of UTIs, having different virulence factors that increase its ability to colonize the urogenital tract (Schilling *et al*., 2001; Finer and Landau, 2004). The uroepithelial surface binding is one of the factors that prevent "washout" through urination, and starts the bacterial invasion(Finer and Landau, 2004). The two *fimbriae* types most commonly found in UPEC isolates are the *Type 1 fimbriae* (mannose-sensitive) and P *fimbriae* (mannose-resistant) which are morphologically similar, but differ in the ability to mediate the hemagglutination in the presence of mannose(Connell *et al*., 1996; Santo *et al*., 2006). According to several authors the *fim* gene that encodes the T*ype 1 fimbriae*, is characterized as the main virulence factor (Connell *et al*., 1996). These *fimbriae* consist of helical filaments composed of repeated subunits of the fimA structural protein, attached to fimH adhesion structures (Eto *et al*., 2007). The fimH adhesion binding to mannosylated receptors present on the uroepithelium is essential for the bladder colonization (Thankavel *et al.,* 1997). The *pap* gene codifies for *P fimbriae*, which contain four subunits, a larger subunit, *PapA*, which constitutes the *fimbriae* structure and three smaller subunits (*PapE*, *PapF* and *PapG*) located at the end of the *fimbriae* extremity(Santo *et al*., 2006; Johnson, 1991).The binding of PapF and PapE to the receptors in Galα (Souza, 2009; Heilberg and Schor, 2003; Martins *et al*., 2010; Moura and Fernandes, 2010) uroepithelial cells prevents the elimination of bacteria from the bladder, breaks the mucosal barrier and encourages the immune response of the host (Bergsten *et al*., 2004).

In turn, the pathogenicity of *Klebisella sp.* is also due to virulence factors such as *fimbriae* or adhesins that bind ABH glycol conjugates expressed in host tissues, the production of urease, the presence of flagellum or "H" antigen (responsible for its mobility) and also capsular antigens (that confer resistance to phagocytosis)(Cao *et al*., 2011; Tarkkanen *et al*., 1997). The adhesion property is mediated by different types of filamentous projections, the *fimbriae*, each with their specific receptor. Thus, there are four types of adhesins involved in the adhesion process; however there are two predominant types. Its principal abilities are based on the fact that they can agglutinate erythrocytes of different animal species (Tarkkanen *et al*., 1997, Podschun and Ullmann, 1998). Depending on whether or not the reaction is inhibited by D-mannose, these adhesins are designated as mannose-sensitive or mannose-resistant (MSHA and MRHA respectively)(Podschun and Ullmann, 1998). *Type 1 fimbriae* (MSHA), encoded by the gene cluster *fim*, seem to recognize the mannose glycoproteins present in various tissues of the host(Rosen *et al*., 2008). This *fimbriae* is involved in pyelonephritis scenarios, where they bind to proximal tubular cells. In contrast, *Type 3 fimbriae* mediate bacterial adhesion in tubular basal membranes, Bowman's capsule and renal vessels, requiring 6 *mrk* genes, in which *mrkA* encodes the main subunit and *mrkD* the adhesion subunit(Tarkkanen *et al*., 1997).

Thus, some studies have pointed out the relationship between an individual's susceptibility to infection according to their blood phenotype (AB0, Rh). Among these studies the identification of the *fimbriae* previously described stands out(Tarkkanen *et al*., 1997).

The AB0 phenotype of an individual is due to the ABH genes which encode glycosyltransferases(enzymes) that add specific sugars to a carbohydrate chain precursor –the H substance(Yamamoto and McNeill, 1996). When this substance is added to an L-fucose, an 0 group is formed, the addition of an N-acetyl D galactosamine forms the A group and the addition of a D-galactose forms the B group (Yamamoto and McNeill, 1996; Yamamoto and Hakomori, 1990). The chains that carry the AB0 antigens can be glycoproteins, glycolipids or glycosphingolipids (Yang *et al*., 1994).

Several studies have been developed over the last few years, but the relationship between UTIs by different bacteria and the expression of AB0 and Rh antigens is not yet fully clarified. Therefore, the present study aims to associate the expression of these antigens and bacteria involved in UTIs.

MATERIAL AND METHODS

Study population

The study took place at the District Hospital of Figueira da Foz, E.P.E. (HDFF, E.P.E.) and at the Coimbra Health School (ESTeSC). The sample processing was performed in the Laboratory of the Biomedical Sciences Department of ESTeSC, with a total of 307 studied patients.

The study was confidential and conducted in accordance with the principles of the Declaration of Helsinki.

Determination of the AB0 and Rh Blood Groups

The determination of the AB0 and Rh blood groups was conducted using the Card-ID (gel-test) methodology, from peripheral blood samples collected into tubes with tripotassium ethylene diaminetetra acetic acid (EDTA K_3). This determination was made using the following cards: ScanGel AB0/Rh Group, ScanGel Monoclonal

RH/K Phenotypes (BioRad®, California, USA). To each sample was assigned a different and confidential code number.

The age and sex parameters and clinical information of patients were obtained from the clinical process.

The filling of a personal and confidential survey also allowed the collection of other useful information for this work.

Identification/Antibiogram of pathogens - Urocultures

The urine samples from patients with suspicion of urinary infection were seeded on CLED AGAR (CONDA Laboratories S.A., Madrid, Spain) with a 24-hour incubation under aerobic conditions (36°C). Only the positive urine cultures, up to three strains, were eligible for identification and antibiogram. Through the letters of identification, GN test kit and GP test kit, we were able to identify the microorganism on the VITEK® 2 Compact equipment (BioMérieux®, Lyon, France).

The obtained results were entered into a database and the collected data was analyzed using the Statistical Package for Social Sciences 18.0 software (SPSS Inc., Chicago, USA) for Windows.

RESULTS

From the universe of individuals who attended HDFF, E.P.E. and ESTeSC, a cohort of 307 patients with UTI (adjusted for study variables) participated in this study. The population consisted of 73% (224) females and 27% (83) males, with a mean age of 68 years (maximum of 99 and minimum of 17). For the AB0 blood group, 51.1% (156) of the individuals presented the A phenotype, 37.7% (115) the 0 phenotype, 8.55% (26) the B phenotype and finally 2.65% (8) the AB phenotype (Figure 1). For the Rh system, 85.9% (262) exhibited a Rh(D) positive phenotype and 14.1% (43) presented a Rh(D) negative phenotype.

Patients came from 21 different services: 0.65% (2) from the Fetal Wellbeing consultation, 1.0% (3) from the Surgery consultation, 1.0% (3) from the Gynecology consultation, 1, 0% (3) from the Medicine consultation, 1.6% (5) from the Obstetrics consultation, 0.65% (2) from the Oncology consultation, 0.32% (1) from the Breast Pathology consultation, 0.32% (1) from the Family Planning consultation, 0.32% (1) from the Cancer Screening consultation, 0.32% (1) from the Day Hospital of Immunohemotherapy consultation, 0.32% (1) from Day Hospital of Oncology consultation, 0.32% (1) from the Cardiology internment, 2.3% (7) from the Surgery internment, 0.65% (2) from the Gynecology internment, 12.7% (39) from the Medicine internment, 4.23% (13) from the Special Medicine internment, 8.5% (26) from the Orthopedics internment, 1.3% (4) from the Surgery Urgency, 32.6% (100) from the Urgency Medicine, 0.3% (1) from the Orthopedics Urgency and 7.5% (23) from the Urgency. The remaining 68 samples (22.1%) were collected in ESTeSC (Figure 2).

From the 307 patients, 223 under went urine cultures followed by the microorganism identification. From the data cross-checking with the AB0 blood group, we obtained the following most relevant results: 4.5% (10) *Acinetobacter baumannii,* from which 3.1% (7) had 0 phenotype, 0.9% (2) A phenotype and 0.5% (1) B phenotype (Figure 3); 4% (9) *Candida albicans*, from wich1.3% (3) had 0 phenotype and 2.7% (6) A phenotype; 48.4% (108) *E. coli.,* being 15.7% (35) 0 phenotype, 26.9% (60) A phenotype, 4.5% (10) B phenotype and 1.3% (3) AB phenotype (Figure 4); 17% (38) *Klebsiella pneumoniae* from which 6.7% (15) were 0 phenotype, 8.5% (19) A phenotype and 1.8%(4) B phenotype (Figure 5); 8,5% (19) *Serratiamarcescens;* being 3.6% (8) 0 phenotype, 4.5% (10) A phenotype and 0.4% (1) AB phenotype; 4.9% (11) *Staphylococcus capitis* from which 0.45% (1) was 0 phenotype, 4% (9) A phenotype and 0.45% (1) B phenotype.

Thus, we note that in this universe of 223 patients, *E. coli* is the pathogen with the highest frequency (48.4%, 108) followed by *Klebsiella pneumoniae* (17%; 38) (Figure 6). Comparing the predominant pathogen in this universe with the blood groups, we found that the largest percentage is from the A phenotype.

DISCUSSION

Considering the number of patients with urinary tract infection, it was found that the prevalence of cases in relation to the sex of the patients, mostly focused in the female population when compared to the males. The results were statistically significant (p<0.001), noting that the female population presented more 2.89% of probability for the occurrence of urinary infections, with a 95% confidence interval (1.63–5.13). Similar results have been reported by Scholes *et al*. 2000, Miranda *et al*. Provide year and Silva *et al*. 2007 indicating a high frequency of urinary infection in the female population, but in a younger population than the studied one

The study of the AB0 blood groups revealed that the prevalence of patients with 0 and the A phenotypes was higher in the study population. For the B and AB phenotypes, the number of cases was low, not favoring a discriminative power for these blood groups. According to *Duran et al. 2007* in Portugal the most common blood group is the A group, with a percentage of 46.6% (which goes against the results obtained in this study - 51.1%), followed by the 0 group with a 42.3% frequency, 7.7% for the B group and 3.4% for the AB group. Globally, the

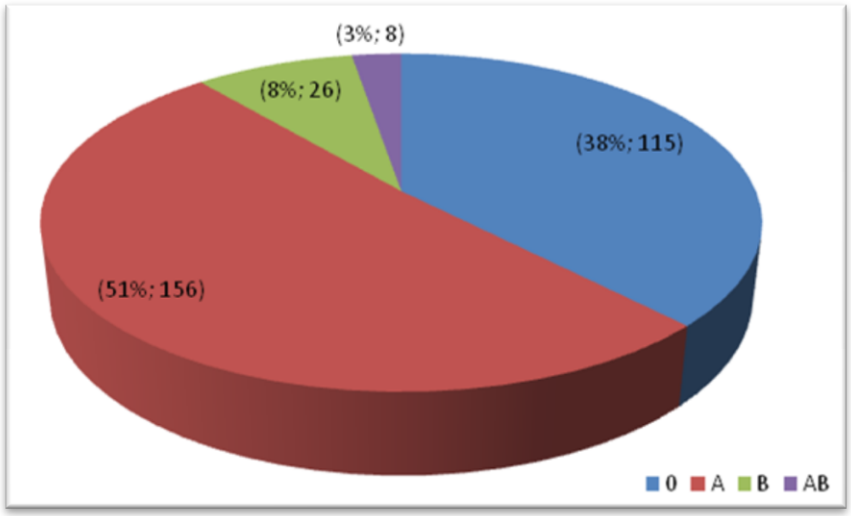


Figure 1. AB0 phenotype distribution in the studied population.

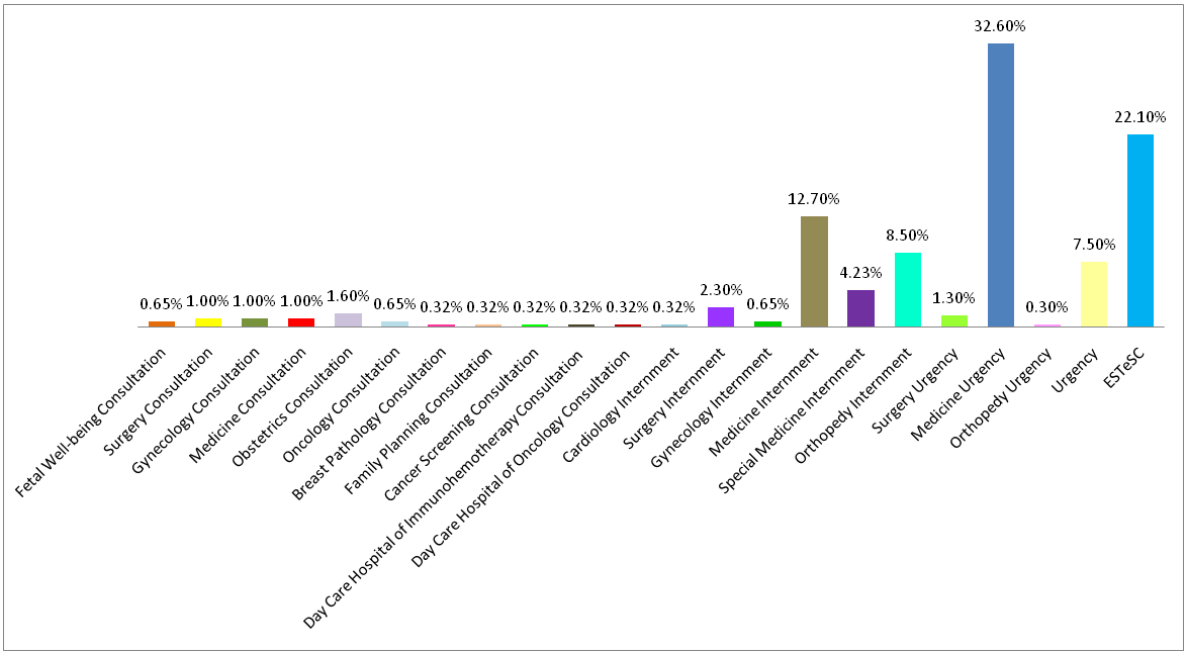


Figure 2. Patient distribution by several Services and College of Health Technology of Coimbra.

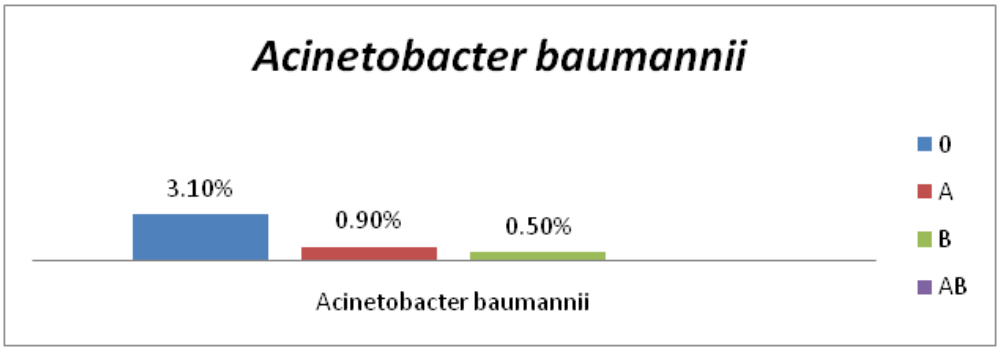
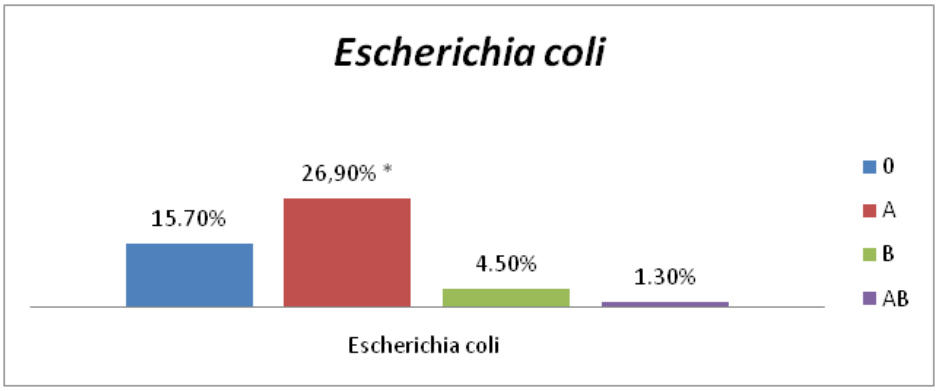


Figure 3. *Acinetobacterbaumannii* distribution in relation with the blood groups.



*p-value<0,0005

Figure 4. *Escherichia coli* distribution in relation with the blood groups.

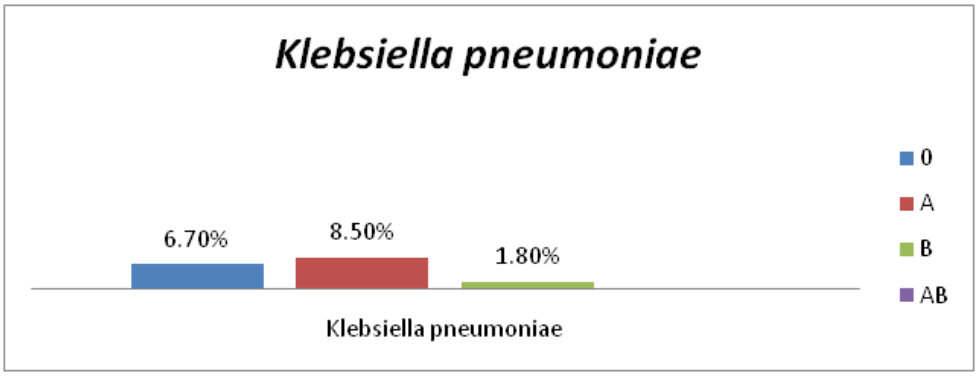


Figure 5. *Klebsiellapneumoniae* distribution in relation with the blood groups.

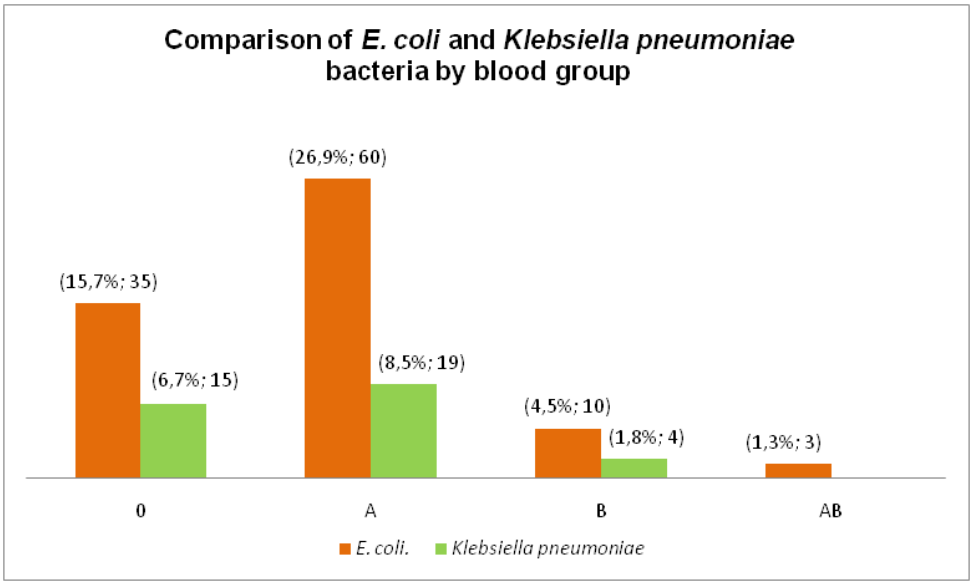


Figure 6. Comparison of *Escherichia coli* and *Klebsiellapneumoniae* with the blood groups.

most common blood group is the 0 group (63% of the population). In Northern Europe there is a western area with very low frequencies of A and B and very high frequencies of 0. When it comes to Brazil, *Novaretti et*

al. 2000 present that 46.5% of the population has the 0 phenotype, 39.45% the A phenotype, 11.5% the B phenotype and finally 2.5% the AB phenotype.

Given this, it is possible to deduce that this study found a higher prevalence of the A phenotype, suggesting the existence of a relationship of association with the susceptibility of these individuals for UTIs, being the results statistically significant (p<0.001). However, other authors such as *Scholes et al. 2000 and Kinane et al. 1982* state that there is no pattern of association between AB0 blood groups and urinary tract infections.

From the 73.1% of patients who underwent the identification of microorganisms, it was found that 48.4% presented *E. coli* as the primary pathogen causing UTI, followed by *Klebsiella pneumonia* (17%). *Kahlmeter 2003* reports similar results, in which *E. coli* is the most common pathogen in European countries, including Portugal with 52.9%.

In this study we considered that the differences founded between the AB0 frequencies and *E. coli* were statistically significant. The largest difference was found when compared to the A phenotype (p<0.0005). *Lindstedt et al. 1991 and Senior et al. 1988* reported similar results, indicating that the chains of *E. coli* recognize the precursor of the A blood group. In this context, for *Klebsiella pneumoniae* it is possible to describe the number of cases; however we didn't found an association pattern.

CONCLUSION

Based on the obtained results, we suggest that both the A phenotype for the AB0 blood group, as well as the female gender, constitute risk for the emergence of urinary tract infections.

On the other hand, we also suggest that the most frequent pathogen is *E. coli*, and individuals with A phenotype are more likely to suffer from urinary tract infection caused by this bacterium.

In order to clarify some discrepancies found in this study we propose to do future investigations in order to assess other aspects that may interfere with the results, namely factors such social status, chronic diseases, geographic and environmental factors, as well as the major virulence factors of the main microorganisms which cause urinary tract infection. We also think that would be interesting to study the existence of a relationship between urinary infections and the use of contraceptives (oral or non-oral) as well as with the number of sexual partners. In order to better understand this relationship we also suggest studies with molecular biology related to the polymorphisms of AB0 blood groups. Once after reviewing the literature relationship between UTIS and the use of contraceptives, being that the predisposition of women to infection worsens with the use of barrier methods (Diaphragm and spermicide use), but this allows the persistence and overgrowth of *E. coli* in the vagina. The woman could be advised to consider alternative methods, such as oral contraceptives. The literatures also mention that sexual intercourse is a strong risk factor for UTI and that there is a positive correlation, statistically significant between the frequency of sex and UTI. However not all reviews declare the effectiveness of urination after sexual act prevent UTI, since it would be interesting to carry out more studies in this direction. Even though most women are followed by family planning methods there should be enhanced health behaviors for the hygienic or safe use.

It is a fact that natural selection of species between humans and infectious diseases exists, a good example is the malaria, being the most significant selective force acting on the blood groups, so probably blood groups and their polymorphisms may contribute to selection.

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