

Incidence and Antibiotics Resistance of *Staphylococci* and *Escherichia coli* Isolated from Diabetic Urinary Tract Infection Patients in Egypt

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Abstract

This study investigated the prevalence, risk factors and antimicrobial resistance of *Staphylococci* and *E. coli* isolated from diabetic urinary tract infection patients. Urine samples collected from 694 cases admitted to the General Health Insurance Authority Hospital in Port Said City, Egypt. A total of 302 bacterial strains were isolated from 292 urine samples with glucosuria and infection positive. The prevalence of the *S. saprophyticus*, *S. aureus*, *E. coli* and other species isolates from the urine samples are 54.7%, 34%, 7.6% and 3.7%, respectively. The antibacterial resistance profile of the isolated bacteria was investigated against different antibiotics. Most bacterial isolates were more susceptible to ofloxacin antibiotic while resistance to ampicillin. Multiple antibiotic resistance (MAR) was found highest for bacterial isolates obtained from urine samples. *S. aureus* showed high resistance percentage than other bacterial strains to studied antibiotics. Vancomycin resistance was detected in 23% of all *S. aureus* isolates. Out of 165 isolates *S. saprophyticus*, 71% were λ -lactamase producers, while all *S. aureus* and *E. coli* isolates were λ -lactamase positive. Also the purpose of this study was to study any relative between the recognized antibiotic resistance of bacteria and the occurrence of plasmids. Molecular sizes of the detected plasmids were 39.306 kbp in *S. aureus* and 44.640 kbp in *E. coli*. Plasmid curing in combination with MIC determination revealed that resistance of staphylococci and *E. coli* isolates was plasmid-mediated linked. The high MAR recognized makes it essential for antibiotic resistance testing to be accompanied prior to antibiotics remedy for diabetic urinary tract infection patients.

Keywords: Antibiotics Resistance, *Staphylococci*, *E. coli*, Diabetic Urinary Tract Infection.

Abbreviations: UTI, urinary tract infection; M, male Patients; F, Female Patients; +, Glucosuria concentration 180-200 mg/dl; ++, Glucosuria concentration 200-250 mg/dl; +++, Glucosuria concentration 250-350 mg/dl; +++++, Glucosuria concentration over 350 mg/dl.

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(Received: 02 August 2019; accepted: 08 September 2019)

Citation: Samy Selim, Mohamed Abdel Aziz, Saher El-Alfay and Hanan Zakaria, Incidence and Antibiotics Resistance of *Staphylococci* and *Escherichia coli* Isolated from Diabetic Urinary Tract Infection Patients in Egypt, *J Pure Appl Microbiol.*, 2019; **13**(3): 1697-1702. <https://doi.org/10.22207/JPAM.13.3.44>

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INTRODUCTION

Diabetes is very public health difficulties that evidently rise in occurrence and frequency with progressing age. Besides organ complications, diabetic patients also hurt extra recurrently after problematical contagions equated with non-diabetic patients (Carten *et al.*, 1992; Foxman, 2002; Geerlings *et al.*, 2002; Hoepelman *et al.*, 2003; Brown *et al.*, 2004; Brown *et al.*, 2005). To complicate substances further, diabetes also may be a risk factor for single and multi-drug resistance. However, all investigators have found increased uropathogen resistance to antibiotics in diabetic patients (Stapleton and stamm, 1997; Fedele *et al.*, 2000; Geerlings *et al.*, 2001; Wullt *et al.*, 2003).

Insufficient articles have observed endemic antimicrobial resistance in Egypt, espically UTI in diabetic patients (Haberberger *et al.* 1994; Oyoyo *et al.* 1995; Ostroff *et al.* 1996; Hilal *et al.* 1997; El-Teheawy *et al.*, 1988; El Kholy and Nassar, 1996; Samuel *et al.*, 1996; El Kholy *et al.*, 2003). This study was therefore supposed to study the occurrence, risk factors and antibiotic resistance of staphylococci and *E. coli* isolated from diabetic urinary tract infection patients in Egypt.

MATERIALS AND METHODS

Sample collection and identification of bacteria

Urine samples were collected as described

by Collins *et al.* 1998 from 694 cases admitted to the General Health Insurance Authority Hospital in Port Said city, Egypt. A total of 388 DM patient's urine samples with glucosuria positive concerned for further bacterial examination. One ml aliquots from urine suspensions were dispensed into CLED and MacConkey media. All plates were incubated face down and the bacteria were allowed to grow at 37°C for 24-48 hours prior to enumeration and further identification. Pure well-isolated colonies were preceded for their biochemical tests according to Bergeys manual of determinative bacteriology (Holt *et al.*, 1994).

Antibiotic resistance testing

All trials were piloted using the inventive typical cultures to escape the unstructured hurt of antibiotic resistance. Antibiotic resistance was tested using a modified Kirby-Bauer disc diffusion method (Robert *et al.*, 2003). λ -lactamase detection and curing test was carried out as described by Odugbemi *et al.*, (1977).

Plasmid Analysis

The plasmid isolated by mini-prep alkaline extraction method (Sambrook *et al.*, 1989). Concentrations and purity of DNA were assessed spectrophotometrically using Spectro 22, Labo Med, Inc., USA. Gels were arranged by adding 1% agarose and 5 μ L ethidium bromide (10 mg/mL) to the TBE buffer. Pure DNA sample

Table 1. Showing distribution of collected urine samples during study

Patients	Age	No. Cases	Urine samples with glucosuria positive	Urine samples with glucosuria and infection positive
Male patients	Less 30	1	1	1
	30-	17	7	7
	40-	96	52	34
	50-	104	54	44
	60-	118	59	48
	70-	39	20	11
	80 – more	15	10	9
	Total	390	203	154
Female patients	Less 30	1	0	0
	30-	16	10	7
	40-	95	54	41
	50-	69	44	34
	60-	81	52	39
	70-	35	21	15
	80 – more	7	4	2
	Total	304	185	138
Total		694	388	292

(3µL) was added to 12µL deionized water and 1µL endonuclease (*EcoR* I, *Hind* III (Sigma Production), *BamH* I (Roche Diagnostics GmbH). Sequential dilutions of acridine orange were used for curing of isolated plasmids.

RESULTS

A full of 292 urine trials were found infection positive from all different ages and cases admitted to the General Health Insurance Authority Hospital (Table 1). The percentage of infection raised by increase the concentration of glucosuria. We detected 100% a bacterial infection in urine samples of ++++ glucosuria level on CLED

medium. Also percentage of counts on MacCckonky medium increased from 35.21% on + glucosuria level to 66.67% on ++++ glucosuria level.

A whole of 302 bacterial isolates were isolated from urine samples. The distribution of staphylococci and *E. coli* is shown in Table 2. The incidence of the *S. saprophyticus*, *S. aureus*, *E. coli* and other species isolates from the urine samples are 54.7%, 34%, 7.6% and 3.7%, respectively (Table 2). Bacterial counts had flocculation on + and ++ glucosuria concentration but other concentration in female patients recorded high bacterial counts than male patients (Table 2).

Table 2. Showing distribution of identified bacterial species in male and female patients accordance to glucosuria level

Glucosuria level Bacterial isolates	+		++		+++		++++		Total (%)
	M	F	M	F	M	F	M	F	
<i>S. saprophyticus</i>	15	8	34	19	40	46	1	2	165 (54.7)
<i>S. aureus</i>	8	11	16	13	21	34	0	0	103 (34)
<i>E. coli</i>	4	1	3	4	5	6	0	0	23 (7.6)
Other Species*	2	1	1	3	1	3	0	0	11 (3.7)
Total	50	93	156	3	302				

* Other species include: *Pseudomonas aeruginosa* and *Streptococcus* sp.

The antibiotic resistance profile of staphylococci and *E. coli* isolates from urine samples is shown in Table 3. Most bacterial isolates were more susceptible to ofloxacin antibiotic while resistance to ampicillin. MAR was main for bacterial isolates gained from urine samples. Greater degrees of resistance were confirmed for *S. aureus* as compared with *S. Saprophyticus* versus most studied antibiotics. *S. aureus* showed high resistance percentage than other bacterial strains. Alls of staphylococci isolates were susceptible to vancomycin, except 23% of *S. aureus* (Table 3). *E. coli* isolates showed low resistance pattern to studied antibiotics. Susceptibility to imipenem and septazole (trimethoprim and sulfamoxazole) antibiotics for *E. coli* was 100% (Table 3). β-lactamase enzyme manufacture was confirmed in all staphylococci and *E. coli* isolates. Out of 165 isolates *S. saprophyticus*, 71% were β-lactamase producers, while all *S. aureus* and *E. coli* isolates were λ-lactamase positive.

Plasmid outlines of the three bacterial

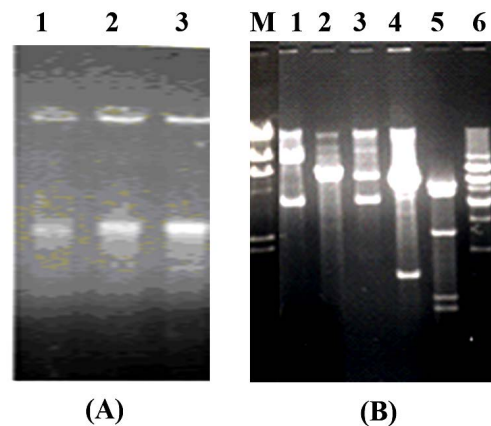


Fig. 1. Agarose gel electrophoresis of pure plasmids preparation from isolated strains. (A) lanes 1-3 pure plasmids of *E. coli*, *S. aureus* and *S. saprophyticus* respectively. (B) The restriction patterns of plasmids isolated from *E. coli* and *S. aureus* bacterial strains (contain only one plasmid) digested with *Hind* III, *EcoR* I and *BamH* I respectively. Where: Lane M: Lambda (ϕ) DNA + *Hind* III + *EcoR* I, lanes 1- 3: *E. coli* and lanes 4- 6: *S. aureus*

isolates below study were strongminded (Table 4). *E. coli* and *S. aureus* contain one plasmid, though *S. saprophyticus* were establish to three plasmids (Fig. 1A). Breakdown of isolated plasmids of *E. coli*

and *S. aureus* isolates presented in fig. 1B. Quantity of recognition sites, amount of fragments and the estimated molecular size of restricted fragments were as shown in Table 4.

Table 3. Antibiotic resistance profiles of isolated bacteria from urine samples

Antibiotics / Isolates	Bacterial isolates resistance to antibiotics (%)		
	<i>S. saprophyticus</i> (no.= 165)	<i>S. aureus</i> (no.= 103)	<i>E. coli</i> (no.= 23)
Nitroforantain (300 µg)	70	79	95
Imipenem (10 µg)	40	19	100
Aztreonam (30 µg)	100	100	76
OFLAXACIN (57g)	0	20	0
Amoxicillin (25 µg)	50	56	60
Erythromycin (57g)	79	100	40
Trimethoprim (1257g)+Sulfamoxazole(23µg)	60	80	100
Amikacin (30 µg)	36	20	60
Cefotaxime (30 µg)	60	100	40
Amoxicillin+Clavulanic acid (30 µg)	60	100	80
Ampicillin (10 µg)	71	100	100
Tobramycin (10 µg)	53	17	39
Norfloxacin (10 µg)	40	54	29
Vancomycin (30 µg)	0	23	ND

N: Number of studied isolates; ND: Not Determined.

Table 4. The restriction patterns of plasmids from *E. coli* and *S. aureus* isolates

Plasmids	Restriction Enzymes	No. of Recognition Sites	No. of Fragments	Size of Fragments (Kbp)	Plasmid Size (Kbp)
<i>E. coli</i>	<i>Hind III</i>	6	5	23000-9416-5148-4361 and 3530	44.64
	<i>EcoR I</i>	6	5	23100-9416-5148-3530 and 3410	
	<i>BamH I</i>	5	4	23000-9416-5804 and 5643	
<i>S. aureus</i>	<i>Hind III</i>	6	5	23000-6557-5148-4973 and 3530	39.306
	<i>EcoR I</i>	6	5	22000-5804-4973-3530 and 2037	
	<i>BamH I</i>	8	7	9416-7421-5148-5100-3430-3530 and 2322	

DISCUSSION

Patients with diabetes frequently have enlarged difficulties of UTI, harshness and unfamiliar expressions (Stepleton, 2002). The risk for UTI complications is higher in people with DM. The foremost reasons of severe and straightforward UTI in ambulatory patients have been informed to be due to *E. coli*, *S. aureus* and *Pseud. Aeruginosa* (Foxman et al., 2000; Hoepelman et al., 2003). *E. coli* origins the common of UTIs between utmost clusters of patients deprived of diabetes and is

likewise the maximum joint cause of UTI between men or women with diabetes (Parker et al., 2004). In our studies find similar results.

From the above data it can be mostly settled that staphylococci and *E. coli* isolates are relatively resistant to commonly used antibiotics. Resistance rates between staphylococci have been testified from other domestic geographical areas with results similar to ours (HEI-Kholy et al., 2003H). Amongst isolates of *E. coli*, 100% were resistance to ampicillin. Completely isolates were

susceptible to imipenem and septazole. *E. coli* isolates in our study were have resistant outline to the antibiotics like to those from the El-Kholy *et al.* 2003. The occurrence of MAR organisms has attracted the attention of many workers and increasing antibiotic resistance is a factual problem in UTI (Foxman, 2002). It occurs from the infected patients who respond poorly to treatment and in a hospital, which may perform infection control and prevention programs. By definition, patients with complex UTI have a superior possibility of infection with an antimicrobial-resistant organism and/or an uncommon organism and also have a larger hazard of treatment disappointment (Patterson and Andriole, 1995; Ronald and Harding, 1997).

Most antibiotic- resistant microbes develop as a consequence of genetic change and following assortment courses by antibiotics. The resistance factor may be chromosomal, that developed as a result of spontaneous mutations and extrachromosomal resistance (Bekowitz, 1995; Selim, 2003). Plasmid- mediated antibiotic resistance in *S. aureus* has been described by many authors (Archer *et al.*, 1986; Lyon and Skurray, 1987; Mansouri and Khaleghi, 1997; Shakibaie *et al.*, 1999; Selim, 2003). The plasmid-linked resistance outlines of three bacterial ampicillin-resistance isolates were examined. For them plasmids were experimental and plasimd-linked resistance to ampicillin were established with relatively high MIC(S). The frequency of penicillin and cephalosporin- resistant clinical isolates of *S. aureus* has enlarged quickly and most of the isolates are -lactamase producers. In greatest strains, the enzyme is determined by plasmid but can also be establish on the chromosome (Shakibaie *et al.*, 1999; Ako-Nai *et al.*, 2005).

In, our data propose that antimicrobial resistance amongst staphylococci and *E. coli* is joint and important in diabetic patients in Egypt. The results obtained here, we confidence, will improve clinicians' ability to improved achieve these diseases and decrease probable development. Our outcomes request for additional molecular biology studies to describe genes involved in antimicrobial resistance patterns in these isolates.

ACKNOWLEDGMENTS

None.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors have made substantial, direct and intellectual contribution to the work and approved it for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

The study was approved from the Universities Ethical Committee (ENREC).

REFERENCES

1. Ako-Nai, A.K., Adeyemi, F.M., Aboderin, O.A., Kassim, O.O. Antibiotic resistance profile of *staphylococci* from Clinical sources recovered from infants. *African Journal of Biotechnology*, 2005; **4**: 816-822.
2. Archer, G., Coughter, J.P., Johnston, J.L. Plasmid encoded trimethoprim resistance in *Staphylococcus aureus*. *Antimicrob. Agent Chemother.*, 1986; **29**: 733-40. <https://doi.org/10.1128/AAC.29.5.733>
3. Bekowitz, F.E. Antibiotic resistance in bacteria. *South Med. J.* 1995; **88**: 797-804. <https://doi.org/10.1097/00007611-199508000-00001>
4. Brown, J.S., Barrett-Connor, E., Nyberg, L.M., JW, K., TJ, O., Ma, Y., Vittinghoff, E. Incontinence in women with impaired glucose tolerance: results of the Diabetes Prevention Program. *J. Urol.*, 2004; **171**: 325–326 (2004). [https://doi.org/10.1016/S0022-5347\(18\)38462-3](https://doi.org/10.1016/S0022-5347(18)38462-3)
5. Brown, J.S., Wessells, H., Chancellor, M.B., Howards, S.S., Stamm, W.E., Staleton, A.E., Steers, W.D., Van Den Edden, S.K., McVary, K.T. Urologic complications of diabetes. *Dia. Care.* 2005; **28**: 177-185. <https://doi.org/10.2337/diacare.28.1.177>
6. Carton, J.A., Maradona, J.A., Nuno, F.J. Diabetes mellitus and bacteraemia: a comparative study between diabetic and nondiabetic patients. *Eur. J. Med.* 1992; **5**: 281-287.
7. Collins, C.H., Lyne, P.M., Grange, J.M. 1998. Microbiological methods, pp178-205. Seventh edition, Butterworth Heinemaa.
8. El Kholy, A.A., Nassar, Y.H. Phenotyping versus plasmid pattern analysis of *Enterobacter cloacae* in an outbreak in a pediatric intensive care unit. *Egyptian Journal of Laboratory Medicine.* 1996; **8**: 467–83.
9. El Kholy, A., Baseem, H., Hall, G.S., Procop, G.W., Longworth, D.L. Antimicrobial resistance in Cairo, Egypt

- 1999-2000: a survey of five hospitals. *J. of Antimicro. Chemoth.* 2003; **51**: 625-630. <https://doi.org/10.1093/jac/dkg101>
10. El-Teheawy, M.M., El-Bokl, M.A., Abd el-Fattah, S.A., Sabbour, M.S. The pattern of antimicrobial use in general hospitals in Egypt. *Chemioterapia.* 1988; **7**: 387-92.
 11. Fedele, D., Bortolotti, A., Coscelli, C., Santeusano, F., Chatenoud, L., Collij, E., Lavezzari, M., Landoni, M., Parazzini, F. Erectile dysfunction in type 1 and type 2 diabetics in Italy. *Int. J. Epidemiol.* 2000; **29**: 524-531. <https://doi.org/10.1093/intjepid/29.3.524>
 12. Foxman, B., Gillespie, B., Koopman, J. Risk factors for second urinary tract infection among college women. *Am. J. Epidemiol.* 2002; **151**: 1194-1999. <https://doi.org/10.1093/oxfordjournals.aje.a010170>
 13. Foxman, B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am. J. Med.* 2002; **113**: 5S. [https://doi.org/10.1016/S0002-9343\(02\)01054-9](https://doi.org/10.1016/S0002-9343(02)01054-9)
 14. Haberberger, R.L., Lissner, C.R., Podgore, J.K., Mikhail, I.A., Mansour, N.S., Kemp, L. Etiology of acute diarrhea among United States embassy personnel and dependants in Cairo, Egypt. *American Journal of Tropical Medicine and Hygiene.* 1994; **51**: 870-874. <https://doi.org/10.4269/ajtmh.1994.51.870>
 15. Geerlings, S.E., Stolk, R.P., Camps, M.J. Consequences of asymptomatic bacteriuria in women with diabetes mellitus. *Arch. Intern. Med.* 2001; **161**: 1421-1427. <https://doi.org/10.1001/archinte.161.11.1421>
 16. Geerlings, S.E., Meiland, R., Hoepelman, A.I.M. Pathogenesis of bacteriuria in women with diabetes mellitus. *Int. J. of Antimicro. Agents.* 2002; **19**: S39-S45. [https://doi.org/10.1016/S0924-8579\(02\)00090-0](https://doi.org/10.1016/S0924-8579(02)00090-0)
 17. Hilal, S., El Kholy, A., El Ansary, M., El Rachidi, N. Comparison of a polymerase chain reaction (PCR) assay and standard susceptibility testing methods for detection of methicillin resistant *Staphylococcus aureus*. *Journal of Cairo University.* 1997; **65**: 67-77.
 18. Hoepelman, A.I.M., Meiland, R., Geerlings, S.E. Pathogenesis and Management of bacterial urinary tract infections in adult with diabetes mellitus. *Int. J. of Antimicro. Agents.* 2003; **22**: S35-S43. [https://doi.org/10.1016/S0924-8579\(03\)00234-6](https://doi.org/10.1016/S0924-8579(03)00234-6)
 19. Holt, J.G., Krieh, N.R., Sneath, P.A., Staley, J., Williams, S.T. Bergey's manual of determinative bacteriology. Ninth edition, Williams and Wilkins Co., Baltimore, MD 1994.
 20. Lyon, B.R., Skurray, R. Antibiotic resistance of *Staphylococcus aureus*. Genetic basis. *Microbiol. Rev.* 1987; **51**: 88-92.
 21. Mansouri, S., Khaleghi, M. Antibacterial resistance pattern and frequency of methicillin resistant *Staphylococcus aureus* isolated from different sources in southeastern Iran. *Iran. J. Med. Sc.* 1997; **22**: 89-93.
 22. Patterson, J.E., Andriole, V.T. Bacterial urinary tract infections in diabetes. *Infect. Dis. Clin. North Am.* 1995; **9**: 25-51.
 23. Odugbemi, T.O., Hafiz, S., McEntegart, M.D. Penicillinase-producing *Neisseria gonorrhoea* detection by Starch-paper technique. *Br. Med. J.* 1977; **2**: 500. <https://doi.org/10.1136/bmj.2.6085.500>
 24. Ostroff, S.M., Harrison, L.H., Khallaf, N., Assaad, M.T., Guirguis, N.I., Harrington, S. Resistance patterns of *Streptococcus pneumoniae* and *Haemophilus influenzae* isolates recovered in Egypt from children with pneumonia. The antimicrobial surveillance study group. *Clinical Infectious Diseases.* 1996; **23**: 1069-1074. <https://doi.org/10.1093/clinids/23.5.1069>
 25. Oyfo, B.A., El Gendy, A., Wasfy, M.O., El Etr, S.H., Churilla, A., Murphy, J. A survey of enteropathogens among United States military personnel during operation bright star 94, in Cairo, Egypt. *Military Medicine.* 1995; **160**: 331-334. <https://doi.org/10.1093/milmed/160.7.331>
 26. Parker, A.S., Cerhan, J.R., Lynch, C.F. History of urinary tract infection and risk of renal cell carcinoma. *Am. J. Epidemiol.* 2004; **159**: 42-48. <https://doi.org/10.1093/aje/kwh014>
 27. Robert, S., Anders, R.L., Niels, F., Frank, E. Evaluation of different disk diffusion/media for detection of methicillin resistance in *Staphylococcus aureus* and coagulase-negative staphylococci. *APMIS.* 2003; **111**: 905-914. <https://doi.org/10.1034/j.1600-0463.2003.1110909.x>
 28. Ronald, A., Harding, G. Complicated urinary tract infections. *Infect. Dis. Clin. North Am.* 1997; **11**: 583-592. [https://doi.org/10.1016/S0891-5520\(05\)70374-3](https://doi.org/10.1016/S0891-5520(05)70374-3)
 29. Sambrook, J., Fritsch, E.F., Maniatis, T. Molecular cloning: A laboratory manual. Second edition, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 1989.
 30. Samuel, S., Haroun, M., El Kholy, A., Mahmoud, S. Epidemiologic aspects of community-acquired pneumonia in infancy and childhood in summer versus wintertime. *Journal of Arab Child.* 1996; **7**: 1-10.
 31. Selim, S. A. Plasmids and Resistance to Antimicrobial Agents in *Pseudomonas aeruginosa* and *Staphylococcus aureus* strains isolated from Burns. The Eleventh Conference of microbiology, Cairo, Egypt, 2003; 139-153.
 32. Shakibaie, M.R., Mansouri, S., Hakak, S. Plasmid Pattern of Antibiotic Resistance in Beta-Lactamase Producing *Staphylococcus aureus* Strains Isolated from Hospitals in Kerman, Iran. *Archives of Iranian Medicine.* 1999; **2**: 4-7.
 33. Stapleton, A., Stamm, W.E. Prevention of urinary tract infection. *Infect. Dis. Clin. of North America.* 1997; **11**: 719-733. [https://doi.org/10.1016/S0891-5520\(05\)70382-2](https://doi.org/10.1016/S0891-5520(05)70382-2)
 34. Stapleton, A. Urinary tract infections in patients with Diabetes. *The Am. J. of Med.* 2002; **113**: 80S-84S. [https://doi.org/10.1016/S0002-9343\(02\)01062-8](https://doi.org/10.1016/S0002-9343(02)01062-8)
 35. Wullt, B., Bergsten, G., Fischer, H., Godaly, G., Karpman, D., Leijonhufvud, I., Lundstedt, A. C., Samuelsson, P., Samuelsson, M., Svensson, M. L., Svanborg, C. The host response to urinary tract infection. *Infect. Dis. Clin. North America.* 2003; **17**: 279-301. [https://doi.org/10.1016/S0891-5520\(03\)00028-X](https://doi.org/10.1016/S0891-5520(03)00028-X)