Prevalence of Uropathogens in Diabetic Patients and their Antimicrobial Susceptibility Pattern.

*Akinnibosun, F. I and Iriakpe, H. J

Department of Microbiology, Faculty of Life Sciences, University of Benin, P.M.B 1154, Benin City, Edo State, Nigeria.

Abstract: The prevalence of bacteria causing UTI in diabetic patients, as well as their susceptibility to commonly used antibiotics was investigated in Benin City. Bacteriological analysis involved standard biochemical tests and comparison of isolates' characteristics with known taxa. Species isolated from the urine samples analysed were *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Proteus mirabilis* and *Pseudomonas aeruginosa*. Gram-negative isolates had a prevalence of 60 %, while Gram-positive isolates had 40 %. *E. coli* were found to be the most prevalence (44.4 %), while the least prevalent were *P. aeruginosa*(11.1 %),*S. aureus*(11.1 %) and *S. saprophyticus* (11.1 %). Isolates were found to be more in females than males. Three out of the six male diabetics sampled had uropathogens, while six out of the fifteen female diabetics sampled had uropathogens. Susceptibility tests were performed by Bauer-Kirby disc-diffusion method with standard antibiotics. The results were expressed as susceptible or resistant. All the isolates were found to be susceptible to ciprofloxacin and gentamicin. They were also found to be multi-drug resistant. This study showed that diabetic patients had increased risk of urinary tract infections due to the presence of uropathogens.

Key words: Diabetes, Urinary tract infection, Multi-drug resistance, Susceptibility pattern, Bacteria.

Introduction

Urinary tract infections (UTI) are serious health problems affecting millions of people each year. They are the second most common type of infections in the body (Stamm *et al.*, 2011). UTIs are one of the most common types of bacterial infections in humans occurring both in the community and the health care settings and ranks high amongst the most common reason that compel an individual to seek medical attention (Susman, 1998; Tice, 1999; El-Sweih *et al.*, 2008; Kolawole *et al.*, 2009).

It encompasses a spectrum of clinical entities ranging in severity from asymptomatic infections to acute cystitis, Prostatitis, Pyelonephritis and Urithritis (Fowler, 1986; Gluisier, 1991; Kunin, 1994; Kolawole, 2009). The structure of the female urethra and vaginal makes it susceptible to trauma during sexual intercourse as well as bacteria being massaged up the urethra and into the bladder during pregnancy and or child birth (El-Sweih *et al.*, 2008; Kolawole *et al.*, 2009; Jones *et al.*, 2006). In pregnancy the physiological increase in plasma volume and decrease in urine concentration develop glycosuria in up to 70% women which ultimately leads to bacterial growth in urine (Lucas and Cunningham, 1993). Worldwide about 150 million people are diagnosed with UTIs each year (Gupta, 2001). Majority of UTIs are not life threatening and do not cause any irreversible damage. However, when the kidneys are involved, there is a risk of irreparable tissue damage with an increased risk of bacteremia (Hvidberg *et al.*, 2000).

*Corresponding author:
*fakinnibosun@yahoo.co.uk; *Akinnibosun, F. I*

Transmission occurs in four ways; namely through sexual intercourse, from mother to the foetus viaplacenta, through poor personal hygiene and via communal sponge and towel usage (Onifade *et al.*, 2011). The most commonly encountered microorganisms in UTI are Gram-negative bacteria including *Escherichia coli, Citrobacter sp, Enterobacter aerogenes, Pseudomonas aeruginosa* and *Proteus vulgaris* whereas *Klebsiella* sp, *Staphylococcus aureus* and *Salmonella* sp. are found rarely (Foxman and Brown, 2003).

Diabetes mellitus is the most common endocrine disease and is associated with organ complications due to microvascular and macrovascular disease. People with diabetes also suffer from simple and complicated infections, although the association between diabetes and increased susceptibility to infection has been questioned (Wheat, 1980; Thornton, 1971). Nevertheless many specific infections are commoner in diabetes and some occur almost exclusively in diabetic subjects. Others may occur with increased severity and may be associated with greater risk of complications (Joshi *et al.*, 1999). UTIs fall into both these categories i.e. exclusive and more severe. Asymptomatic bacteriuria, acute pyelonephritis and complications of UTI are reported to be more common in patients with diabetes. Despite the clinical and economic significance, there is a paucity of research.Patients with diabetes have a 10-fold increased risk of UTI when compared to non-diabetics (Goswani *et al*, 2001) and diabetics have a longer hospitalization than non-diabetics (Moreno *et al*, 1999). Diabetics are more prone to UTIs and to upper UTI (Geerlings, 2008). The reason for this predisposition is not

completely understood, but the most important is likely to be bladder dysfunction caused by diabetic neuropathy. In diabetic women, there is higher incidence of bacteriuria and of asymptomatic kidney infection.

Increasing multidrug resistance in bacterial uropathogens is an important and emerging public health problem. In the last three decades there have been a lot of reports in the scientific literature on the inappropriate use of antimicrobial agents and the spread of bacterial resistance among microorganisms causing urinary tract infections (Tenever and McGowan, 1996; Hryniewicz *et al.,* 2001; Kurutepe *et al*., 2005). This is a serious issue particularly in the developing world were apart from high level of poverty, ignorance and poor hygiene practices, there is also high prevalence of fake and spurious drugs of questionable quality in circulation. Epidemiological surveillance of antimicrobial resistance is indispensible for empirically treating infections, implementing resistance control measures and preventing the spread of antimicrobial-resistant microorganisms (Oteo *et al*., 2005; Okonko *et al*., 2009). The changing pattern in the etiology of UTI and their sensitivities to commonly prescribed antibiotics have been reported (Jacoby and Archer, 1991; Hryniewicz *et al.,* 2001; Kurutepe *et al.,* 2005; Mordi and Erah, 2006). The worldwide escalation in both community and hospital acquired antimicrobial resistant bacteria is threatening the ability to effectively treat patients, emphasizing the need for continued surveillance, more appropriate antimicrobial prescription, prudent infection control, and new treatment alternatives (Mulvey, 2004; Rhomberg *et al*., 2006; Chikere *et al*., 2008; Okonko *et al.,*2009).

This study, therefore, was undertaken to determine the prevalence of uropathogens in diabetic patients in Benin City, Nigeria and to evaluate the antimicrobial susceptibility pattern of the bacterial isolates.

Materials and Methods

Sample Collection

Fresh mid-stream urine was collected from each patient into a 20 ml calibrated sterile screw-capped universal container which was distributed to the patients. The specimens were labelled transported to the laboratory and analysed within 6 hrs. In each container boric acid (0.2 mg) was added to prevent the growth of bacteria in urine samples. All patients were well instructed on how to collect sample aseptically prior to sample collection to avoid contaminations from urethra. Verbal informed consent was obtained from all patients prior to specimen collection. The study was conducted after due ethical approval. Twenty-one samples (six males and fifteen females) were collected.

Media Preparation

The media used in this study were nutrient agar and MacConkey agar. All media were prepared according to manufacturer's instruction.

Isolation and Identification of Isolates

The samples were inoculated on MacConkey agar and Nutrient agar. The inoculum on the plate was streaked out for discrete colonies with a wire loop following standard procedures (Cheesbrough, 2006; Mordi and Erah, 2006). The culture plates were incubated at 37 °C for 24 hrs and observed for growth through formation of colonies. Isolates were sub-cultured and pure cultres were identified using morphology, microscopy and biochemical tests following standard procedures described by Cowan and Steel (1974) and Cheesbrough (2006). 10^5 colony forming units per ml urine (cfu/ml) obtained in a clean midstream specimen is a sign of a clinically significant UTI.

Antibiotic Susceptibility Test

This was carried out using the Kirby-Bauer disc diffusion method (Bauer *et al.,* 1966), according to National Committee for Clinical Laboratory Standards (NCCLS, 2002). Multidrug resistance was defined as resistance to ≥3 of the antimicrobial agents tested (Oteo *et al*., 2005). The antibiotics used for the isolates were: Amoxicillin (30µg), Chloramphenicol (30µg), Augmentin (30µg), zinnacef (20 µg), rocephin (25µg), ciprofloxacin (l0 µg), streptomycin (30µg), erythromycin (l0µg), gentamycin (I0µg), septrin (30 µg), perfloxacin (l0µg), ampiclox (30µg) sparfloxacin (30µg) and ofloxacin (30µg)

Results and Discussion

The study assessed the presence of bacteria in urines of diabetic patients. Twenty-one(21) samples for both male and female were collected (6 males and 15 females). Out of the 21 diabeticspatients sample collected, only 9 (42.85 %) (3 male and 6 females) had growth of uropathogens (Table 1). Results revealed that 50 % of the diabetic males had UTI while 40 % of the diabetic females had UTI. *Escherichia coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus saprophyticus* were isolated (Table 2). This agrees with the findings of Horcajada *et al.*(1999) that the incidence of bacteriuria is high in diabetics; and with that of Geerlings (2008) that diabetics are more prone to UTIs. This is because diabetes affects many systems that protects against infection in general, and against UTI specifically (Goswami *et al*, 2001). Poor circulation in diabetes reduces the ability of infection-fighting white blood cells to get where they are needed, and even when they do, they are less able to ingest the offending bacteria and kill them than normal white blood cells. It may also be due to bladder dysfunction caused by diabetic neuropathy which allows urine to remain in static pools for long periods of time, providing luxurious ponds for bacteria to grow in. *E.coli* was the most commonly isolated organism

(44.4%) followed by *Proteus mirabilis* (22.2%), *Staphylococcus aureus* (11.1%) *Staphylococcus saprophyticus* (11.1%) and *Pseudomonas aeruginosa* (11.1%) (Table 2). The results of this study showed that the etiologic agents of UTIs mainly belonged to the Gram-negative bacteria, with *E. coli* being the most prevalent. This agrees well with the previous studies conducted (Braunwald *et al*., 2001; Connell *et al*., 2000; Johnson *et al*., 1999; Oelschlaeger *et al*., 2002).*E.coli* is a normal intestinal flora found in humans and is therefore expected to be more prevalent in urinary tract of immunologically suppressed patients. There seems to be an increased risk of the infection spreading upwards into the kidneys in diabetic patients especially in those whose condition has lasted for long periods of time and in those poorly managed for the condition. All the bacteria isolated occurred in the females except *S. aureus*, while *S. aureus* and *E. coli*, only occurred in the males (Table 3).This is similar to the findings of Braunwald *et al.*, 2001. The uropathogens isolated and identified in this study, were similar to those of many other studies conducted in different countries, either in the region or internationally (Braunwald *et al.*, 2001; Hooton *et al.*, 2012). The similarities and differences in the type and distribution of uropathogens may result from different environmental conditions, and host factors practices such as health care and education programmes, socio-economic standards and hygiene practices in each country.The enterobacteriaceae were the most common microorganisms isolated in this study. This is in agreement with the result of Dimittrov *et al.*(2004); Mordi and Erah,(2006); Dash *et al*. (2013); Abubakar, (2009); Johnson *et al.*(1999); Omigie *et al*.(2009). This high incidence of *E. coli* and other enterobacteriaceae could be attributed to the fact that they are commensals of the bowels and that infections is mostly by faecal contamination due to poor hygiene. This is owned to the fact that commensals of the intestines are more involved in the UTI because of the anatomy proximity to the genitourinary area (Hooton *et al*., 2012).

The results of antibiotic susceptibility test with Gram-negative bacteria (Table 4), showed that *E. coli* was resistant to 7 (70 %) and susceptible to 3 (30 %) of the antibiotics. This goes in agreement with earlier studies by Wazait *et al.* (2003). *P. aeruginosa* was found to be resistant to 7 (70 %) and susceptible to 3 (30 %) of the antibiotics. This is similar to the results of Mazzulli *et al.* (2001). *P. aeruginosa* maintains antibiotic resistance plasmids and are able to transfer these genes by bacterial processes of transduction and conjugation (Nwanze *et al*., 2007). *Proteus mirabilis* showed resistance to 5 (50 %) and susceptible to 5 (50 %) of the antibiotics. *Proteus* sp has the ability to produce urease which helps them to survive in the urinary tract, and they have flagella that enable them to swim about their environment and also contribute to their virulence nature (Wilson and Gaido, 2004; Johnson *et al.*, 1999; Braundwald *et al*., 2001). Antibiotic susceptibility test with Gram-positive bacteria (Table 5), showed that *S. aureus* was foundto be resistant to 6 (60 %) and susceptible to 4 (40 %) of the antibiotics. *S. saprophyticus* was also found to be resistant to 6 (60 %) and susceptible to 4 (40 %) of the antibiotics. These findings were similar to those observed by Nkang *et al.* (2009) but contrary to Bischoff *et al*. (1999). This might be due to environmental differences. *S. aureus* has been reported to exhibit resistance to beta-lactam antibiotics of which benzyl penicillin is one Outbreaks of *S. aureus* resistant to beta-lactam antibiotics have been frequently associated with devastating nosocomial infections (Depardieu *etal*., 2007; Buhlmann *et al*., 2008; Chikere *et al*., 2008). Both Gram-negative and positive bacteria were 100 % susceptible to ciprofloxacin and gentamicin as shown in Tables 4 and 5.This result is similar to that reported by Resih *et al*. (1993) and Okonko *et al.* (2009). Multidrug resistance was observed for some of the isolates as they were resistant to more than one drug (Wasfy *et al*., 2000; Akpomie and Akpan, 2013). Drug abuse and indiscriminate misuse of antibiotics among the general population has favoured the emergence of resistant strains.

Table 1: Incidence of Urinary tract infection among male and female diabetics

Sex	No. of diabetics sampled	No. of diabetics with UTI	% of diabetics with UTI
Male	6	3	50
Female	15	6	40

TABLE 2: Bacteria isolated and their percentage occurrence in the samples

Bacteria isolated	Percentage of Isolates
Escherichia coli	44.4%
Proteus mirabilis	22.2%
Pseudomonas aeruginosa	11.1%
Staphylococcus aureus	11.1%
Staphylococcus saprophyticus	11.1%

Table 3: Occurrence of isolated bacteria among male and female patients

Bacterial Isolates	Males	Females
S.aureus	+	_
S. saprophyticus	_	+
E. coli	+	+
Proteus mirabilis	_	+
Pseudomonas aeruginosa	_	+

Key: - = absent; + = present

Table 4: Antibiotic susceptibility pattern of Gram-negative (-ve) bacteria

Gram –ve	AM	AU	CN	PEF	OFX	S	SXT	CH	SP	CPX
P. mirabilis	S	S	S	R	S	R	R	R	R	S
E.coli	R	R	S	R	S	R	R	R	R	S
P. aeruginosa	R	R	S	R	S	R	R	R	R	S

Key: R = Resistant; S = Sensitive; AM= Amoxicillin; AU= Augmentin; CN= Gentamycin; PEF= Pefloxacin; OFX= Ofloxacin; S= Streptomycin; SXT= Septrin; CH= Chloramphenicol; SP= Sparfloxacin; CPX= Ciprofloxacin

Table 5: Antibiotic susceptibility pattern of Gram-positive (+ve) isolates

Gram+ve	AM	R	CPX	S	SXT	E	PEF	CN	APX	Z
S.aureus	R	S	S	R	R	S	R	S	R	R
S. saprophyticus	S	R	S	R	R	S	R	S	R	R

Key: R = Resistant; S = Sensitive; AM= Amoxicillin; R = Rocephin; CN= Gentamycin; PEF= Pefloxacin; APX= Ampiclox; S= Streptomycin; SXT= Septrin; E = Erythromycin Z = Zinnacef; CPX= Ciprofloxacin

Conclusion

UTI may result as a complication of diabetes and this study confirms that diabetes predisposes humans to the risk of urinary tract infections due to the changes in bladder function and in circulation. The susceptibility and resistance profile of all isolates in this study have shown that ciprofloxacin and gentamicin are the most effective antibiotics of choice. Diabetic patients infected with UTIs should therefore be promptly treated with these antibiotics to prevent development of kidney damage or more serious infections. The findings of this study also confirm that some bacteria, still are resistant to antibiotics and frequently used drugs in many parts of the world.

Acknowledgement

The authors would like to thank the Department of Microbiology, Faculty of Life Sciences, University of Benin, Benin city, for providing materials for this work.

References

Abubakar E. M. (2009) Antimicrobial susceptibility pattern of pathogenic bacteria causing urinary tract infection at the specialist hospital Yola Adamawa state Nigeria. *Journal of Clinical Medical Research* **1**(1): 1-8.

Akpomie, O. O., and Akpan, I. (2013). Multi-drug resistant among bacteria isolated from some foods sold in restaurants in Abraka, Nigeria.*InternationalJournal of Microbiological Research and Reviews* **2**(6): 97-102.

Bauer, A. W., Kirby, W. M., Sherries, J. C. and Turck, M. (1966). Antibiotics susceptibility testing by a standard single Disc method. *American Journal of Pathology* **451**: 493- 496.

Bischoff, W.E., Reynolds, T.M., Hall, G.O.,Wenzel, R.P. and Edmond, M.(1999). Molecular epidemiologyof vancomycin - resistant *Enterococcus faecium* in a large urban hospital over a 5-year period. *Journal of Clinical Microbiology*. **37**:3912-3916.

Braunwald, E., Fauci, A.S., Kasper, D.L., Hauser, S.L., Longo, D.L. and Jameson, J.L. (2001). Principles of Internal Medicine. McGraw-Hill New York, USA 15th ed.pp1620- 1625.

Cheesbrough, M. (2006). District laboratory practice in tropical countries. Cambridge University Press 434pp.

Chikere, C. B., Chikere, B. O. and Omoni, V. T. (2008). Antibiogram on clinical isolates from a hospital in Nigeria. *African Journal of Biotechnology* **7**(24): 4359-4363.

Connell, H., Poulsen, L. K. and Klemm, P. (2000); Expression of type 1 and P fimbrie *in situ* and localization of a uropthogenic *Escherichia coli* strain in the murine bladder and kidney. *International Journal of Medical Microbiology*. **290**:587-597.

Cowan, S. J. and Steel, K. J. (1974). Cowan and steel manual for identification of medical bacteria 2nd edition Cambridge University Press London pp 176-232.

Dash, M., Padhi, S., Mohanty, I., Panda, P., and Parida, B. (2013). Antimicrobial resistance in

pathogens causing urinary tract infections in a rural community of Odisha India. *Journal of Family and Community Medicine***20**(1): 20-26.

Depardieu, F., Podglajen, I., Leclercq, R., Collatz, E. and Courvalin, P. (2007). Modes and modulations of antibiotic resistance genes expression clinical microbiology revised **20**(1): 79-114.

Dimitrov, T. S., Udo, E. E., Awni, F., Emara, M. and Passadilla, R. (2004). Etiology and antibiotic susceptibility patterns of community-acquired urinary tract infections in a Kuwait hospital.*Medical Principles and Practices* **13**(6): 334-339.

El-Sweih, N., Jamal, W. and Rotimi, V. O. (2008). Spectrum and antibiotic resistance of uropathogens isolated from hospital and community patients with urinary tract infections in two large hospitals in Kuwait. *Medical Principle Practical* **14**:401-407.

Foxman, B. (2003). Epidermiology of urinary tract infections: incidence morbidity and economic costs. *Disease-a-Month Journal* **49**(2): 53-70.

Fowler, J. E. (1986). Urinary tract infection in women *Urologic Clinics of North American* **13**: 673 - 676.

Geerlings, S.E. (2008). Urinary tract infections in patients with diabetes mellitus Epidemiology Pathogenesis and Treatment. *International Journal of Antimicrobial Agent***31** (1): 54-57.

Gluisier, M.P. C. (1991). Urinary tract infection and pyelonephritis. In Braude, A. I. P.and Sander, W. B. (ed). Medical Microbiology and infectious diseases. W B Comp Philadelphia 1172-1183pp.

Goswami, R., Bal, C.S., Zateri, R.B., Punjabi, G.V. (2001). Prevalence of urinary tract infection and renal scars in patients with diabetes mellitus. *Infectious Disease Clinic North America***18:** 52- 41.

Hooton, T.M. (2012). Fluoroquenolones and resistance in the treatment of uncomplicated urinarytract infection. *International Journal on Antimicrobial Agents* **2**:65-72.

Horcajada, S.K., Patel, K.C., Jain, U.S., Johnson, J.R. (1999). Laboratory diagnosis of urinary tract infections in adult patients. *Clinical Infectious Diseases***39**(6): 873-877.

Hryniewicz, K., Szczypa, K., Sulilowska, A., Jankowski, K., Betlejewska, K. and Hryniewicz, W. (2001). Antibiotic susceptibility of bacteria strains isolated from urinary tract infections in Poland. *Journal on Antimicrobial Chemotherapy* **47**(6): 773-780.

Hvidberg, H., Struve, C., Krogfelt, K. A., Christensen, N., Rasmussen, S. N. and Frimodt-M ler, N. (2000). Development of a long term ascending urinary tract infection mouse model for antibiotic treatment studies. *Antimicrobial Treatment Chemotherapy* **44**: 156-163.

Johnson, J.R., Delavari, P. and Azar, M. (1999). Activities of a nitrofurazone-containing urinarycatheter and a silver hydrogel catheter against multidrug-resistant bacteria characteristic of catheter-associated urinary tract infection. *Antimicrobial Agents and Chemothermophiles*. **43**:2990-2995.

Jones, R. N., Inabo, H. I. and Obanibi, H. B. I. (2006). Antimicrobial susceptibility of some urinary tract clinical isolates to commonly used antibiotics. *African Journal of Biotechnology* **5**(5): 487-489.

Joshi, N., Caputo, G.M., Weitekamp, M.R., Karchmer, A.W. (1999). Infections in patients with diabetes mellitus. *New England Journal of Medicine***341**:1906-12.

Kolawole, A. S., Kolawole, O. M., Kandaki-Olukemi, Y. T., Babatunde, S. K., Durowade, K. A. and Kolawole, C. F. (2009). Prevalence of urinary tract infections among patients attending dalhatu Araf Specialist Hospital, Lafia, Nasarawa State, Nigeria. *International Journal on Medicines and Medical Sciences* **1**(5): 163-167.

Kunin, C. M. (1994). Urinary tract infections in females. *Clinical Infectious Disease* **18**:1-12.

Kurutepe, S., Surucuoglu, S., Sezgin, C., Gazi, H., Gulay, M. and Ozbakkaloglu, B. (2005). Increasing antimicrobial resistance in Escherichia coli isolates from community acquired urinary tract infections during 1998-2003 in Turkey. *Japan Journal on Infectious Diseases* **58**: 159-161.

Lucas, M. J. and Cunningham, F. G. (1993). Urinary tract infections in pregnancy. *Clinical Obstetrics and Gynecology* **36**(4): 855-868.

Mazzulli, T., Skulnick, M., Small, G., Marshall, W., Hoban, D. J., Zhanel, G. G., Finn, S. and Low, D. E. (2001). Susceptibility of community Gram negative urinary isolates to mecillinam and other oral agents. *Canadian Journal on Infections* **12**(5): 289-292.

Mordi, R. M. and Erah, P. O. (2006). Susceptibility of common urinary tract isolates to the commonly used antibiotics in a tertiary hospital in southern Nigeria .*African Journal Biotechnology* **5**(11): 1067-1071.

Moreno, A.P., Krieger, J.N., Kim, Y.Y., Park, S.K. (1986). Complications and treatment of urinary tract infections during pregnancy. *Urologic Clinics of North America* **16:** 685-693.

Mulvey, M. R., Bryce, E., Boyd, D., Ofner-Agostini, M., Christianson, S. and Paton, S. (2004). The Canadian hospital epidermiology committe of the Canadian nosocomial infection surveillance program, health Canada ambler class A extended-spectrum beta-lactam producing *Escherichia coli* and *Klebsiella* sp.

in Canadian hospital. *Antimicrobial Agents Chemotherapy* **48**: 1204-1214.

National committee for clinical laboratory standards (NCCLS) (2002) Performance standards for antimicrobial susceptibility testing twelfths informational supplement NCCLS document M100-S12 PA USA.

Nwanze, P., Nwaru, L. M., Oranus, S., Dimkpa, U., Okwu, M. U., Babatunde, B. B., Anke, T. A., Jatto, W. and Asagwara, C. E. (2007). Urinary tract infection in okada village: Prevalence and antimicrobial susceptibility pattern. *Science Research Essays* **2**(4): 112-116.

Oelschlaeger, T.A., Dobrindt, U. and Hacker, J. (2002). Virulence factors of uropthogens. *Current Opinion on Urology*.**12**:33-38.

Okonko, I. O., Donbraye-Emmanuel, O. B., Ijandipe, L. A., Ogun, A. A., Adedeji, A. O., and Udeze, A. O. (2009). Antibiotics sensitivity and resistance patterns of uropathogens to nitrofurantoin and nalidixic acid in pregnant women with urinary tract infections in Ibadan, Nigeria. *Middle East Journal of Scientific research* **4**(2): 105-109.

Omigie, O., Okoro, L., Umolu, P. and Ikunh, G. (2009). Increasing resistance to quinolones a four year prospective study of urinary tract infection pathogens. *International Journal of General Medicines* **2**:171-175.

Onifade, A. K., Anibijuwon, I. I. and Azariah, E. J. (2011). Urinary tract infection in apparently healthy individuals in ile-ife Nigeria: Detection of predominant microorganisms and antibiotics susceptibility profile. *African Journal of Microbiology Research* **5**(20): 3233-3236.

Oteo, J., Lazaro, E., Abajo, F. J., Baquero, F. and Campos, J. (2005). Antimicrobial resistant invasive Escherichia coli Spain. *Emerging Infectious Diseases* **11**(9): 546-553.

Resih, O., Ashkenazi, S., Naor, N., Samra, Z. and Merlob, P. (1993). An outbreak of multi-resistant Klesiella in a neonatal intensive care unit. *Journal on Hospital Infections* **25**(4): 287-291.

Rhomberg, P. R., Fritsche, T. R., Saden, H. S. and Jones, R. N. (2006). Antimicrobial susceptibility pattern Comparison among intensive care unit and general ward Gram-negative isolates from meropanem yearly susceptibility test information collection program (USA). *Diagnosis of Microbiological Infectious Disease* **56**:57-62.

Stamm, W.E. (1982). Urinary traction infections from pathogenesis to treatment. *Journal of Infectious Diseases,* **159:** 400-406.

Susman, M. (1998). Urinary tract infections In Collierr L Balows A and Sussman M Eda topley and Wilson, microbiology and microbial infections 9th edition. pp601-621.

Tenever, F. C. and McGowan, J. E. Jr. (1996). Reasons for the emergence of antibiotic resistance. *The American Journal on the Medical sciences* **311**:9-16.

Thornton, G.F. (1971). Infections and diabetes. *Medical Clinics of North America***55**:931-8.

Wasfy, M. O., Oyofo, B. A., David, J. C., Ismail, T. F., Elgendy, A. M. and Peniski, L. F. (2000). Isolation and antibiotic susceptibility of *Salmonella*, *Shigella* and *Campylobacter* from acute enteric infections in Egypt. .*Journal on Environmental Sciences* **18**(11): 35-38.

Wazait, H.D., Patel, H.R., Veer V., Kelsy, M., Van Der Meulen, J.H., Miller, R.A. and Emberton, M.(2003); Catheter - associated urinary tract infections: prevalence of uropathogens and pattern.of antimicroloial resistance in a UK hospital (1996-2001). *BJU International* **91(**9):806-809.

Wilson, M.L. and Gaido, L. (2004); Laboratory diagnosis of urinary tract infections in adultpatients. *Clinical Infectious Disease* **38**:1150-1158.

Wheat, L.J. (1980). Infection and diabetes mellitus. *Diabetes Care***3**:187-97.