Emerge of multidrug resistance in uropathogenic *Escherichia coli*

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Abstract: In this study, a total of 132 uropathogenic *E.coli* isolates were recovered from patients suffering from UTIs attending in Shebien El Kom Teaching Hospitals, and Monofeya University Hospitals from May 2014 till August 2016. All the isolates were identified based on their colonial characteristics on MacConkey's agar, Gram staining, conventional biochemical identification tests and Microbact ™12A identification system. The susceptibility of the recovered ceftazidime resistant *E.coli* isolates to 24 antibiotics was determined using disc diffusion method. Out of 132 tested isolates, 84(63.63%) exhibited multidrug resistant (MDR) character, 66 (50%) were extensive drug resistant (XDR) and there is no pandrug resistant (PDR) isolates. Resistance patterns were set for tested isolates which include 15 heterogeneous pattern. The isolates showed multiple antibiotic resistant (MAR) index values ranged from 0.25 to 0.916. MAR index values of isolates were divided to four levels, low, moderate, high and sever high resist. Emerge of high and multidrug resistance among the bacterial pathogens leads to failure of drug therapy and increase the severity degree of outcome of infection according to high risk source of contamination, misused for antibiotics and control of antimicrobial use is not strictly followed by clinicians. So, ensure proper use of antimicrobials to preserve their efficacy and minimize the development of antimicrobial resistance.

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Keywords: UTI; *Escherichia coli*; MAR indeces; MDR; XDR; PDR

1. Introduction:

Urinary tract infections (UTI) are the most prevalent infections worldwide, mostly caused by *Escherichia coli*. Accounting for more than 70% of uncomplicated cases both in outpatients and inpatients **(Gupta *et al*.,2001).** Clinically, UTIs are categorized as uncomplicated, complicated and recuurent infection. Uncomplicated UTIs typically affect individuals who are otherwise healthy and have no structural or neurological urinary tract abnormalities. These infections are differentiated into lower UTIs (cystitis) and upper UTIs (pyelonephritis) **(Hannan, 2012 & Hooton, 2012).** Complicated UTIsare defined as UTIs associated with factors that compromise the urinary tract or host defence, including urinary obstruction, urinary retention caused by neurological disease, immunosuppression, renal failure, renal transplantation, pregnancy and the presence of foreign bodies such as calculi, indwelling catheters or other drainage devices **(Lichtenberger *et al*., 2008 & Levison *et al.*, 2013).** UTI is defined as 2 uncomplicated UTIs in 6 months or, more traditionally, as ≥ 3 positive cultures within the preceding 12 months **(Annette *et al*., 2015).** Several risk factors are associated with cystitis, including female gender, a prior UTI, sexual activity, vaginal infection, diabetes, obesity and genetic susceptibility **(Hannan, 2012 & Foxman, 2014).** UTIs are usually treated with broad-spectrum cephalosporins flouroquinolones and aminoglycosides. The rapid spread of resistance to broad-spectrum beta-lactams in pathogenic strains of bacteria has recently become a major health problem in the world. It causes antibiotics ineffectiveness, increased severity of illness and cost of treatment **(Yazdi *et al.*, 2012 & Harada *et al.*, 2013).** MAR index is a tool to analyze health risk and is helpful to check the spread of bacterial resistance in a given population **(Osundiya *et al.*, 2013).** The Multi-Drug Resistance (MDR) character of the isolates was identified by observing the resistance pattern of the isolates to the tested antibiotics. Multiresistance was considered on the basis that the studied clinical isolates were resistant to antibiotics belonging to at least 3 classes and up to all tested antibiotics **(El-Nakeeb *et al*., 2011).**

2. Material and Methods:

Between May 2014 and August 2016, One thousand fresh mid-stream urine samples from urinary tract infected patients were collected. The samples were as following 407 urine sample were collected from male patient and 593 urine sample were collected from female patient. Urine samples were collected aseptically in a sterile clean catch container.

1- Isolation and Identification of Pathogens:

The pathogens were isolated by following standard protocol using sterile bacteriological media. Each sample were inoculated on MacConkey's agar using calibrated loop delivering 0.01ml of the sample. Then, plates were incubated overnight at 37°C for 24 hrs. Identification of the organisms were done on the basis of Gram stain and routine biochemical tests including, reaction on triple sugar iron (TSI) producing acids, citrate utilization test, methyl red test, Voges Proskauer test and indole test. Microbact 12A™ was used as a confirmatory identification. Bacterial growth, only for strains of *E.coli* with clinically growth (>10^5 CFU/m) were included in this study.

2- Ceftazidime resistant isolates among the tested *E. coli* isolates was screened by using breakpoint method:

Culture on Muller Hinton agar supplemented with 2 mg/liter Ceftazidime. The plates were incubated overnight at 35ºC in ambient air and then examined for any growth **(Khater *et al.*, 2014).**

3- Antimicrobial susceptibility testing by disc diffusion method for *E.coli* isolates:

Routine disc diffusion susceptibility testing was performed by modified Kirby Bauer's disc diffusion method **(Yazdi *et al.*, 2012).** Susceptibility of the tested isolates to 24 different antimicrobial agents including 17 β-lactam and 7 non β-lactam drugs; (AX) Amoxicillin, (PRL) Pipracillin, (P) Penicillin G, (CFR) Cefadroxil (AMC) Amoxicillin/Clavulinicacid, (CZ) Cefazolin, (CEC) Cefaclor, (MA) Cefamandolin, (FOX) Cefoxetin, (CTX) Cefotaxime, (CAZ) Ceftazidime, (CRO) Ceftriaxone, (CFM) Cefixime, (FEP) Cefepime, (IPM) Imipenem, (MEM) Meropenem, (ATM) Azetreonam, (CIP) Ciprofloxacin, (OFX) Ofloxacin, (AK) Amikacin, (TE) Tetracycline, (G) Gentamycin, (C) Chloramphenicol, (SXT) Trimethoprim/Sulfamethaxole. The results were interpreted according the clinical and laboratory standards institute **(CLSI, 2014).**

4- Antimicrobial resistance pattern of *E.coli* isolates:

Based on the previous disc diffusion data, the patterns of resistance of all tested isolates to the studied antimicrobial drugs were determined.

5- Determination of multiple antibiotic resistance (MAR) index, multi-drug resistance, extensively drug resistance and pandrug resistance among ceftazidime resistant *E.coli* isolates:

MDR index is a tool that reveals the spread of resistant bacteria in a given population. The MAR index values for each isolate and each antibiotic were calculated according to **Tambekar *et al.*, 2006 and Mthembu, 2008** using the following formulas:

$$\text{MAR index for isolates} = \frac{\text{Number of antibiotics to which the isolate was resistant}}{\text{Total number of antibiotics to which the isolate was exposed}}$$

$$\text{MAR index for antibiotics} = \frac{\text{Number of antibiotic resistant isolates}}{\text{number of antibiotics} \times \text{number of isolate}}$$

Greater MAR index values for bacterial isolates than 0.2 reveals that they have originated from an environment where several antibiotics were used**.**

MDR was considered on the basis that the studied clinical isolates were resistant to antibiotics belonging to at least 3 classes and up to all tested antibiotics **(El-Nakeeb *et al.*, 2011).** XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e. bacterial isolates remain susceptible to only one or two categories) and PDR was defined as non-susceptibility to all agents in all antimicrobial categories.

3. Results:

Isolation and Identification of Pathogens:

Urine samples were cultured on MacConkey's agar. Out of the developed colonies, the lactose fermenter; flat, dry, pink colonies were selected for further identifications using gram staining, traditional biochemical identification tests and Microbact™ 12A Biochemical Identification Kit. It was found that 132 were *E.coli* isolates.

Ceftazidime resistant isolates among the tested *E.coli* isolates was screened by using breakpoint method

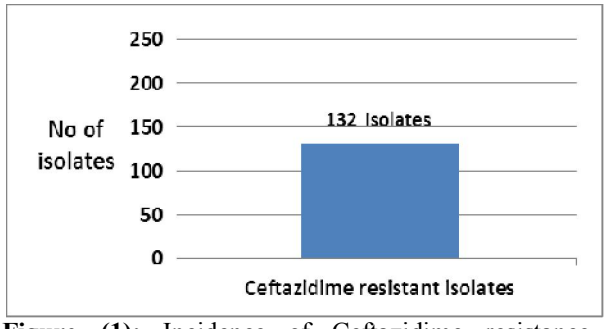

Figure (1): Incidence of Ceftazidime resistance among the detected *E.coli* isolates

Antimicrobial susceptibility testing by disc diffusion method for Ceftazidime resistant *E.coli* isolates for other antimicrobials:

Resistance to tested antibiotics were distributed among recovered isolates as shown in Figures (2 & 3).

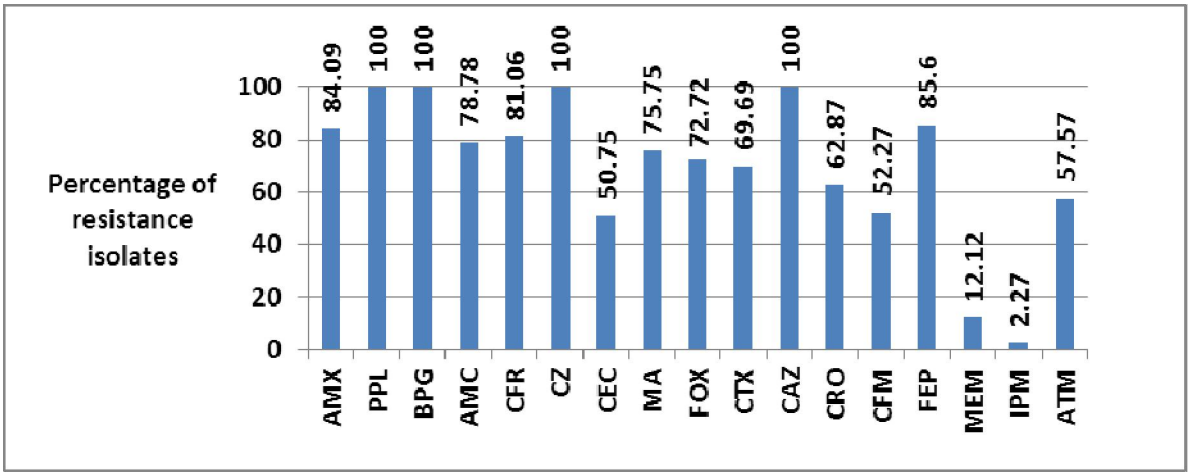

Figure (2): Histogram showing resistance of Ceftazidime resistant *E.coli* isolates to different β-Lactam antibiotics.

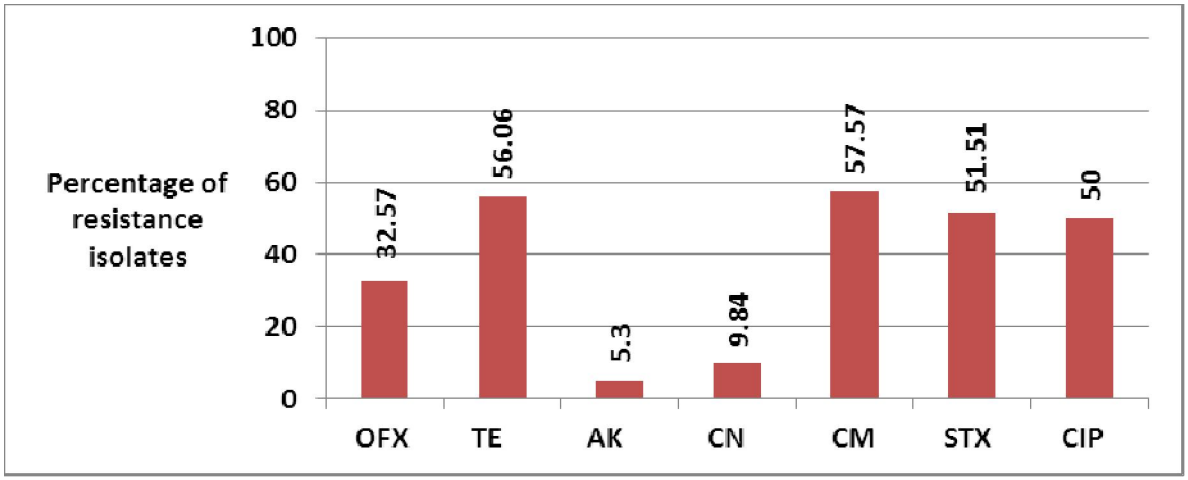

Figure (3): Histogram showing resistance of Ceftazidime resistant *E.coli* isolates to different non β-Lactam antibiotics.

Determination of resistance patterns of *E.coli* isolates:

Based on the previous disc diffusion data, the patterns of resistance of all *E.coli* isolates to the studied antimicrobial drugs were determined and presented in Table (1).

E.coli isolates exhibited 15 major resistance patterns according to number of resistance markers and each pattern included subpatterns or subgroups. All isolates were resistant to up to 6-22 out of the tested 24 antimicrobial agents. Tested isolates were very heterogeneous where not more than 7 isolates shared the same resistance pattern.

5. Determination of MAR indices, MDR, XDR and PDR among ceftazidime resistant *E.coli* isolates:

MAR index values of bacterial isolates are presented in Table (1) and its analysis revealed that all the isolates had a high MAR index value (>0.2). The isolates showed MAR index values ranged from 0.25 to 0.916. Only 6 isolates showed MAR index values < 0.3 and only 3 isolates showed MAR index values of 0.916.

MAR index values of isolates were divided to four levels, low, moderate resist, high and sever high Low, moderate, high and sever high MAR index values of isolates were ranged from 0.25 to 0.357, 0.416 to 0.5, 0.514 to 0.75 and 0.79 to 0.916 respectively as shown in Figure (4).

Low, moderate, high and sever high MAR index values of isolates exhibited number of markers of antimicrobial agents which were up to 9, 12, 18 and 22 respectively as shown in Figure (5).

Table (1): Multiple Antibiotic Resistance (MAR) indexes and antimicrobial resistance patterns of *Ceftazidime* resistant *E.coli* isolates

Pattern code		Antimicrobial Resistance pattern*	No of markers	isolates exhibiting pattern	Pattern incidences	MAR index
I		AMX-PRL-PG -CZ-MA-CAZ	6	E290- E456-E597- E763-E904-	5	0.25
II		PR L-PG-CFR-CZ-MA-CAZ-TE	7	E149	1	0.29
III	a b c	PRL-PG-CFR-CZ-CAZ-FEP-OFX-CM-SXT AMX-PRL-PG -CFR-CZ- MA- CTX-CAZ- FEP AMX-PRL-PG -CFR-CZ-MA-FOX-CAZ- FEP	9	E89-E396-E703-E945 E102-E409-E716-E726 E112-E419	4 4 2	0.375
IV	a b	AMX-PRL-PG-AMC-CFR-CZ-MA-CAZ-FEP-MEM- AMX-PRL-PG-AMC-CZ-MA-FOX-CTX-CAZ-CRO	10	E274-E581 E285-E601-E888-E908	2 4	0.416
V	a b	AMX-PRL-PG-AMC-CZ-MA-FOX-CAZ-CFM-FEP-SXT PRL-PG-CFR-CZ-MA-FOX-CAZ-ATM-CIP-TE-CM	11	E282-E608-E915 E301-E589-E896	3 3	0.458
VI		PRL-PG-AMC-CFR-CZ-MA-FOX-CTX-CAZ-FEP-ATM-CIP	12	E178-E485-E792	3	0.5
VII	a b c	AMX-PRL-PG-AMC-CFR-CZ- MA-FOX-CTX-CAZ-CRO-CFM-FEP AMX-PRL-PG-AMC-CFR-CZ-CEC-MA -CTX-CAZ-CFM-FEP-OFX AMX-PRL-PG-AMC-CFR-CZ-MA-FOX-CTX-CAZ-CRO-FEP-SXT	13	E257-E564-E871 E152-E459-E766 E10-E317-E624-E974	3 3 4	0.541
VIII	a b c d e	AMX-PRL-PG-AMC-CZ-FOX-CTX-CAZ-CRO-FEP-ATM-TE-CM-SXT AMX-PRL-PG-AMC-CZ-FOX- CTX-CAZ-CRO-FEP-ATM-CIP-TE-CM PRL-PG-AMC-CFR-CZ-CEC- CAZ- FEP-ATM-CIP-OFX-AK-CM-SXT AMX-PRL-PG-AMC- CZ-CEC-MA-FOX-CTX-CAZ-CFM-FEP-OFX-CM AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-CAZ-CFM-FEP-TE-CM-SXT	14	E255-E562-E869 E278-E585-E892 E254-E561-E868-E980 E120a-E427-E734 E233-E540-E847	3 3 4 3 3	0.583
IX	a b c d e	AMX-PRL-PG-AMC-CFR-CZ-FOX-CTX-CAZ-CRO-IPM-ATM-CIP-TE-CM AMX-PRL-PG-AMC-CFR-CZ- FOX-CTX-CAZ-CRO- FEP-ATM-CIP-TE-CM AMX-PRL-PG-AMC-CFR-CZ-CEC-FOX-CTX-CAZ- CFM-FEP-TE-CM-SXT AMX-PRL-PG-AMC-CFR-CZ-FOX-CTX-CAZ-CRO-FEP-ATM-CIP-OFX-CM PRL-PG-AMC-CFR-CZ-MA-CTX-CAZ-CRO-CFM-FEP –ATM-TE-CM-SXT	15	E294-E592-E899 E156-E463-E770-E953-E998 E218-E525-E832 E281-E588-E895 E243-E550-E857	3 5 3 3 3	0.625
X	a b	AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM-CIP AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CAZCFM-FEP-MEM-TE-CM-SXT	16	E53-E360-E667-E937-E993 E69-E376-E683	5 3	0.666

XI	a b c	AMX-PRL-PG-AMC-CFR-CZ-MA-FOX-CTX-CAZ-CRO- FEP-OFX-TE-CN-CM-SXT AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CAZ-CRO-CFM-FEP-CIP-TE-CM-SXT AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CAZ-CRO-CFM-FEP-ATM-TE-CM-SXT	17	E307-E614-E921 E204-E511-E818 E226- E533-E840-E956	3 3 4	0.708
XII	a b c d	AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO -FEP-ATM-CIP-TE-CM-SXT AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM-CIP-OFX-SXT AMX-PRL-PG-CFR-CZ-CEC-MA-CTX-CAZ-CRO-CFM-FEP-MEM-ATM-CIP-TE-CN-CM- AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM- TE-CM-SXT	18	E11a-E318-625 E93-E400-Ez07 E277-E584-E891-E933 E221-E528-E835	3 3 4 3	0.75
XIII	a b	AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM-CIP-OFX-TE-CM AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM-CIP-OFX-TE-SXT	19	E291-E598-E905-E987 E74- E119-E381-E426-E688-E733-E951	4 7	0.79
XIV	a b c	AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-MEM-ATM-CIP-TE-CN-SXT AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-MEM-ATM-CIP-OFX-TE-SXT AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM-CIP-OFX-TE-CM-SXT	20	E210-E517-E824 E146-E453-E760-E960 E17b-E324-E631-E950-E955	3 4 5	0.833
XV		AMX-PRL-PG-AMC-CFR-CZ-CEC-MA-FOX-CTX-CAZ-CRO-CFM-FEP-ATM-CIP-OFX-TE-AK-CN-CM-SXT	22	E207-E514-E821	3	0.916

*(AMX) Amoxicillin, (PRL) Pipracillin, (P) Penicillin G, (AMC) Amoxicillin/Clavulinicacid, (CZ) Cefazolin, (CEC) Cefaclor, (CFR) Cefadroxil, (MA) Cefamandolin, (FOX) Cefoxetin, (CTX) Cefotaxime, (CAZ) Ceftazidime, (CRO) Ciprofloxacin, (CFM) Cefixime, (FEP) Cefepime, (MEM) Meropenem, (IPM) Imipenem, (ATM) Azetreonam, (OFX) Ofloxacin, (TE) Tetracyclin, (AK) Amikacin, (CN) Gentamycin, (CM) Chloramphenicol, (SXT) Trimethoprim/Sulphamethaxole, (CIP) Ciprofloxacin

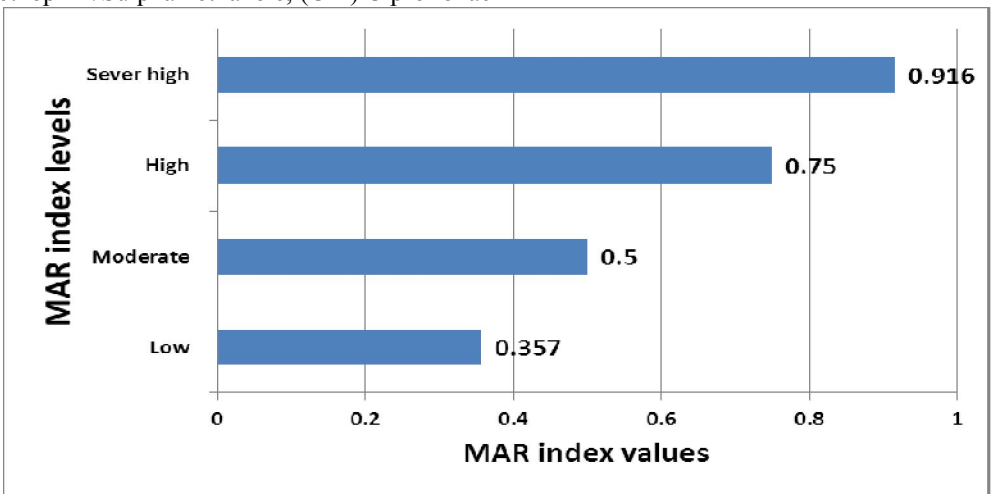

Figure (4): Different MAR index levels of isolates

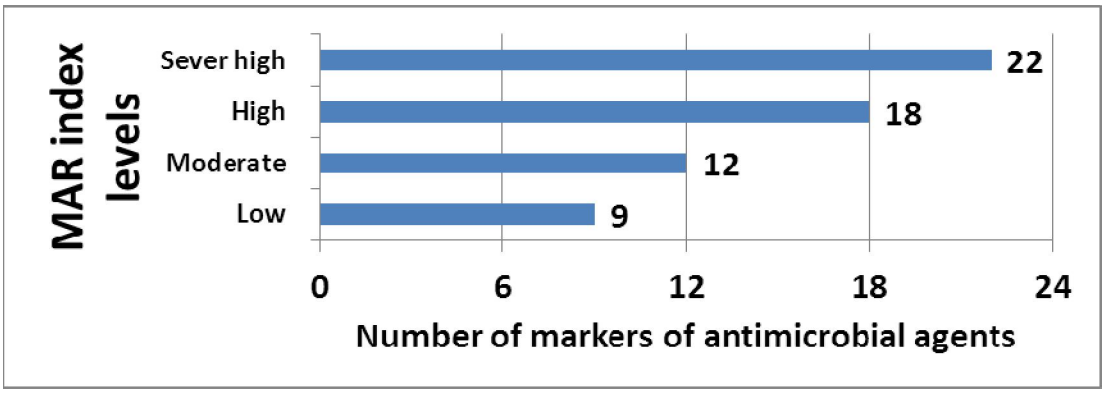

Figure (5): Relationship between MAR index levels and number of markers of antimicrobial agents.

From the above data, number of isolates exhibiting low, moderate, high and sever high MAR index values were 16, 15, 61 and 26 isolates respectively as shown in Figure (6)

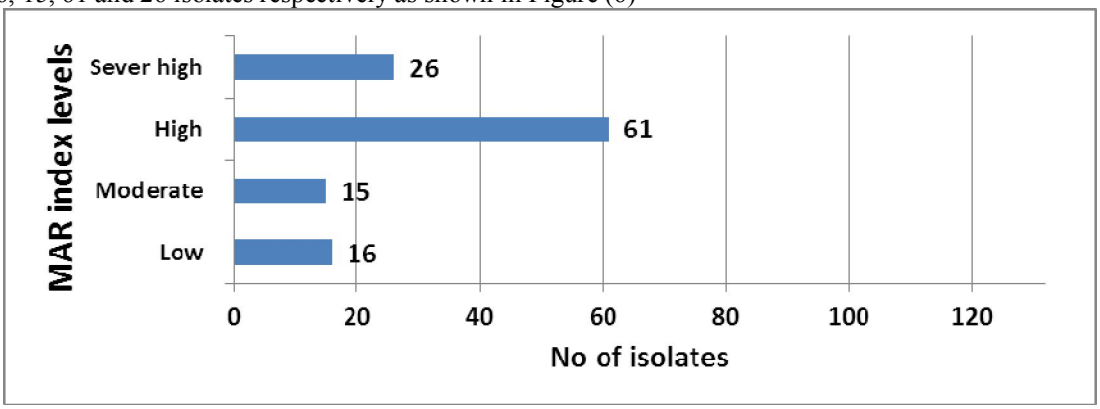

Figure (6): Relationship between MAR index levels and number of isolates

MAR index values of each antimicrobial agent are shown in Figure (7). MAR index values ranged from 0,0009 and 0.416. This figure shows that imipenem, amikacin, gentamicin and meropenem are the most effective drugs on ceftazidime resistant E.coli isolates as these antimicrobials had the least MAR index values of 0.0009, 0.0022, 0.0041 and 0.005 respectively.

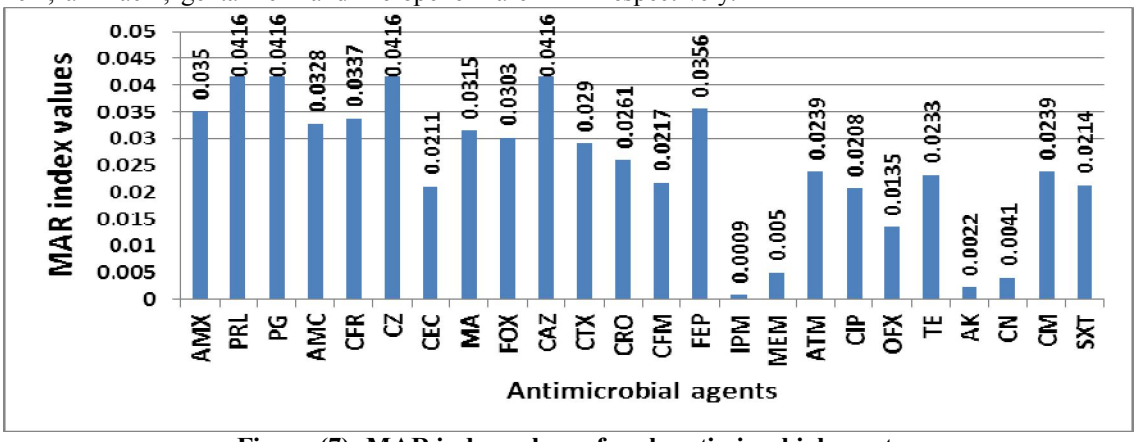

Figure (7): MAR index values of each antimicrobial agent

(AMX) Amoxicillin, (PRL) Pipracillin, (P) Penicillin G, (AMC) Amoxicillin/Clavulinicacid, (CZ) Cefazolin, (CEC) Cefaclor, (CFR) Cefadroxil, (MA) Cefamandolin, (FOX) Cefoxetin, (CTX) Cefotaxime, (CAZ) Ceftazidime, (CRO) Ciprofloxacin, (CFM) Cefixime, (FEP) Cefepime, (MEM) Meropenem, (IPM) Imipenem, (ATM) Azetreonam, (OFx) Ofloxacin, (TE) Tetracyclin, (AK) Amikacin, (CN) Gentamycin, (CM) Chloramphenicol, (CIP) Ciprofloxacin, (SXT) Trimethoprim/Sulphamethaxole

In present study, MAR index values of each antimicrobial agent can be divided to three levels, (high MAR index values, moderate MAR index values and low MAR index values) shown in Figure (8).

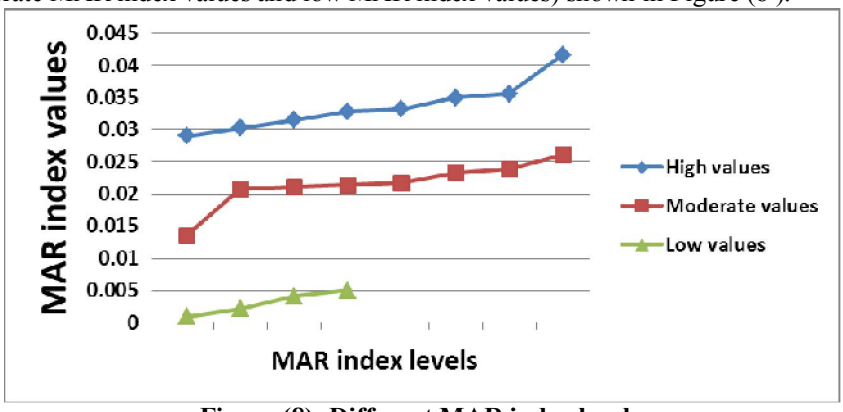

Figure (8): Different MAR index levels

High MAR index values of each antimicrobial agent were ranged from 0.029 to 0.0416. It found that the tested isolates were high resist to cefotaxime, cefoxitin, cefamandolin, amoxicillin/clavulanic acid, cefadroxile, amoxicillin, cefepime, pipracillin, penicillin G, cefazolin and ceftazidime as shown in Figure (9).

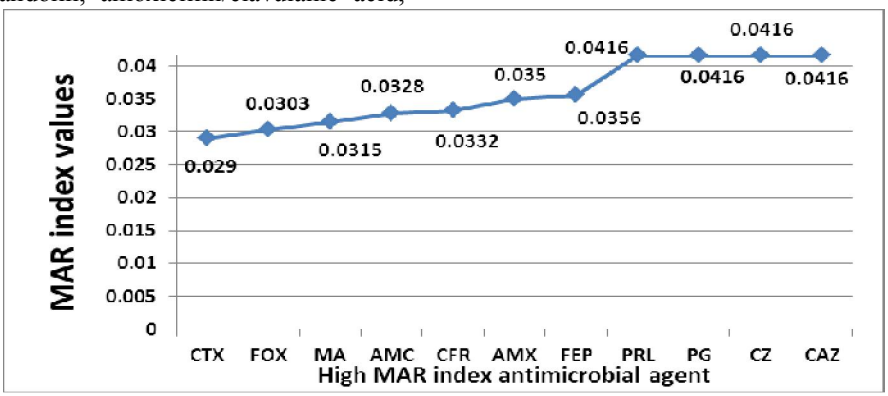

Figure (9): High MAR index antimicrobial agents

(CTX: cefotaxime, FOX: cefoxitin, MA: cefamandolin, AMC: amoxicillin/clavulanic acid, CFR: cefadroxile, AMX: amoxicillin, FEP: cefepime, PRL: pipracillin, PG: penicillin G, CZ: cefazolin, CAZ: ceftazidime.

Moderate MAR index values of each antimicrobial agent were ranged from 0.0135 to 0.0261. It found that the tested isolates were moderate resist to ofloxacin, ciprofloxacin, cefaclor, trimethoprime/Sulphamethaxole, cefexime, tetracyclines, azetreonam, chloramphenicol and ceftriaxone as shown in Figure (10).

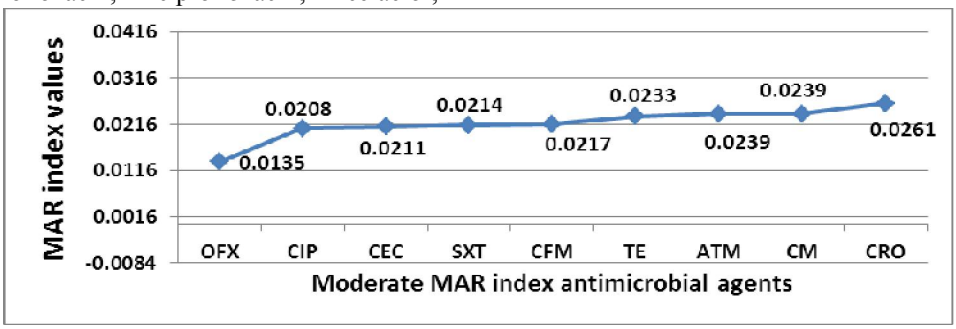

Figure (10): Moderate MAR index antimicrobial agents

(OFX: ofloxacin, CIP: ciprofloxacin, CEC: cefaclor, SXT: trimethoprime/Sulphamethaxole, CFM: cefexime, TE: tetracyclines, ATM: azetreonam, CM: Chloramphenicol, CRO: Ceftriaxone

Low MAR index values of each antimicrobial agent were ranged from 0.0009 to 0.005. It found that the tested isolates were low resist to imipenem, amikacin, gentamicin, meropenem as shown in Figure (11).

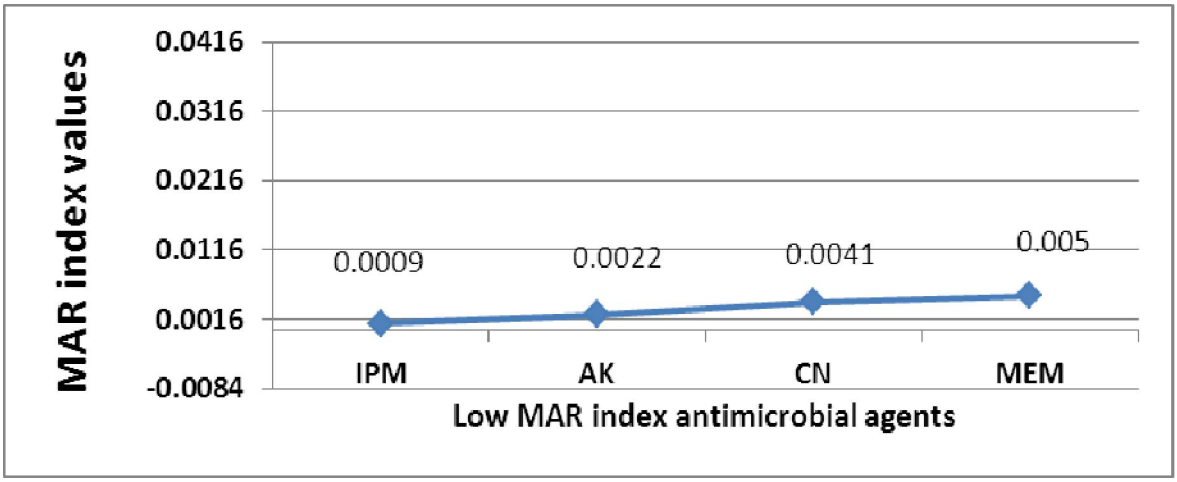

Figure (11): Low MAR index antimicrobial agents
(IPM: imipenem, AK: amikacin, CN: gentamicin, MEM: Meropenem)

From the above data, the isolate that showed resistance to at least one agent in ≥ 3 antimicrobial categories was considered MDR. Accordingly, 84 (63.63%) ceftazidime resistant *E.coli* isolates exhibited MDR character, 66 (50%) ceftazidime resistant *E.coli* isolates were extensively drug resistant (XDR) and there is no PDR isolates as shown in Figure (12).

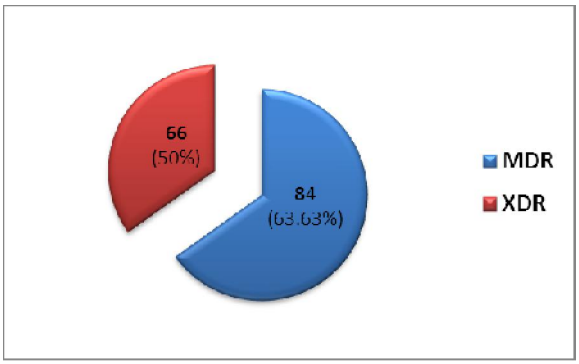

Figure (12): Incidence of MDR and XDR

4. Discussion:

In present study, a total of 132*E.coli* isolates collected from patients suffering from UTIs attending from Shebien El Kom Teaching Hospitals, and Monofeya University Hospitals from May 2014 till August 2016. Isolates were determined as *E.coli* by culturing on MacConkey's agar, gram staining, conventional biochemical identification tests and Microbact 12A™ biochemical identification kits. This kit offers manual identification of microorganisms for: Infectious disease diagnosis and identification of important industrial microorganisms and strips give accurate identifications based on extensive databases and are standardized, easy-to-use test systems.

The present study focused on assessment of the efficacy of 24 different antimicrobial agents by using disc diffusion method. In present study, based on the previous disc diffusion data, the patterns of resistance of all Ceftazidime resistant *E.coli* isolates to the studied antimicrobial drugs were determined. *E.coli* isolates exhibited 15 major resistance patterns according to number of resistance markers and each pattern included subpatterns or subgroups **(Magiorakos *et al*., 2012).** All isolates were resistant to up to 6-22 out of the tested 24 antimicrobial agents. Tested isolates were very heterogeneous where not more than 7 isolates shared the same resistance pattern.

It worth mentioning that antimicrobial resistance among the tested isolates was very heterogeneous where not more than 7 of *E.coli* tested isolates exhibited the same resistance pattern. All isolates were group into 15 resistance patterns according to number of resistance markers and each pattern included subpatterns or subgroups **(Magiorakos *et al*., 2012)**, depending upon their resistance profiles to different

antimicrobial agents. All isolates were resistant to up to 6-22 out of the tested 24 antimicrobial agents. Tested isolates were very heterogeneous where not more than 7 isolates shared the same resistance pattern.

MAR index is a tool to analyze health risk and is helpful to check the spread of bacterial resistance in a given population **(Osundiya *et al.*, 2013).** Analysis of MAR index of isolates revealed that (96.21%) isolates a high MAR index value (> 0.2). This suggested that all isolates would have originated from a high risk source of contamination. Only 5 isolates ranged between 0.2 and 0.25 are in a range of ambiguity, and samples in this range require careful scrutiny. According to **(Krumperman. 1983)** the choice of MAR index of 0.2 to differentiate between low and high risks contamination is arbitrary. Indices between 0.2 and 0.25 are in a range of ambiguity, and samples in this range require careful scrutiny. The MAR indexing of the isolates in our study ranged from 0.33 to 1 and it is greater than 0.25 and probability originated from high risk source of contamination. **(Chandran *et al.,2008*) and (*Ranjini et al., 2015*)**.

In present study, MAR index values were ranged from 0.25 to 0.916 and this finding agreed with results detected by ***(*Chandran *et al.,2008*)** in India which MAR index values ranged from 0.25 to 1 and by **(*Sharma et al., 2013*)** ranged from 0 to 1. In our study, there is no PDR isolates and this result not agreed with **(Chandran *et al.,*2008**) in India which recorded only one isolate was PDR and by **(Sharma *et al., 2013*)** recorded 5 isolates exhibited 1 MAR index value and were considered PDR. The MAR indices of *E. coli* obtained in this study is a possible indication that a very large proportion of the bacterial isolates have been exposed to several antibiotics.

Unfortunately, low, moderate, high and sever high MAR index values of isolates exhibited number of markers of antimicrobial agents which were up to 9, 12, 18 and 22 respectively and the number of isolates exhibiting low, moderate, high and sever high MAR index values were 16, 15, 61 and 26 isolates respectively, from this data, major of tested isolates 87/132 (65.90%) were resist to high number of antimicrobial agent ranged from 13 to 22 antimicrobial agents. So, this is possible indication for a very large proportion of the bacterial isolates have been exposed to several antibiotics.

Unfortunately, high MAR index values of antimicrobial agents ranged from 0.029 to 0.0416 which included cefotaxime, cefoxitin, cefamandolin, amoxicillin/clavulanic acid, cefadroxile, amoxicillin, cefepime, pipracillin, penicillin G, cefazolin and ceftazidime, so tested isolates were high resist to penicillins, 1st generation cephalosporins and some of 2nd, 3rd generation cephalosporins and 4th generation cephalosporin.

Moderate MAR index values of antimicrobial agents ranged from 0.0135 to 0.0261 which included ofloxacin, ciprofloxacin, cefaclor, trimethoprime/Sulphamethaxole, cefexime, tetracyclines, azetreonam, chloramphenicol and ceftriaxone, so it found that the tested isolates were moderate resist to quinolones, sulfonamides, tetracycline, chloramphenicol, monobactam and some of 2nd & 3rd generation cephalosporins.

In contrast, low MAR index values of antimicrobial agents ranged from 0.0009 to 0.005. It found that the tested isolates were low resist to imipenem, amikacin, gentamicin, Meropenem. So, carpabenems and aminoglcosides are the most effective drugs against urinary tract infections by uropathogenic *E.coli* and this finding agreed with **(Anago *et al*., 2015)** and **(Zaki. 2007).**

The Multi-Drug Resistance (MDR) character of the isolates was identified by observing the resistance pattern of the isolates to the tested antibiotics. Multiresistance was considered on the basis that the studied clinical isolates were resistant to antibiotics belonging to at least 3 classes and up to all tested antibiotics **(El-Nakeeb *et al*., 2011).**

In present study, number of MDR isolates was 63.63% and was agreed with the result of **(Zakaria *et al.,* 2015)** in Ismailia-Egyptwhich found that near to 93% of the Isolated *E.coli* were multidrug resistant (MDR) and **(Shalaby *et al.,* 2016)** in Cairo found that 52 % was MDR.

The findings alarm to a serious impact in limiting the selection of treatment drug. This finding corroborated with the study reported by **(Mubita *et al*., 2008)**, who reported that both clinical and environmental strains displayed MDR phenotype to most of the previously mentioned antibiotics. Many authors documented that the use of antibiotics is strongly associated with the prevalence of antimicrobial resistance in *E. coli* isolates in food-producing animals **(kang *et al*., 2005).**

The current results were in harmony with other studies from Egypt **(Shaheen *et al*., 2004) and (Putnam *et al*.,2004)** and different parts of the world **(Okeke *et al*.,2000), (Hoge *et al*., 1998), (Shapiro *et al.,* 2001) and (Turner *et al*., 1998).** There is an increasing isolation rate of MDR strains belonged to enteropathogenic *E. coli* in Nigeria **(Okeke *et al*., 2000),** Thailand **(Hoge *et al*., 1998),** Kenya **(Shapiro *et al*., 2001)** and Israel **(Turner *et al*., 1998)**, 90.8% by **(Sharma *et al., 2013*)** and in India **(Ranjini *et al., 2015*) and (Chandran *et al*., 2008)** reported that 82.6% and 92% respectively of *E.coli* isolates were MDR. A total of 66 (50%) ceftazidime resistant *E.coli*

isolates were extensively drug resistant (XDR) and there is no PDR isolates.

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