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NOSOCOMIAL BLOOD STREAM INFECTIONS IN ADULT PATIENTS ADMITTED TO AL JUMHORIA HOSPITAL -BENGHAZI-LIBYA

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Abstract:-

As little information of antibiotic resistance in Libya is known.This study included 937 patients admitted to Al Jamhoryia hospital, Benghazi during 20092010.The results showed that rate of nosocomial blood stream infection (BSI) was 28% in 2009 and 27% in 2010 with the highest percentage of ICU (61%) in 2009. This study also showed that in 2009, the most frequently isolated bacteria among staphylococci was methicillin resistance Staphylococcus aureus (MRSA). However methicillin resistant Coagulase negative staphylococci accounted for (27.4%) Klebsiellapneumoniaere presented the highest percentage followed by Escherichia coli, S. hominis, S. aurues, S. epidermides, and Acinetobacterbaumannii. The rate of infection recorded in 2010 was (52.5%). This study showed that MRSA was the most prevalent pathogen. S. aurues isolates represented the highest percentage among all bacteria isolated (24.8%) followed by E. coli % S. hominis and S. epidermides. The occurrence of Extended Spectrum Beta-lactamase (ESBL) producing bacteria was 15.9% and 14.9% in 2009 and 2010 respectively. Antimicrobial sensitivity testing showed that Grampositive isolates exhibited higher sensitivity patterns toward Rifampin (95.8%) followed by Teicoplanin (91.6%), Ciprofloxacin (90.2%), Vancomycin (87.4%), and Linezolid (84). High rate of resistance was observed against penicillins and 3rd generation cephalosporins. The rate of antibiotic resistant bacteria causing NBSI is increasing among Grampositive and negative bacteria and creates a serious health problem in hospitals.

Keywords:-*Nosocomial blood stream, Intensive care unit, Methicillin resistance staphylococcusaureus, Antibiotic Susceptibility.*

INTRODUCTION:

Nosocomial infections (NIs) are infections that became clinically evident after 48 hours of hospitalization and was not originated from patient's original admitting diagnosis [1-3]. In the last few years these infections cause significant morbidity and mortality and have a considerable impact on health care costs indeed, among all types of NIs, nosocomial blood stream infection (BSI) creates a serious health problem in hospitals all over the world. In addition, patients admitted to intensive care units (ICU) carry an even higher risk of nosocomial (BSI) than those admitted to other types of units [47]. Nosocomial BSI is the 10th leading cause of death in the U.S.A approximately 250,000 cases of BSI occur in the U.S.A annually [8, 9].

Methicillin resistant ***Staphylococcus aureus*** (MRSA) is the most widely prevalent pathogen among NBSI followed by Methicillin resistant Coagulase negative ***Staphylococci*** [6, 7]. For many years, MRSA has been prominent among hospital-acquired microorganisms responsible for nosocomial infections Of 65% of ***S. aureus*** blood-stream isolates were resistant to methicillin [10, 11] . On the other hand, the incidence of methicillin resistance was also high among coagulase negative ***staphylococci***, with 53% of CNS being resistant to methicillin coincides, where the MRSA rate was(46%) invasive ***S. aureus*** infection is increasingly recognized as an important cause of serious sepsis across the developing world, with mortality rates higher than those in the developed world the prevalence of MRSA among both nosocomial and community-acquired infections has increased throughout the world and the factors determining mortality in developing countries have not been identified [12-14].

Acinetobacterspp have been implicated in a variety of nosocomial infections including blood stream infection (BSI), ***pneumonia***, ***meningitis***, intravascular devices and implant treated infection and its resistance to commonly used antimicrobial agents is arising problem, also A. baumannii may survive much longer on inanimate environmental surfaces [8,15,16] .

Different studies demonstrated that ***Acinetobacter*** infection associated with high mortality rates as high as 17–52% in BSI ,increased duration of intensive care admission and increase cost of care, the risk factors for ***Acinetobacter*** BSI include prior exposure to antimicrobial agents such **as penicillins**, **aminoglycosides** and **cephalosporins**, **mechanical ventilation**, presence of nasogastric tube, arterial catheter and urinary catheter [8,15,17,18]

K.pneumoniae is an important bacterial pathogen associated with community and nosocomial infections especially in immune compromised patients to cause severe morbidity and mortality, particularly in ICU and pediatric and surgical wards with the emergence of multidrug-resistant (MDR) and extended-spectrum β-lactamase (ESBL) producing ***Klebsiellapneumoniae*** poses a serious antibiotic management problem as resistance genes are easily transferred from one organism to another [19-23]

Several authors reported that mortality and morbidity are greater when caused by antimicrobial-resistant bacteria. Enterobacteriaceae and non-fermentative Gram-negative bacilli are great of concern because antimicrobial therapy for infections due to these resistant pathogens remains a clinical dilemma in hospitalized patients It is also noted that there is an increase in the resistance among Gram-negative bacilli to third generation cephalosporin's which is caused by expression of Extended-Spectrum β-lactamase (ESBL) enzymes [14][24-31]. However, few data exist on bacteria that cause blood stream infection in the studied hospitals. This study was designed to determine the prevalence of bacteria that cause blood stream infection in Al Jamhoryia hospital, Benghazi-Libya and its susceptibility to the commonly used antibiotics.

Materials and methods

Patients:

The study was conducted over a period of 24 month (from January 2009 to December 2010) on 937 patients were admitted at different medical units of the hospital including Coronary care units (CCU), isolation units (ISO), neurological units(B.C), Medicine units(B.B), intensive care units (ICU), gynecology units(G.B), oncology units and hematology units(B.A). All patients admitted to units were monitored daily by attending physicians for subsequent development of nosocomial BSI, which must meet at least one of the following criteria; the first that the Patient has at least one of the following signs or symptoms: fever (38°C), chills, or hypotension, the second criteria was that the Patient has a recognized pathogen cultured from one or more blood cultures and the organism cultured from blood is not related to an infection at another site.

Sample collection:

Blood samples: 5 to10 ml of venous blood were collected from patients using sterile syringes. Blood samples were inoculated immediately under complete aseptic conditions into bottles containing 50 ml of brain heart infusion broth. The purpose of using cultural techniques in microbiology is to demonstrate the presence of micro-organisms that may cause disease, and to test the susceptibility of pathogens to antimicrobial agents. Blood culture bottles were incubated aerobically at 37°C for 5days; the bottles were examined daily for evidence of bacterial growth as haemolysis, gas production or turbidity above the red cell line. Subcultures using sterile syringes were performed daily for 5 days before reporting blood cultures as negative. Isolation of anaerobes is not considered. All bacterial isolates were stain using Gram staining technique to differentiate either Gram negative or Gram positive. Culture media used were blood Agar, Chocolate Agar MacConkey Agar.

According to the protocol of infection control lab, the following antibiotics were used-:

Antimicrobials for Gram positive -bacteria-:

- B-Lactams (Ampicillin, Penicillin G, Cefoxitin, Amoxicillin/clavulanic acid, Ceftriaxone, Cefotaxime ,Oxacilin and Imipenem).
- Macrolides (Erythromycin and clarithromycin).
- Aminoglycosides (Gentamicin -syn, Gentamicin).
- Tetracyclines (Tetracycline).
- Quinolones (Ciprofloxacin,).
- Others (Clindamycin,Vancomycin,Teicoplanin, Trimethoprim / sulfamethoxazole, Daptomycin,Linezolid).

Antimicrobials for Gram negative –bacteria-:

- β-Lactams (Ampicillin, Cephalothin, Cefoxitin,Amoxicillin / clavulanic acid, ,Ceftazidime, Piperacillin, Cefotaxime, Cefepime, Cefuroxime, Aztreonam, Imipenem and Meroprnem).
- Aminoglycosides (Amikacin, Gentamicin,).
- Tetracyclines (Tetracycline).
- Quinolones (Ciprofloxacin,).
- Others (Trimethoprim/sulfamethoxazole, Colistin, Piperacillin-Tazobactam)

Detection of β-lactamase and extended spectrum β-lactamase enzymes and MRSA B lactamase enzyme produced by some Gram positive cocci and extended spectrum B – lactamase enzyme produced among some Gram- negative bacilli were detected by using of Phonex technique .and Detection of MRSA was performed by Phoenix technique. -Data analysis; Data were analyzed by using statistical package for social science (SPSS) version 18.

Table 1: Distribution of bacterial isolates collected in 2009.

Type of pathogen	Gram-positive		Gram-negative	
	NO	%	NO	%
A.bummannii			14	8.9%
E. coli			20	12.7%
E. cloace			1	0.6%
E. casseliflavus	1	0.6%		
E. faecalis	7	4.5%		
K. pneumonia			25	15.9%
K. oxetoca			1	0.6%
S. aurues	17	10.8%		
S. epidermidis	15	9.6%		
S. haemolyticus	4	2.5%		
S. hominis	18	11.5%		
S. warenrii	5	3.2%		
S. saprophyticus	6	3.8%		
S. cohnii	1	0.6%		
S. capitis	9	5.7%		
S. marcscense			7	4.5%
S. typhii			3	1.9%
P. aeruginosa			3	1.9%
Total	83	52.9%	74	47.1%

RESULTS:

The results showed that the rate of nosocomial (BSI) in 2009 was(28%) ,while the infection rate in 2010 was (27%) with the highest percentages (61%) in ICU in 2009, however in 2010 the infection rate was lower (52.5%) . Of all positive cases of the bacterial isolates for BSI occurrence of Gram-positive bacteria reached (52.9%). This study also showed that methicillin resistant ***S. aureus*** (MRSA) represented (5.7%) from all bacterial isolates tested. However methicillin resistant coagulase negative ***Staphylococci***occurred high percentage (27.4%) than MRSA. Gram negative- bacilli were reported in 2009 as (47.1%). In 2010 analysis occurrence micro-organisms causing BSI showed that Gram positive were reported as (59.4%). ***MRSA*** was the most prevalent (13.9%), whereas methicillin resistant coagulase negative ***Staphylococci*** rate was (28.7%). In 2010 the percentage of Gram- negative was reported as(40.6%).This study showed that Gram- negative producing ESBLs was counted (15.9%) in 2009, (14.9%) in 2010.

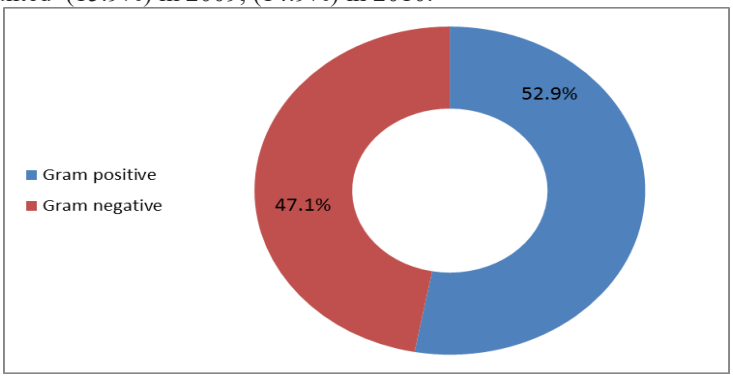

Figure 1 Distribution of bacterial isolates collected in 2009.

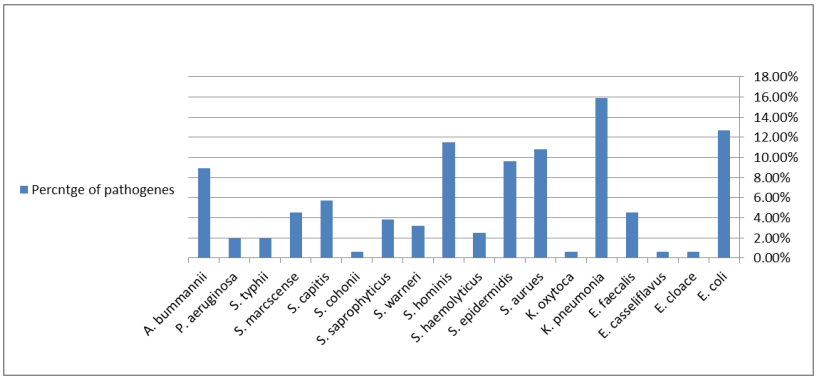

Figure 2 Distribution of bacterial isolates collected in 2009

Distribution of bacterial isolates:

Distrubution of bacterial isolates in 2009 was BSI causing by Gram- positive bacteria was higher (52.9%) more than Gram negative bacteria (47.1%) as shown in figure 1

K.pneumonia represented the highest percentage (15.9%) followed by ***E.coli*** (12.7%), ***S.aurues*** (10.8%) and ***Enterobacterspp*** were (0.6%) as shown in figure.2. Distribution of bacterial isolates collected in 2010 shown in table 2, the percentage of Gram positive bacteria isolated) 59.4%) in 2010 was higher than in 2009 (6.5%) was (40.6%). Among all isolates collected in 2010 ***S.aurues*** represented the highest percentage (24.8%) followed by *E .coli* (15.8%), ***K.pneumonia*** (11.9%), and ***Enterobacterspp*** were (1.0%).

Table 2: Distribution of bacterial isolates collected in 2010.

Type of pathogen	Gram-positive		Gram-negative	
	NO	%	NO	%
A. bummannii			7	6.9%
E. coli			16	15.8%
E. cloace			1	1.0%
K. pneumonia			12	11.9%
K. oxetoca			1	1.0%
S. aurues	25	24.8%		
S. epidermidis	13	12.9 %		
S. haemolyticus	3	3.0%		
S. hominis	13	12.9%		
S. kloosii	1	1.0%		
S. capitis	3	3.0%		
S. marcscense			4	4.0%
S. pneumoniae	2	2.0%		
Total	60	59.4%	41	40.6%

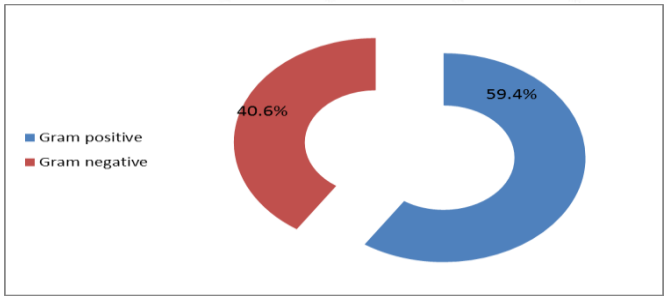

Figure 3 Distribution of bacterial isolates collected in 2010

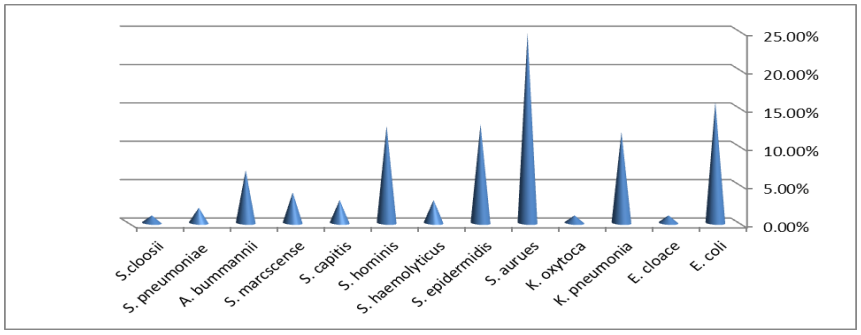

Figure 4 Distribution of bacterial isolates collected in 2010

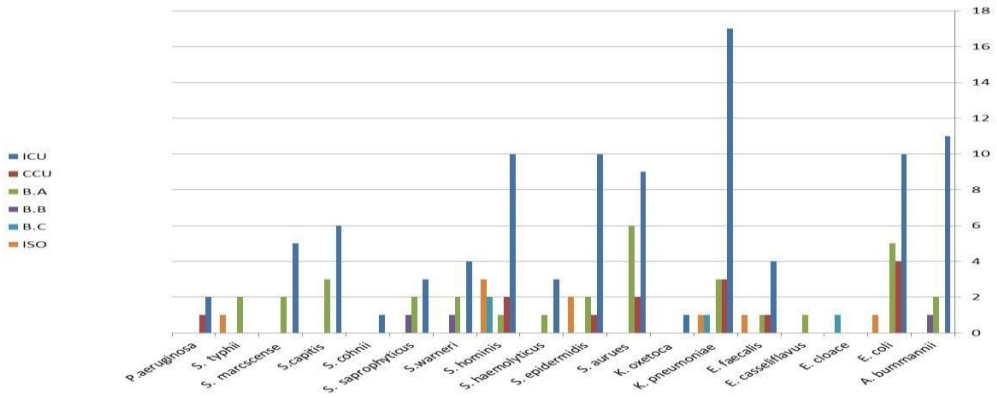

Fig 5 Distribution of bacteria according to departments in 2009

This study clearly demonstrated that BSI in ICU the highest compared other departments (61.1%) and the most causative bacterial agent was ***K.pneumoniae*** (10.8%) followed by ***A.baumannii*** (7.0%) whereas the spread of BSI was equal for ***E. coli***, ***S.epidermides***, ***S.hominis*** (6.4%) respectively ***S.aureus*** (5.7%) and ***K.oxetyaca*** (0.6%) as shown in figure.5 The prevalence of BSI causing bacteria according to departments in 2010 is shown in figure 6 During this study was highest infection occurred in ICU (52.5%), followed by CCU (8.8 %).

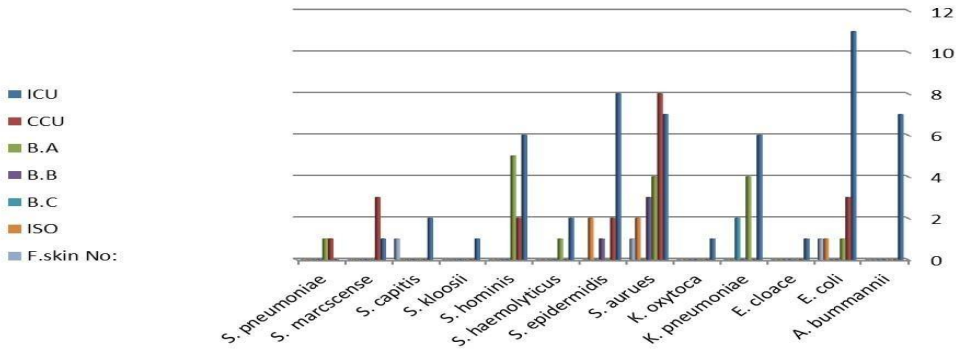

Figure 6 Distribution of bacterial isolates according to Departments in 2010.

According to the results shown in fig 6 the ICU recorded the highest occurrence of BSI than another departments (52.5%) and the most causative bacterial agent was ***E. coli*** (10.9%*)* followed by ***S.epidermides*** (7.9%), ***A.baumannii*** and ***S.aureus*** (6.9%) whereas the percentage of infection was equal for***K.pneumoniae*** (5.9%), ***S.hominis*** (5.9%) on the other hand the rate of infection was low by ***S.marcscens*** ,***K oxytoca*** and***S.kloosii*** (1.0%) .

Distribution of bacterial isolates according to production of resistance enzymes in 2009

The rate of Staphylococci producing (BLCT) enzymesa (7.%) is shown in table 5**. S.*aurues*** was the most frequently isolated strains (3.2%) than any other coagulase negative Staphylococci followed by ***S.hominis***(1.9%). whereas the rate of prevalence of (MRS) was (33.1%). The incidenc of coagulase negative *Staphylococci* was by ***S.epidermidis*** and ***S.hominis*** (8.3%) followed by ***S.aurues*** (5.7%).

The rate of prevalence of ***Klebsiella*spp** and ***E. coli*** producing (ESBL) enzyme was high (15.9%). ***K.pneumoniae*** producing (ESBL) enzyme occurred for (9.6%) followed by ***E. coli*** (5.7%) as shown in figure 9.

Distribution of bacterial isolates according to production of resistance enzymes in 2010.

The rate of Staphylococci producing (BLCT) enzymes was (14.9%) ***S.aurues*** producing (BLCT) enzyme was more than other coagulase negative Staphylococci producing (BLCT) enzyme (10.9%) followed by ***S.hominis*** (3.0%), Wherase the rate of prevalence of (MRS) was very high (42.6%). MRSA was more than another coagulase negative Staphyiococci .This study also showed the rate of prevalence of ***Klebsiellaspp*** and ***E. coli***producing ESBL enzymes was high (14.9%) Tab 6, fig 10.

Table 3 Prevalence of Gram- positive isolates according to susceptibility to antimicrobials agents

Antimicrobial	Susceptible	Intermediate	Resistant
Imepinim	25.2%		74.8%
Cefotaxim	3.5%	2.1%	94.4%
Ampicillin	0.7%		99.3%
Penicillin	6.3%		93.7%
Augmentin	35.0%		65.0%
Daptomycin	65.0%		35.0%
Trimethoprim-	86.0%	2.1%	11.9%
Teicoplanin	91.6%	3.5%	4.9%
Vancomycin	87.4%	2.1%	10.5%
Ciprofloxacin	90.2%	2.8%	7.0%
Rifampin	95.8%	0.7%	3.5%

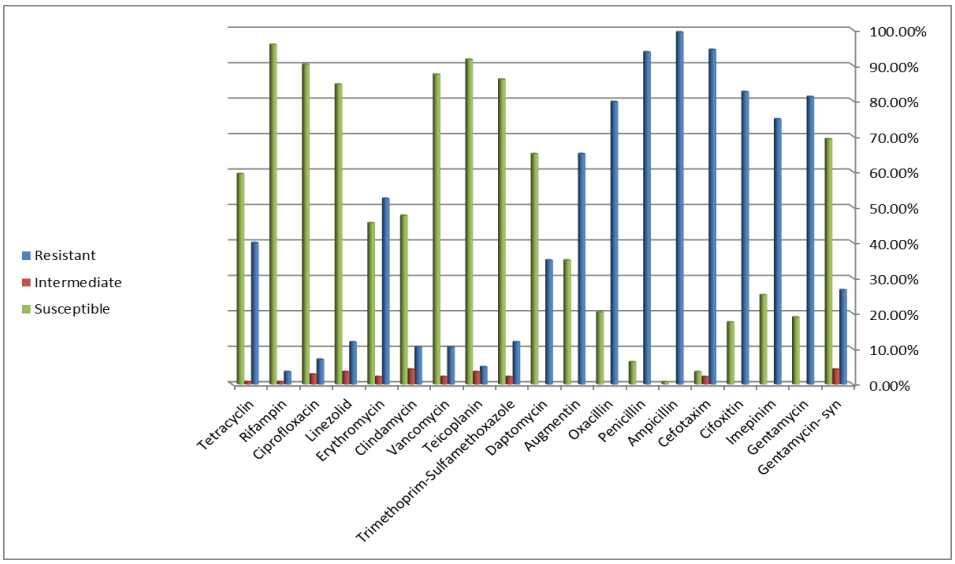

Figure 7 Prevalence of Gram- positive isolates according to Susceptibility to antimicrobials agents

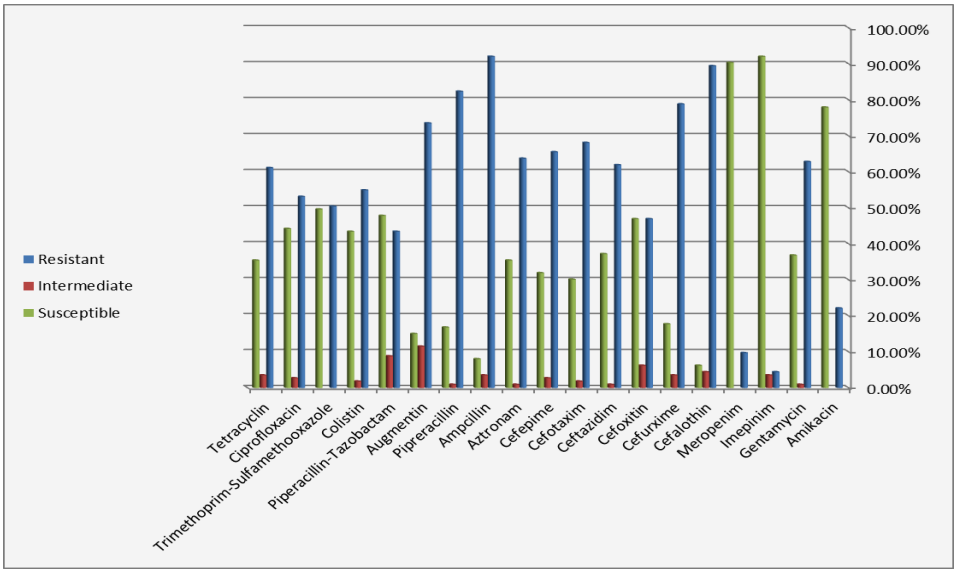

Figure 8 Prevalence of Gram- negative isolates according to susceptibility to antimicrobials agents

Prevalence of Gram-positive isolates according susceptibility antimicrobials agents:
These results show that rifampin was the most effective antibacterial (95.8%) against Gram-positive isolates followed by**teicoplanin** (91.6%) ciprofloxacin (90.2%), v**ancomycin** (87.4%), t**rimethoprim- sulfamethoxazole** (86.0%), g**entamicin syne** (69.2%), **daptomycin** (65.%) , (6.3%) and **ampcillin**(0.7%) . Fig. 7.
Prevalence of Gram -negative isolates according to susceptibility to antimicrobials agents. Table 4 showed the most antibacterial effect wasi**mepenim** by (92.0%) followed by **meropenem** (90.3%), **amikacin** (77.9%) t**rimeyhoprim - salfamethoxaole** (49.6%), **piperacillin /tazobctam** (47.8%) ,**augmentin** (15.0%) , **ampcillin** (8.0%) and **cephalothin** (6.2%).

Table 4 Prevalence of Gram- negative isolates according to susceptibility to antimicrobials agents

Antimicrobial	Susceptible	Intermediate	Resistant
Amikacin	77.9%		22.1%
Gentamycin	36.8%	0.9%	62.8%
Imepinim	92.0%	3.5%	4.4%
Meropenim	90.3%		9.7%
Cefotaxim	30.1%	1.8%	68.1%
Cefepime	31.9%	2.7%	65.5%
Ampcillin	8.0%	3.5%	92.0%
Pipreracillin	16.8%	0.9%	82.3%
Augmentin	15.0%	11.5%	73.5%
Piperacillin-Tazobactam	47.8%	8.8%	43.4%
Trimethoprim-	49.6%		50.4%
Ciprofloxacin	44.2%	2.7%	53.1%

Table 5: Distribution of bacterial isolates according to production of resistance enzymes in 2009.

Type of pathogen	Non No: (%)	ESBL No: (%)	BLCT- No: (%)	MRS No: (%)	Total No: (%)
E. coli	11 7.0%	9 5.7%			20 12.7%
K. pneumoniae	10 6.4%	15 9.6%			25 15.9%
K. oxytoca		1 0.6%			1 0.6%
S. aurues	3 1.9%		5 3.2%	9 5.7%	17 10.8%
S. epidermidis	1 0.6%		1 0.6%	13 8.3%	15 9.6%
S. hominis	2 1.3%		3 1.9%	13 8.3%	18 11.5%

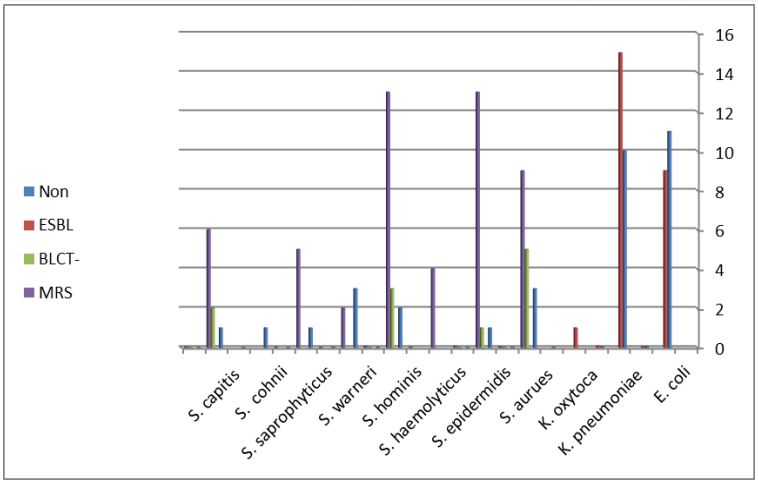

Figure 9 Distribution of bacterial isolates according to production of resistance enzymes in 2009

Table 6 Distribution of bacterial isolates according to production of resistance enzymes in 2010.

Type of pathogen	Non No. (%)	ESBL No: (%)	BLCT-- No: (%)	MRS No: (%)	Total No: (%)
E. coli	9 8.9%	7 6.9%			16 15.8%
K. pneumoniae	5 5.0%	7 6.9%			12 11.9%
K. oxytoca		1 1.0%			1 1.0%
S. aurues			11 10.9%	14 13.9%	25 24.8%
S. epidermidis			1 1.0%	12 11.9%	13 12.9%
S.hominis			3 3.0%	10 9.9%	18 11.5%

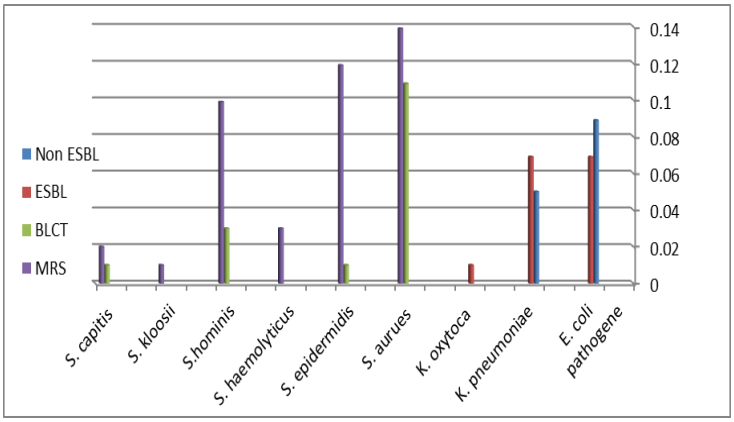

Figure 10 Distribution of bacterial isolates according to the production of resistance enzymes in 2010

Discussion:

Nosocomial BSI represents a current problem in the hospitals worldwide. Problems associated with BSI include infection with multidrug resistant pathogens especially (ESBLs) which are difficult to treat. In the present study showed that the rate of nosocomial BSI was the highest percentage (61%) in ICU in 2009 and (52.5%) in 2010 [5]. The leading pathogens caused clinically significant nosocomial BSI in this study during 2010, were coagulase negative staphylococci (34.8%) and ***S.aureus*** (24.8%) these results are similar to the SCOPE (Surveillance and Control of Pathogens of Epidemiologic Importance) which revealed that the most common pathogens causing nosocomial (BSI) were coagulase-negative staphylococci (32%) and ***S.aureus***(16%). In addition, data published from the National Nosocomial Infections Surveillance System (NNIS) for ICU-associated primary blood stream infections identified coagulase-negative staphylococci (37%) and ***S.aureus*** (12.6%) as the leading pathogens of (BSI).

The leading pathogens causing clinically significant nosocomial BSI in this study during 2009 were ***K.pneumoniae*** (15.9%) followed by ***E. coli*** (12.7) similar results was found by Ahmad *et al* .(2009) who reported that the most common Gram- negative causative agent was ***K.pneumoniae*** (10.3%) followed by ***E. coli*** (8.6%) . These results are similar to recent nosocomial BSI studies [32]. who found that Gram-negative pathogens and the leading cause of (BSI) .
Antibiotic resistance is a growing problem in hospitals everywhere,[26] .This study showed that (19.6%) of the ***S.aureus*** isolated from blood-stream were resistant to methicillin . The incidence of methicillin resistance was also high among coagulase negative (CNS) being resistant to methicillin, with percentage (55.2%), coincides with that reported in a French general hospital, where the rate of (MRSA) rate was (46%) [6] .who found that (65%) of the ***S.aureus*** bloodstream isolates were resistant to methicillin.

Gram – negative rods showed high resistance rates against the majority of antimicrobial agents. This may be explained by the late introduction of infection control programs in studied hospital, and the high percentage of extended spectrum beta lactamases among Gram- negative bacilli reach (30.8%) in Jumohouria hospital, which limits the therapeutic options in infections caused by such strains due to two broad factors: cross-resistance (e.g. to aminoglycosides or fluoroquinolones) and the high hydrolytic affecting of these enzymes. The results of this work are similar to the work conducted by reference [6]. Who reported that high percentage of extended spectrum beta lactamases among Gram-negative bacilli (64.7%) could limit the therapeutic options in infections caused by Gram-negative isolates.

The present study also showed that among all ***K.pneumoniae*** isolated there were 22 (MDR) (16.5%). resistant to three or more classes of antimicrobial agents. In contrast,with reference [19] , reported that the rate of (MDR) ***K.pneumoniae*** strains in Malaysia is relatively low (53 %) when compared to the (94%) .

Acinetobacterspp is one of the most important pathogens in clinical practice, in this study the prevalence of Acinetobacter BSI in Jumhoria hospital was (15.8%) and in ICU was (13.9%) in both years. These findings are comparable with previous study of Dersi[19] who reported that the prevalence of Acinetobacter BSI in Hospital UniversitiSains Malaysia(HUSM) was (6.11%) and in ICU was (8.32%). However, there were other previous studies in ICU that showed higher prevalence (10.2-18.0%) [34, 33, 35].

In this study 19 antimicrobial agents tested against blood isolates of ***Acinetobacterspp*** in Jumohouria hospital. Four active antimicrobial agents were amikacin, imipenem, meropenim and colistin. Most of the penicillins andcephalosporins were not active against ***Acinetobacter spp***. similar Deris[19] reported that performance of 16 antimicrobial agents tested against blood isolates of ***Acinetobacter spp***. in HUSM show that five active antimicrobial agents with susceptibility equal or more than 70% were amikacin ciprofloxacin, imipenem, netilmycinandcefoperazone / sulbactam. Most of the penicillin sand cephalosporins were not active against Acinetobacter spp. With susceptibility less than 60%.

Conclusion:

The results showed that the rate of nosocomial (BSI) was (28%) in 2009, while the infection rate in 2010 was (27%) with the highest percentages (61%) in ICU in (2009). However in 2010 the infection rate in (ICU) was 52.5%. Nosocomial (BSI) represents a current problem in Jumhoria Hospital. Problem associated with (BSI) include infection with multidrug resistant pathogens particularly ESBLs which are difficult to treatments.
K.pneumoniae represent the highest percentage reach to (15.9%) among all bacteria isolated in 2009 while ***S.aurues*** represented the highest percentage among all bacteria isolated (24.8%) in 2010.
Carbapenems are the most active and reliable treatment options for infections caused by ESBL producing isolates, however, overuse of carbapenems may lead to resistance of other Gram -negative organisms.
Rifampin is the most active treatment options for Gram positive isolated bacteria. This study showed that MRSA which known of prevalent bacteria represent infection reach (19.6%) from all bacteria. During this study methicillin resistant coagulase negative Staphylococci occurred in high percent (56.1%) than (MRSA). Also showed that the percent Gram-negative isolates for the production of the (ESBL) enzyme reach to (30.8%.

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