COMMON BACTERIAL ORGANISMS IN CRITICALLY ILL SEPTIC PATIENTS IN THE CRITICAL CARE DEPARTMENT: A PROSPECTIVE EPIDEMIOLOGICAL OBSERVATIONAL STUDY

Eslam M. Fathi*, Tayseer M. Zaitoun*, Amr H. Dahroug*, Marwa A. Meheissen**

*Department of Critical Care Medicine, Faculty of Medicine, Alexandria University, Egypt
**Department of Microbiology Medicine, Faculty of Medicine, Alexandria University, Egypt

Abstract

Background: Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation).Sepsis occurs due to the imbalance between proinflammatory mediators like tumor necrosis factor-alpha (TNF alpha) and interleukin-1 (IL-1) and antiinflammatory mediators like(IL-6) and (IL-10) which regulates the inflammatory processes, If the proinflammatory mediators exceeds antiinflammatory one, sepsis will be appeared. The approach to treatment of sepsis involves initial resuscitation and detection of causative organisms by doing cultures and starting antibiotics as early as possible according to antibiotic policy.

Objectives: The aim of this prospective observational epidemiological study was to describe the clinical profile of patients with sepsis and/or septic shock attending critical care department of Alexandria Main University Hospital, determine the microbial etiology of culture positive community and/or hospital acquired severe sepsis and septic shock cases and determine the antimicrobial resistance pattern of etiological agents in an attempt to establish an empirical protocol of antibiotic treatment for sepsis in Alexandria Main University Hospital (AMUH) ICUs. This study was conducted for a six months period starting from the 1st of April through the end of September 2014.

Methods: The present study was conducted on 188 patients fullfilling all criteria of sepsis divided into two groups: group I (community acquired infection) included 46 patients group II (hospital acquired infection) included 142 patients. Assessment of APACHE II score and using history taking, clinical data, laboratory investigation and cultures from infected sites like (miniBAL,urine,blood, wound) to detect the causative organism of sepsis.

Results: Lower respiratory tract infection was the most common cause of sepsis in both groups. In miniBAL cultures, acinetobacter was the most common g–ve isolate representing 58 patients (40.8%) in group II and 4 patients in group I (8.7%) with statistical significance difference (P<0.001)and most common antibiotics sensitive to acinetobacter spp were imipenem/cilastatin with 58.1% followed by meropenem with 46.8% and lastly amikacin with 37.1% while methicillin resistant staph.aureus (MRSA) was the most common g+ve isolate representing 22 cases (15.5%) in group II with P=0.004 which denote significance difference in comparison to group I and vancomycin was the most sensitive antibiotic to MRSA in miniBAL cultures with 90.9% followed by linezolid with 54.5% and lastly teicoplanin with

45.5%. In blood cultures, acinetobacter was the most common g-ve isolate and meropenem,imipenem/cilastatin and cefepime were sensitive with the same percentage 50% while MRSA was the most common g +ve isolate and vancomycin was the most sensitive one with 90.9% followed by linezolid with 81.8% and lastly teicoplanin with 72.7%. In urine cultures, acinetobacter was the most common g –ve one and cefoperazone/sulbactam was the most sensitive antibiotic with 75% followed by both meropenem and tigecycline were sensitive in the same percentage with 37.5% while MRSA was the most common g+ve one and both vancomycin and linezolid were sensitive with the same percentage 100%. In wound cultures, acinetobacter was the most g-ve one and all amikacin,meropenem and imipenem/cilastatin were sensitive with the same percentage 20% while MRSA was the most common g+ve organism and all vancomycin,clindamycin and levofloxacin were sensitive with the same percentage 50%. Serum CRP level was the most accurate parameter for monitoring sepsis. Automated blood cultures was more sensitive in detection of micro-organisms than conventional blood culture.

Conclusions: Acinetobacter spp was most commonly isolated gram –ve pathogen in AMUH ICUs while MRSA was most commonly isolated gram +ve organism in all cultures.Gram –ve organisms were sensitive mostly to amikacin followed by meropenem and lastly imipenem/cilastatin while gram +ve organisms were sensitive to vancomycin followed by linezolid and lastly teicoplanin.septic shock was the most common cause of death in both groups.

Keywords: Sepsis,antibiotic policy, anti-inflammatory mediators.

{**Citation:** Eslam M. Fathi, Tayseer M. Zaitoun, Amr H. Dahroug, Marwa A. Meheissen. Common bacterial organisms in critically ill septic patients in the critical care department: a prospective epidemiological observational study. American Journal of Research Communication, 2016, 4(4): 44-64} www.usa-journals.com, ISSN: 2325-4076.

Introduction

Sepsis is defined as the presence of infection together with systemic manifestations of infection. Severe sepsis is defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion. Sepsis induced hypotension is defined as a systolic blood pressure (SBP) < 90 mm Hg or mean arterial pressure (MAP) < 70 mm Hg or a SBP decrease > 40 mm Hg or less than two standard deviations below normal for age in the absence of other causes of hypotension.Septic shock is defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation. Sepsis induced tissue hypoperfusion is defined as infection induced hypotension, elevated lactate, or oliguria.[(1)]

Identifying the most likely source of infection differs in patients admitted to the ICU.

Respiratory tract infection

Community-acquired pneumonia (CAP) is a common and potentially serious illness. It is associated with considerable morbidity and mortality, particularly in elderly patients and those with significant comorbidities.[(2)]

Hospital-acquired (or nosocomial) pneumonia (HAP) is pneumonia that occurs 48 hours or more after admission and did not appear to be incubating at the time of admission.[3]

Ventilator-associated pneumonia (VAP) is a type of HAP that develops more than 48 to 72 hours after endotracheal intubation.[3]

Healthcare-associated pneumonia (HCAP) is defined as pneumonia that occurs in a non-hospitalized patient with extensive healthcare contact, as defined by one or more of the following:

Intravenous therapy, wound care, or intravenous chemotherapy within the prior 30 days.

Residence in a nursing home or other long-term care facility.

Hospitalization in an acute care hospital for two or more days within the prior 90 days.

Attendance at a hospital or hemodialysis clinic within the prior 30 days.[4]

Catheter related infection

Approximately 80,000 central venous catheter-related bloodstream infections occur in United States intensive care units each year. In general, the diagnostic approach to catheter-related blood stream infection (CRBSI) consists of clinical evaluation and microbiologic confirmation with blood and catheter cultures.[5]

Urinary tract infections (UTI)

Associated with urinary catheters are the leading cause of secondary nosocomial bacteremia. Approximately 20% of hospital-acquired bacteremias arise from the urinary tract, and the mortality associated with this condition is about 10%.[6]

Infectious pressure ulcers

Pressure ulcers are localized areas of tissue necrosis that tend to develop when soft tissue is compressed between a bony prominence and an external surface for a prolonged period of time. They are a significant problem in critically ill patients, the elderly, and in persons with spinal cord injury (SCI).[7]

Prevention of sepsis

Infection control is a discipline that applies epidemiologic and scientific principles and statistical analysis to the prevention or reduction in rates of nosocomial infections. [8]

Management of sepsis & septic shock

Initial Resuscitation and Infection Issues

A. Initial Resuscitation

Protocolized, quantitative resuscitation of patients with sepsis- induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:

1.Central venous pressure 8–12 mm Hg
2.Mean arterial pressure (MAP) ≥ 65 mm Hg
3.Urine output ≥ 0.5 mL/kg/hr
4.Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively.[9]

In patients with elevated lactate levels targeting resuscitation to normalize lactate.[9]

B. Screening for Sepsis and Performance Improvement

1. Routine screening of potentially infected seriously ill patients for severe sepsis to allow earlier implementation of therapy.
2. Hospital–based performance improvement efforts in severe sepsis.[10]

C. Diagnosis

1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s).

At least 2 sets of blood cultures (both aerobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted.

Use of the 1,3 beta-D-glucan assay, mannan and anti-mannan antibody assays, if available and invasive candidiasis is in differential diagnosis of cause of infection

2. Imaging studies performed promptly to confirm a potential source of infection.[11]

D. Antimicrobial Therapy

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock and severe sepsis without septic shock as the goal of therapy.

2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis.

2b. Antimicrobial regimen should be reassessed daily for potential deescalation.

3. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection.

4a. Combination empirical therapy for neutropenic patients with severe sepsis and for patients with difficult-to-treat, multidrug- resistant bacterial pathogens such as Acinetobacter and Pseudomonas spp.

For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is for P. aeruginosa bacteremia. A combination of beta-lactam and macrolide for patients with septic shock from bacteremic Streptococcus pneumoniae infections.

4b. Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known.

5. Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with S. aureus; some fungal and viral infections or immunologic deficiencies, including neutropenia.

6. Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin.

7. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause.[12]

Antibiotic policy

Antibiotic resistance:

The increasing prevalence of resistance to antimicrobial agents amongest micro-organisms is believed to be driven by a number of factors:

- The overall amount of antimicrobials used both in medicine and in non medical applications such as animal husbandry and aquaculture.
- Patterns of use which result in prolonged exposure of micro-organisms to low levels of antimicrobials.
- Use of inadequate dosages or ineffective agents.
- Use of broad spectrum agents, and particularly those which interfere with the normal bacterial flora of the gut.
- Failure to consider the pharmacodynamics of the drug. Some antimicrobials, such as the β-lactams (penicillins and cephalosporins), exhibit "time-dependent" killing. Their effect on susceptible organisms is dependent on the proportion of a dosage interval for which tissue levels are above minimal inhibitory concentration (MIC).
- Poor infection control, allowing resistant organisms, once emerged, to become established within a facility.[13]

Aim of the study

The aim of this prospective observational epidemiological study was to describe the clinical profile of patients with sepsis and/or septic shock attending Alexandria Main University Hospital ICUs, determine the microbial etiology of culture positive community and/or hospital acquired severe sepsis and septic shock cases and determine the antimicrobial resistance pattern of etiological agents in an attempt to establish an empirical protocol of antibiotic treatment for sepsis in (AMUH).

Patients and Methods

All patients admitted to AMUH critical care units with diagnosis of severe sepsis &/or septic shock were included in a prospective observational study. An informed written consent was obtained from the patients or their families to be included in the study

Inclusion criteria: Patients with symptoms and signs of severe sepsis &/ or septic shock diagnosed as community acquired (≤ 48 hours from admission) or hospital acquired infections (> 48 hours from admission) and culture positive cases.

Exclusion criteria included Patients aged less than 18 years, patients who already received antibiotic treatment, pregnant females and patients with clinical presentations suggesting viral infections.

All selected patients were subjected to:

- **Complete history taking**:

A structured sheet was taken from all patients and will include: demographics; critical care unit of admission; presence of underlying chronic diseases and severity, invasive procedures; antimicrobial use in the preceding 3 months; source of infection.[14]

- **Complete clinical examination**
- **Laboratory investigations**

Chemical

- Liver function tests: AST, ALT, albumin, bilirubin total and direct
- Kidney function tests: BUN, creatinine.
- Random blood glucose.
- Electrolytes: Na (mEq/l) and K (mEq/l).
- Arterial blood samples will be collected for measuring:
  - Arterial lactate level (mmol/l).
  - Arterial blood gases.
- Central venous blood samples from the central venous catheter will be collected for measuring central venous oxyhaemoglobin saturation (ScvO2).[14]

Haematological

- Daily CBC.
- Coagulation panel: PT, PTT, INR, fibrinogen levels.

Acute phase reactants

- Daily CRP (mg/dl) using commercial available kits following the instructions of the manufacturers.
- Daily ESR.

Microbiological

Cultures including (miniBAL,urine,blood,wound) were performed before administration of antibiotic or after stoppage of antibiotic for at least 48 hours.[15]

Statistical analysis

Using appropriate statistical test as needed, statistical analysis was carried out using statistical SPSS software package version 20.0.

Results

Demographic data and aetiology

Age and sex: there were 15 male patients of group I with a percentage 32.6%and 31 females (67.4%) while those of group II there were 84 male patients (59.2%) and 58 females (40.8%).There was a mean age of 56.07 ± 15.18 years in group I patients and 51.19 ± 18.93 years in group II with median age of 55 for both groups of patients with P value= 0.079 which denote no statistical difference in age between the two studied groups.

Past medical history (DM, HTN, IHD): As regards to past medical history there were only 14 patients (30.4%) had no past history in group I and 32 patients (69.6%) had past history while in group II there were 70 patients (49.3%) had no past history and 72 patients (50.7%) had past history with P value =0.025 which denote statistical difference of the two groups as regard past medical history.

Diagnosis: The most common diagnosis in group I patients was respiratory failure which represent 24 patients (52.2%) followed by septic shock 9 patients (19.6%) while in

group II patients the most common diagnosis was traumatic brain injury (TBI) representing 48 patients(33.8%) followed by respiratory failure 35 patients (24.6%) and cerebrovascular stroke (CVS) 20 patients(14.1%) with P value <0.001.

APACHEII score: There was a mean APACHE score of 15.91 ± 6.25 in group I (median 16) and 16.96 ± 6.0 in group II (median 18) with P value =0.266 which denote no statistical difference between two studied groups.

Site of infection

Figure (1) show that the most common sites of infection in group I was chest infection representing 28 patients (60.9%) followed by urinary tract infection (UTI) representing 10 patients (21.7%) while in group II the most common site was chest infection representing 96 patients (67.6%) followed by combined UTI and chest infection representing 13 cases (9.2%) and third site was combined chest and wound infection representing 12 cases (8.5%) with P value of 0.004 which denote statistical predominance of chest infection as common site of infection in both groups.

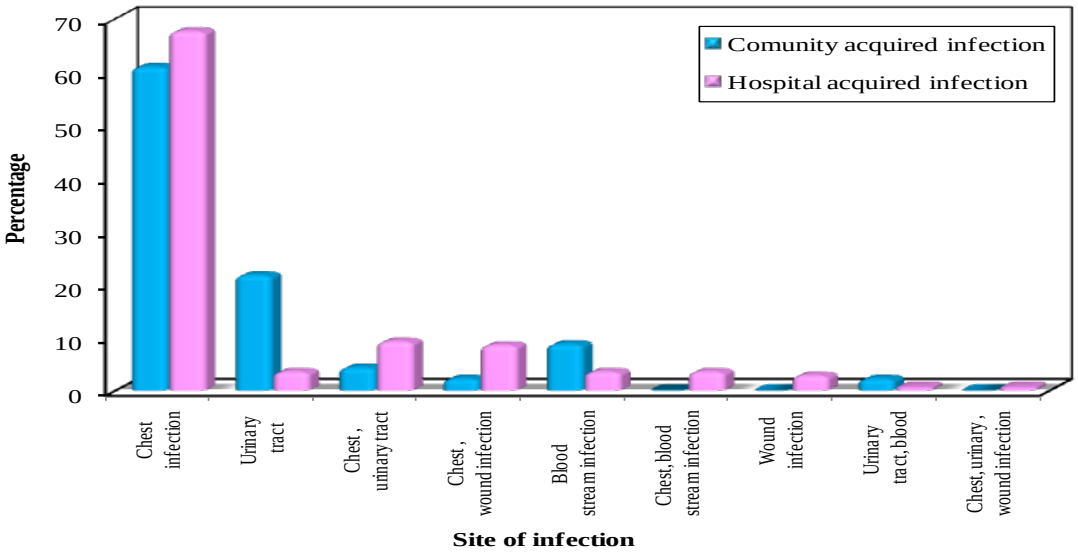

Figure (1): Comparison between two studied groups according to infection site.

MiniBAL cultures'results

Figure (2) show the most common organisms isolated from miniBAL cultures of each group:

Group I: Pseudomonus and Klebsiella were the common two species isolated from miniBAL cultures representing 10 cases for each one (21.7%) followed by Acinetobacter representing 4 cases (8.7%%), E. Coli representing 3 cases (6.5%), Staph. aureus representing 3 cases(6.5%), Proteus, Citrobacter, Enteroccocus pneumoniae and Streptococcus pneumoniae all representing 1 case for each one (2.2%), also there were 15 cases has no organisms and 4 cases with contaminated cultures.

Group II: Acinetobacter was the most common isolate in miniBAL cultures representing 58 patients (40.8%) with statistical significance difference (P<0.001) in comparison to group I followed by Pseudomonus representing 42 cases (29.6%), Klebsiella representing 32 cases (22.5%), MRSA representing 22 cases (15.5%) with P=0.004 which denote significance in comparison to group I, Proteus representing 14 cases(9.9%), E. coli representing 13 cases (9.2%), Citrobacter representing 7 cases(4.9%), Staph. aureus representing 2 cases (1.4%), and Enterococci representing only 1 case (0.7%) and there were 9 cases with no growth of organisms with and 4 case with contaminated cultures.

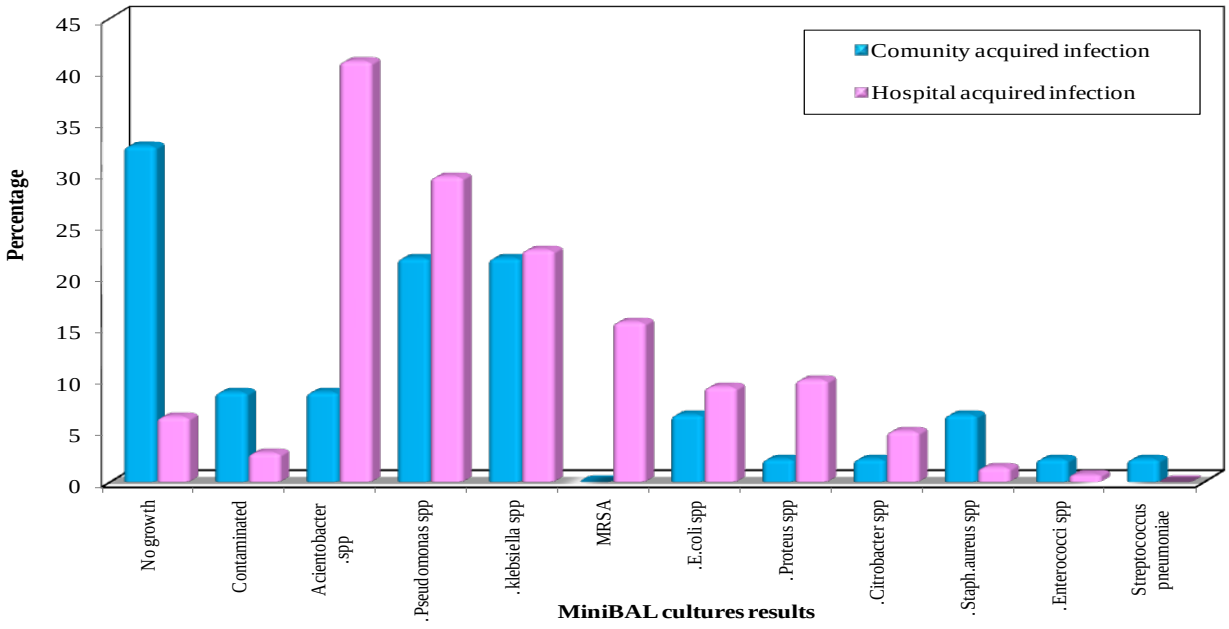

Figure (2): Comparison between two studied groups according to miniBAL cultures results.

Figure (3) show the common antibiotics sensitive to gram +ve and gram –ve organisms in mini BAL cultures as follows:

Gram –ve organisms:

Acinetobacter: Most antibiotics sensitive were imipenem/cilastatin with 58.1% followed by meropenem with 46.8% and lastly amikacin with 37.1%.

Pseudomonas: Most antibiotics sensitive were levofloxacin with 46.2% followed by both amikacin and meropenem with the same percentage 38.5%.

Klebsiella: Most antibiotics sensitive were amikacin with 52.4% followed by both meropenem and imipenem/cilastatin with the same percentage 45.2%.

E.coli: Both amikacin and imipenem/cilastatin were sensitive in the same manner with 50% and lastly cefoperazone/sulbactam with 37.5%.

Proteus**:** Amikacin was the most sensitive one with 46.7% and both meropenem and ampicillin/ sulbactam were sensitive in the same manner with 6.7%.

Citrobacter: Most antibiotics sensitive were levofloxacin with 75% and both ciprofloxacin and cefepime were sensitive in the same percentage 50%.

Gram +ve organisms:

MRSA: Vancomycin was the most sensitive one with 90.9% followed by linezolid with 54.5% and lastly teicoplanin with 45.5%.

Staph.aureus: Tiecoplanin was the most sensitive one with 100% followed by vancomycin with 66.7% and cefepime with 33.3%.

Enterococci: All amikacin, piperacillin/ tazobactam and ciprofloxacin were sensitive with 100%.

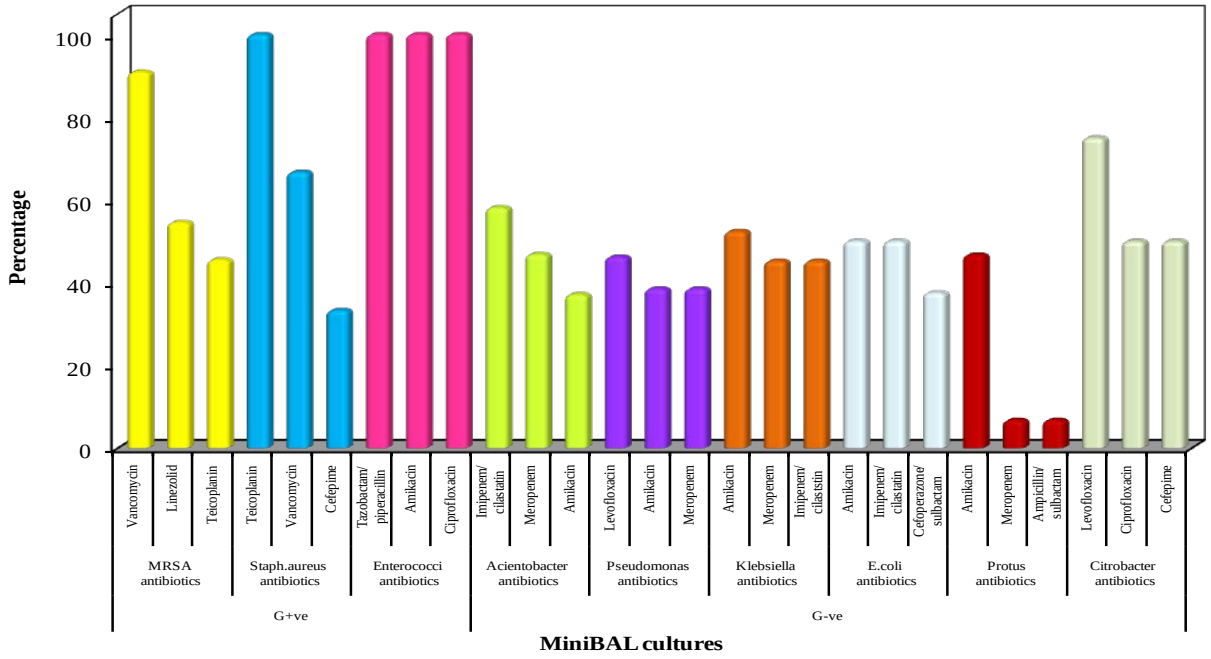

Figure (3): Antimicrobial suseptability pattern of gram –ve and gram +ve organisms in miniBAL cultures.

Blood cultures' results

31 patients were subjected to blood cultures using BACT/ALERT system together with conventional blood cultures 6 out of 31 patients had positive BACT/ALERT system results and negative conventional blood cultures results with P value = 0.024.

Figure (4) show the most common species isolated from blood cultures in both groups:

A total of 21 patients had laboratory confirmed blood stream infections, 6 of these were community acquired and 15 were hospital acquired infections.

Group I (46 cases)

39 patients had negative blood cultures' results with (84.4%), MRSA was the most common isolated organism in this group which isolated from

4 cases with 8.4% followed by both Klebsiella and E.coli were isolated only in one case representing (2.2%) for each one and only one case of contaminated culture with (2.2%).

Group II (142 cases)

126 patients had negative blood cultures'results with (88.7%) , MRSA was most common organism isolated in this group which isolated from 7 cases(4.9%) followed by Klebsiella representing 4 cases (2.8%), Acinetobacter 2 cases(1.4%) and both Pseudomonas and Enterobacter representing one case with (0.7%) for each one and there were 3 cases had contaminated cultures with(2.1%).

There was no statistical significance difference between both groups regarding blood cultures' results.

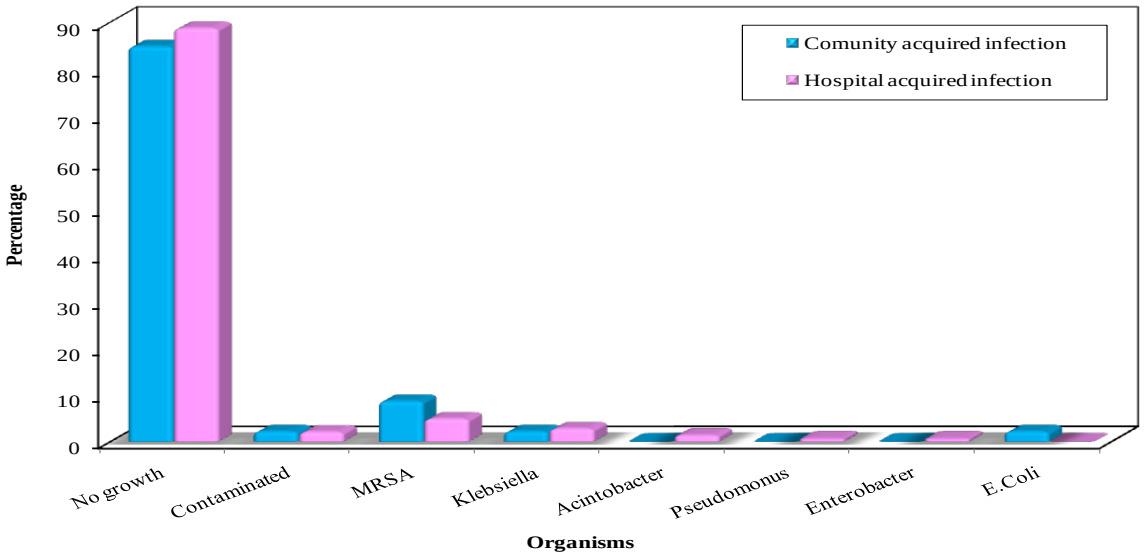

Figure (4): The frequency of different pathogens isolated from blood cultures in the two studied groups.

Figure (5) shows the common antibiotics sensitive to gram +ve and gram –ve organisms in blood cultures as follows:

Gram –ve organisms

Acinetobacter: Meropenem, imipenem/cilastatin and cefepime were sensitive with the same percentage 50%.

Pseudomonas: Only amikacin was sensitive with 100%.

Klebsiella: Amikacin, imipenem/ cilastatin and meropenem were sensitive with the same percentage 80%

E.coli: Meropenem, imipenem/ cilastatin and trimethprim/ sulphamethoxazole were sensitive with the same percentage 100%.

Gram +ve organisms:

MRSA: Vancomycin was the most sensitive one with 90.9% followed by linezolid with 81.8% and lastly teicoplanin with 72.7%.

Enterococci: Both imipenem/cilastatin and doxycycline were sensitive with 100%.

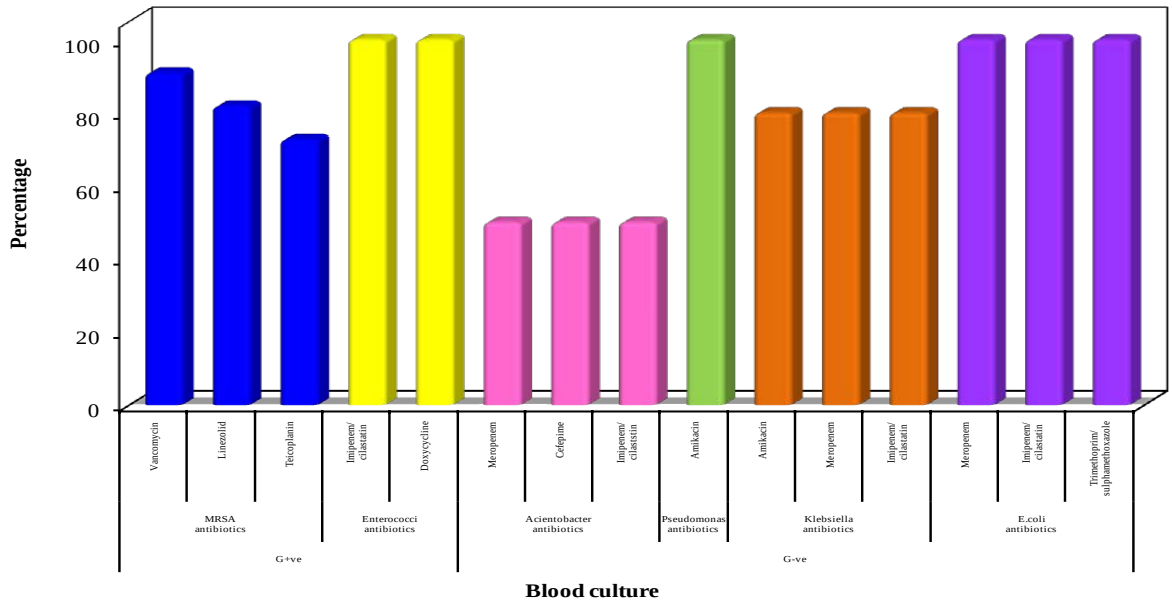

Figure (5): Antimicrobial suseptability pattern of gram –ve and gram +ve organisms in blood cultures.

Urine cultures' results

Figure (6) show the most common organisms isolated from urine cultures in both groups:

A total of 38 cases had laboratory confirmed urinary tract infections, 9 of these were community acquired and 29 were hospital acquired infections.

In group I: 30 cases had negative urine cultures'results with (62.2%) and the most common organism isolated in this group was E.coli (4 cases) with 8.7% followed by Klebsiella (2 cases) 4.3%, Proteus (1 case) 2.2%, Staph. aureus (1 case) 2.2% and Enterococci pneumonia (1 case) 2.2%, there were 5 cases with contaminated cultures representing 10.9%.

In group II: 110 cases had negative urine cultures'results with (77.5%) and the most common organism isolated in this group was Acinetobacter (8 cases) with 5.6% followed by both Klebsiella and Pseudomonas (6 cases) with 4.2%, E.coli (5 cases) with 3.5%, Proteus (3 cases) with 2.1% and MRSA (1 case) with 0.7%, there were 4 cases with contaminated urine cultures representing 2.8%.

There was no statistical significance difference between both groups regarding urine cultures' results.

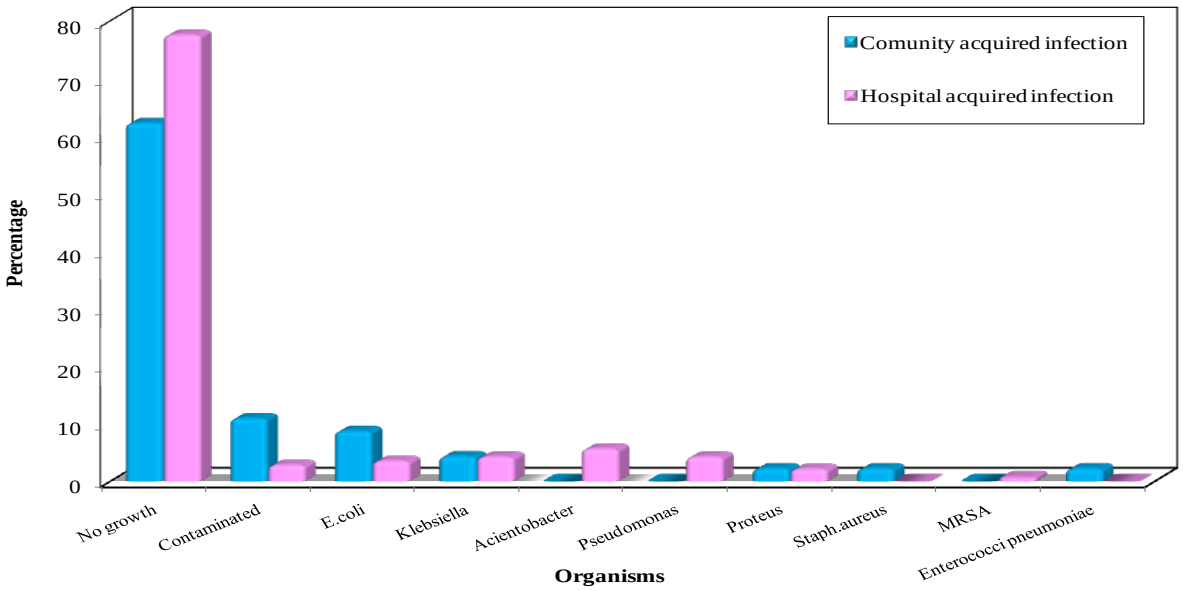

Figure (6): The frequency of different pathogens isolated from urine cultures in the two studied groups.

Figure (7) show the common antibiotics sensitive to gram +ve and gram –ve organisms in urine cultures as follows:

Gram –ve organisms:

Acinetobacter: Cefoperazone/sulbactam was the most sensitive antibiotic with 75% followed by both meropenem and tigecycline were sensitive in the same percentage with 37.5%.

Pseudomonas: Amikacin was the most sensitive antibiotic with 50% followed by both meropenem and imipenem/cilastatin were sensitive with 33.3% for each other.

Klebsiella: Meropenem was the most sensitive antibiotic with 50% followed by imipenem/ cilastatin with 37.5% and lastly ciprofloxacin with 25%.

E.coli: Both amikacin and imipenem/cilastatin were sensitive with the same percentage 55.6% followed by ciprofloxacin with 44.4%.

Proteus: Ciprofloxacin was the most sensitive antibiotic with 50% followed by both cefoperazone and cefepime with 255 for each one.

Gram +ve organisms:

MRSA: Both vancomycin and linezolid were sensitive with the same percentage 100%.

Staph. aureus: Amikacin, chloramphenic-ol and linezolid were sensitive in the same manner 100%.

Enterococci: All ampicillin / sulbactam, imipenem / cilastatin and ciprofloxacin were sensitive with 100%.

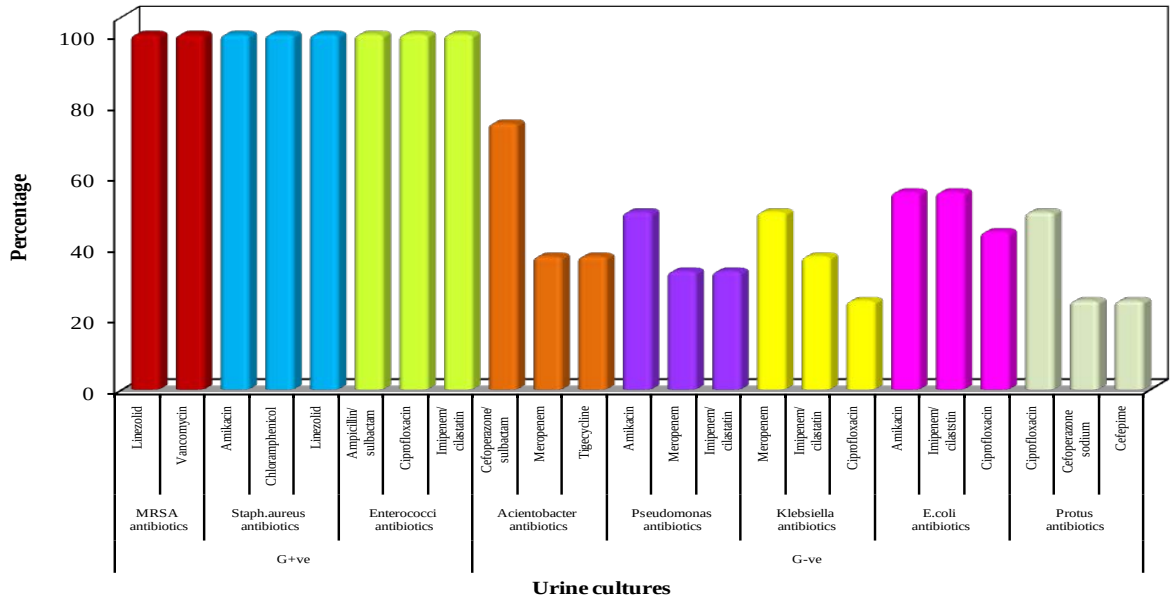

Figure (7): Antimicrobial suseptability pattern of gram –ve and gram +ve organisms in urine cultures.

Wound cultures' results

Figure (8) show the most common organisms isolated from wound cultures in both groups:

A total of 17 cases had laboratory confirmed wound infection, one of these was community acquired and 15 were hospital acquired infections and only one case had a contaminated culture.

Group I (1 case): Only one case had positive wound culture's results, both Klebsiella and Pseudomonas were isolated from that case with 100% .

Group II (16 cases):15 cases had positive wound cultures' results , the most common isolate was Klebsiella 8 cases with 50% followed by Acinetobacter 5 cases (31.3%), E.coli 5 cases (31.3%), Proteus 4 cases (25%), Pseudomonas 2 cases (12.5%), MRSA 2 cases (12.5%),

Citrobacter 1 case (6.3%), Enterobacter 1 case (6.3%) and there was only 1 case contaminated in this group with (6.3%).

There was no statistical significant difference between both groups regarding wound cultures' results.

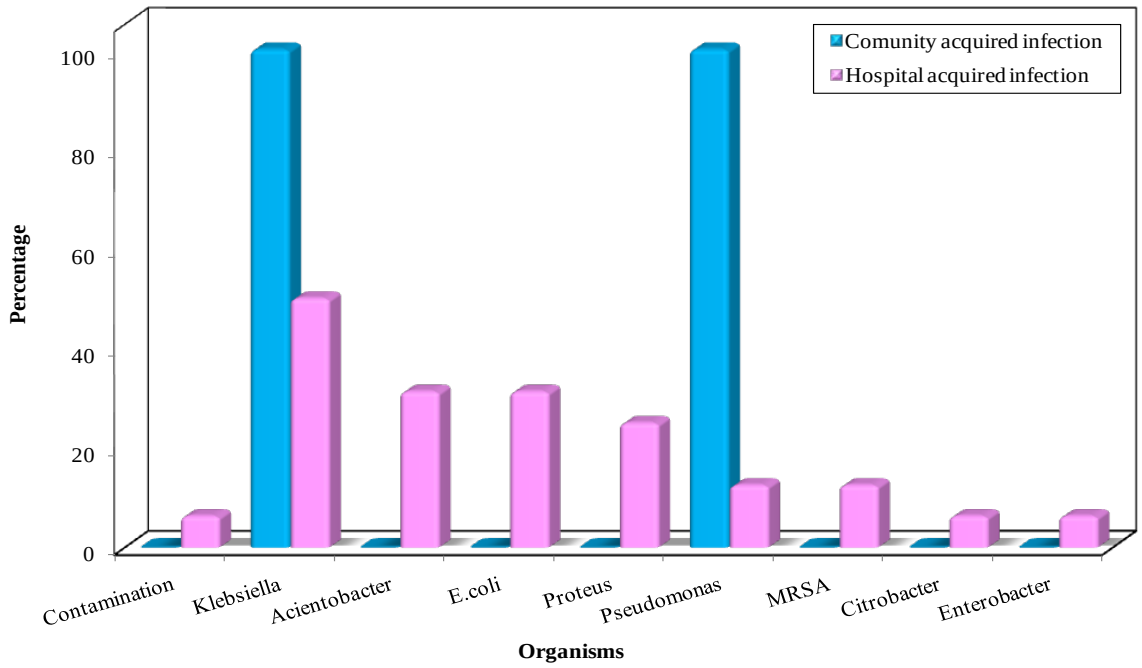

Figure (8): The frequency of different pathogens isolated from wound cultures in the two studied groups.

Figure (9) show the common antibiotics sensitive to gram +ve and gram –ve organisms in miniBAL cultures as follows:

Gram –ve organisms

Acinetobacter: All amikacin, meropenem and imipenem/cilastatin were sensitive with the same percentage 20%.

Pseudomonas: All amikacin, meropenem and cefepime were sensitive with the same percentage 33.3%.

Klebsiella: Most antibiotics sensitive were amikacin with 33.3% followed by meropenem with 22.2% and lastly cefepime with 11.1%.

E.coli: Both amikacin and meropenem were sensitive in the same manner with 60% and lastly cefepime with 20%.

Proteus: Amikacin was the most sensitive one with 50% and both meropenem and cefepime were sensitive in the same manner with 25%.

Citrobacter: Both levofloxacin and tigecycline were sensitive with the same percentage 100%.

Gram +ve organisms

MRSA: All vancomycin, clindamycin and levofloxacin were sensitive with the same percentage 50%.

Enterococci: Both doxycycline and tetracycline were sensitive with the same percentage 100%.

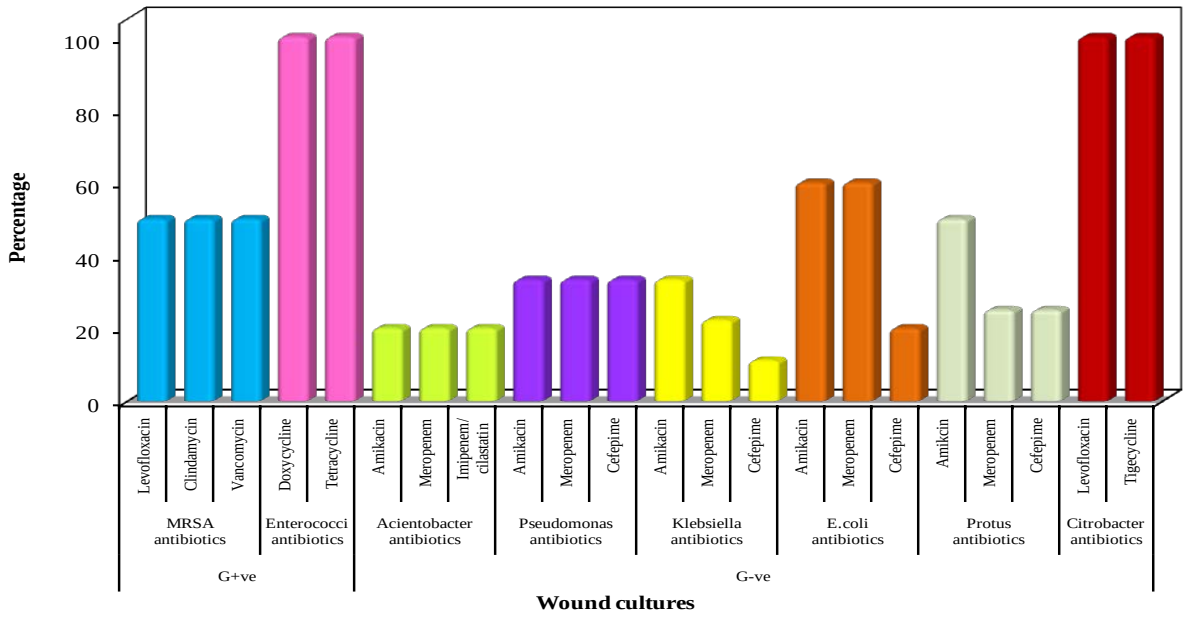

Figure (9): Antimicrobial suseptability pattern of gram –ve and gram +ve organisms in wound cultures.

Outcome

Group I (46 cases) there were 14 cases died with (30.4%) and 32 cases survived with (69.6%) while in group II (142 cases) there were 74 cases died (52.1%) and 68 cases survived (47.9%) and this was significant with (P value =0.010).

The mean duration of ICU stay in group I were 18.80 ± 10.52 with median of 17 days while in group II the mean duration were 29.08 ± 19.93 with median of 23 days and this was significant with (P <0.001).

The mean number of days on mechanical ventilation(M.V) in group I were 19.85 ± 9.88 with median 18 days while in group II were 25.58 ± 16.91 with median 20 days but this was non-significant with (P value=0.100).

In community acquired infection group

First patients who used antibiotics different from cultures' results (4 cases) 3 cases survived with 75% and 1 case died with 25% ,the mean ± SD of duration of ICU stay was

21.50 ± 5.80 with median 19.50 days and the mean ± SD of days on M.V was 19.75 ± 8.18 with median 19.50 days.

Second patients who used antibiotics like cultures' results (42 cases) 29 cases survived with 69% and 13 cases died with 31%, the mean ± SD of duration of ICU stay was 18.55 ± 10.87 with median 15.50 days and the mean ± SD of days on M.V was 19.87 ± 10.21 with median 17.0 days.

There were no significance difference between the two types of patients in group I according to usage of empirical antibiotics regarding prognosis with P=1.000,duration of ICU stay with P=0.250 and days on M.V with P=0.894.

In hospital acquired infection group

First patients who used antibiotics different from cultures' results (12 cases) 6 cases survived with 50% and 6 case died with 50%, the mean ± SD of duration of ICU stay was 41.25 ± 19.79 with median 34.50 days and the mean ± SD of days on M.V was 31.11 ± 10.68 with median 33 days.

Second patients who used antibiotics like cultures' results (130 cases) 62 cases survived with 47.7% and 68 cases died with 52.3%, the mean ± SD of duration of ICU stay was 27.96 ± 19.94 with median 23 days and the mean ± SD of days on M.V was 25.17 ± 17.24 with median 20 days.

Parameters of monitoring sepsis

In group I patients the differences between parameters used to diagnose improvement of sepsis at the 4^{th} reading:

CRP has a sensitivity of 90.62%, specificity of 92.86%, youden index 0.906 with P value of <0.001.

Serum lactate has a sensitivity of 84.37%, specificity of 78.57%, youden index 0.629 with P value of <0.001.

WBCs level has a sensitivity of 93.75%, specificity of 92.86%, youden index 0.866 with P value <0.001.

In group II the differences between parameters used to diagnose improvement of sepsis at the 4^{th} reading:

CRP has a sensitivity of 83.82% , specificity of 95.95%, youden index 0.797 with P value of <0.001.

Serum lactate has a sensitivity of 82.35%, specificity of 62.16%, youden index 0.445 with P value of <0.001.

WBCs level has a sensitivity of 94.12%, specificity of 67.57%, youden index 0.616 with P value <0.001.

Discussion

Site of infection

- The most common site of infection in community acquired infection patients was chest infection (28 cases) due to increase risk of upper respiratory tract infection especially viral

pneumonia and bronchopneumonia, also it was the common site of infection in hospital acquired infection patients (96 cases) with 67.6% due to increased risk of VAP in patients on M.V and inefficient infection control protocol while using suction technique form ETT in patients on M.V. Similary, Angus et al [15] who found that chest infection was the most common cause of sepsis.

- The second common site of infection in community acquired infection patients was UTI because of increase number of patients with kidney diseases like chronic renal failure and nephrolithiasis, also it was the second common cause in hospital acquired infection patients due to inefficient sterilization technique in insertion of urinary catheters, Like Ranieri et al[16] in where UTI was the second common cause of sepsis.

MiniBAL cultures' results

The most common organisms isolated from minibal culturres in community acquired infection patients were Pseudomonas (10 patients,21.7%) and Klebsiella(10 patients,21.7%), like Ranieri et al[16] in which Klebsiella and Pseudomonas were the most common gram –ve organisms isolated from chest. While the most common organisms isolated from hospital acquired infection patients were acinetobacter(58patients,40.8%),Pseudomonas(42 patients,29.6%) and Klebsiella(32 patients, 22.5%), like El Menshawi et al[17] who found that most of infected cases with late onset of VAP were due to Acinetobacter, Pseudomonas and Klebsiella species Pseudomonas species were sensitive to amikacin and carbapenems in both groups, while Klebsiella species were sensitive to amikacin,levofloxacin, carbapenems and cefoperazone/sulbactam in both groups. Hospital acquired infection patients showed multi-drug resistant strain like MRSA isolated from this group and mainly sensitive to vancomycin, like El Menshawi et al[17] who found all gram positive organisms implicated in VAP were sensitive to vancomycin.

Blood cultures' results

Automated blood cultures(BACT/ALERT)

There is a 31 patients in sepsis from both groups subjected to do automated blood cultures in BACT/ALERT system and in the same time conventional (routine) blood cultures and results were as following:

1- No positive results appeared in routine blood cultures.
2- But there are 6 patients appeared positive in automated blood cultures and negative in conventional blood cultures due to aggressive use of antibiotics before withdrawal of blood cultures samples.

So automated blood culture is more sensitive than routine blood culture in detection of micro-organisms in blood especially in patient taking antibiotics.

Out of 188 patients, 39 patients(84.8%) in community acquired infection group and 126 patients(88.7%) in hospital acquired infection group had negative cultures' results, that's due to early use of empirical antibiotics in emergency departments before taking blood samples for cultures. Like Opal et al[18] in which most blood cultures were negative and only one third of septic patients were positive in results.

The most common organism isolated from blood cultures in community acquired infection patients was MRSA while the most common organisms in hospital acquired infection patients were MRSA and Klebsiella. While in Orsini et al[19] the most common

organism in blood cultures was Coagulase –ve Staphylococci followed by *Staphylococcus aure, Enterococcus spp* and *Streptococcus pneumoniae.*

The most sensitive antibiotics to MRSA strain in community acquired infection and hospital acquired infection patients were vancomycin, linezolid and teicoplanin, while antibiotics sensitive to Klebsiella strains in hospital acquired infection group were amikacin, carbapenems, levofloxacin and ciprofloxacin. While in Orsini et al[19] all Coagulase –ve staphylococci were susceptible to vancomycin, and 75% were resistant to methicillin.

Urine cultures' results

There were many patients in both groups,30 patients (62.2%) in community acquired infection group and 110 patients(77.5%) in hospital acquired infection group had negative cultures and 9 patients had contaminated cultures, that's due to early use of empirical antibiotics in emergency departments before taking urine samples for cultures and inefficient sterilization techniques before taking samples.

The most common organism isolated from urine cultures in community acquired infection patients was E.coli like Abraham et al[20] in which E.coli most common isolate in UTI in community acquired infection but the most common organisms in hospital acquired infection patients were Acientobacter, Pseudomonas, Klebsiella and E.coli, unlike Smith et al[21] who showed E.coli the most common isolate in hospital acquired infection group.

The most sensitive antibiotics to E.coli were imipenem/cilastatin, piperacillin/ tazobactam and ciprofloxacin in community acquired infection patients but in hospital acquired infection patients were sensitive to amikacin and cefoperazone/sulbactam, unlike Hooten et al[22] in which E.coli were sensitive to second generation cephalosporins.

In hospital acquired infection patients, Acinetobacter species were sensitive to cefoperazone/ sulbactam, meropenem and tigecycline while Klebsiella were sensitive to carbapenems and tigecycline, Pseudomonas were sensitive to amikacin, carbapenems and levofloxacin.

Wound cultures' results

There was only one patient who had positive wound culture in community acquired infection group and 16 patients in hospital acquired infection group 15 cases of them had positive culture result and only one case with contaminated culture, that's due to deficiency in numbers of air mattreses in our ICUs which protect the patients from bed sores which make them liable for infection.

The most common organisms isolated from wound cultures in community acquired infection patients were Klebsiella and Pseudomonas, while the common isolates from wound cultures in hospital acquired infection patients were Klebsiella, Acinetobacter, E.coli, Proteus, Pseudomonas, MRSA, Citrobacter and Enterococci, unlike Giacometti et al[23] in which the common pathogens were *Staphylococcus aureus* followed by *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus epidermidis* , and *Enterococcus faecalis.*

In community acquired infection group the most common antibiotic sensitive to Klebsiella was amikacin while to Pseudomonus was meropenem, unlike Giacometti et al[23] in which the most sensitive antibiotics to Klebsiella were imipenem and ceftriaxone and Pseudomonas was sensitive to both imipenem and ceftazidime.

In hospital acquired infection group the most sensitive antibiotics to Klebsiella were levofloxacin, cefoperazone/ sulbactam, meropenem and amikacin, Acinetobacter species were sensitive to cefoperazone/ sulbactam and levofloxacin, E.coli were sensitive to carbapenems

and amikacin, Proteus were sensitive to amikacin and cefoperazone/sulbactam, unlike Giacometti et al[23] in which Acinetobacter was sensitive to imipenem and ciprofloxacin, both E.coli and Proteus were sensitive to imipenem and ceftriaxone

Cause of death

As regard causes of death the most common cause of death in both groups was septic shock and that's due to increase risk of sepsis and easly transmission of hospital acquired pathogens between patients and increase rate of co-morbidites in these patients. Similary, Meduri et al [24] stated that the presence of sepsis was the only clinical variable predictive of death whatever the morbidity.

Parameters of sepsis

Using of ROC curve to compare between 3 parameters (WBCs, CRP, serum lactate) to detect which one was the best predictor of improving sepsis after taking antibiotics in both groups, regarding the fourth reading, we found that CRP level was the best one in sensitivity and specificity in both groups, Like Pinkaew et al [25] in which predictive value of CRP could be enhanced by serial rather than a single measurement. Serial CRP showed very high predictive values for diagnosis of sepsis and were better than those of leukocyte indices of CBC.

Empirical antibiotics treatment

In community acquired infection patients there was a comparison between two types of patients who were using empirical antibiotics like culture results and who used antibiotics different from culture results , we found that there were no statistical significant difference in outcome (prognosis, ICU duration, days on M.V) and that's because of most patients in this group had a multiple co-morbidities and recurrent attacks of community acquired infections which made them immuno-compromised and easily liable for severe infection and resistant to antibiotics.

In hospital acquired infection patients, there were a comparison between two types of patients who were using empirical antibiotics like culture results and who used antibiotics different from culture results, we found that there was no statistical significant difference in mortality between these two types of patients, but there was a difference in duration of ICU stay and period on M.V and that's due to change antibiotics like culture results assist in resolving sepsis and to early disconnection from M.V and discharge from ICU but mortality rate the same because they died from multiple co-morbidities which complicate hospitalized patients.

Conclusions

Lower respiratory tract infection was the most common source in both community acquired and hospital acquired sepsis patients.

Acinetobacter spp was most commonly isolated gram –ve pathogen in AMUH ICUs while MRSA was most commonly isolated gram +ve organism.

Gram –ve organisms were sensitive mostly to amikacin followed by meropenem and lastly imipenem/cilastatin while gram +ve organisms were sensitive to vancomycin followed by linezolid and lastly teicoplanin.

The most common cause of death in both groups was septic shock.

CRP level was superior to other parameters in monitoring improvement from sepsis.

In both groups, there were 91.5% of patients used empirical antibiotics like culture results.

In both community acquired and hospital acquired groups there was no statistical signficanct difference in term of mortality between patients having culture and sensitivity results matching with empirical treatment and patients who don't.

Concerning hospital acquired infection group, duration of ICU stay and days on M.V were significantly shorter in patients having culture and sensitivity results matching with empirical treatment.

References

1. Dellinger RP: Cardiovascular management of septic shock. Crit Care Med 2003; 31:946–55.
2. Brancati FL, Chow JW, Wagener MM, Vacarello SJ, Yu VL. Is pneumonia really the old man's friend? Two-year prognosis after community-acquired pneumonia. Lancet 1993;342:30-3.
3. Wilson KC, Schünemann HJ. An ap- praisal of the evidence underlying performance measures for community-acquired pneumonia. Am J Respir Crit Care Med 2011;183:1454-62.
4. Waterer GW, Kessler LA, Wunderink RG. Delayed administration of antibiotics and atypical presentation in community- acquired pneumonia. Chest 2006;130:11.
5. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 49:1.
6. Gould CV, Umscheid CA, Agarwal RK, et al. Guideline for prevention of catheter-associated urinary tract infections 2009. Infect Control Hosp Epidemiol 2010; 31:319.
7. Perencevich EN, Sands KE, Cosgrove SE, et al. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis 2003; 9:196.
8. Moore LJ, Jones SL, Kreiner LA, et al: Validation of a screening tool for the early identification of sepsis. J Trauma 2009; 66:1539–46; discussion 1546.
9. Jones AE, Shapiro NI, Trzeciak S, et al; Emergency Medicine Shock Research Network (EMShockNet) Investigators: Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: A randomized clinical trial. JAMA 2010; 303:739–46.
10. Jansen TC, van Bommel J, Schoonderbeek FJ, et al; LACTATE study group: Early lactate-guided therapy in intensive care unit patients: A multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med 2010; 182:752–61.

11. Cinel I, Dellinger RP: Current treatment of severe sepsis. Curr Infect Dis Rep 2006; 8:358–65.

12. Moore LJ, Jones SL, Kreiner LA, et al: Validation of a screening tool for the early identification of sepsis. J Trauma 2009; 66:1539–46; discussion 1546.

13. Morrell M, Fraser VJ, Kollef MH: Delaying the empiric treatment of candida bloodstream infection until positive blood culture results are obtained: A potential risk factor for hospital mortality. Antimicrob Agents Chemother 2005; 49:3640–45

14. Tille PM. Bailey & Scott's Diagnostic Microbiology. 13th edition. Philadelphia, PA, USA: Mosby ELSEVIER; 2013.

15. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001; 29:1303-10.

16. Ranieri VM, Thompson BT, Barie PS, Dhainaut JF, Douglas IS, Finfer S, et al. Drotrecogin alfa (activated) in adults with septic shock. N Engl J Med 2012; 366(22):2055-64.

17. Elmenshawy AM, Elbadawy TH, Abu khaber H, Hafez SF, Fayed AM, Ibrahim EH. The impact of VAP staff education on VAP morbidity and mor- tality in Alexandria University. Pulm Res Respir Med Open J. 2014; 1(1): 32-45.

18. Opal SM, Garber GE, LaRosa SP, Maki DG, Freebairn RC, Kinasewitz GT, et al. Systemic host responses in severe sepsis analyzed by causative microorganism and treatment effects of drotrecogin alfa (activated). Clin Infect Dis 2003; 37(1):50-8

19. Orsini J, Blaak C, Shamian B, Fonseca X, Salem A, Chen YL. Assessing the utility of ICU admission for octogenarians. Aging Clin Exp Res 2015

20. Abraham E, Reinhart K, Opal S, Demeyer I, Doig C, Rodriguez AL, et al. Efficacy and safety of tifacogin (recombinant tissue factor pathway inhibitor) in severe sepsis: a randomized controlled trial. JAMA 2003; 290(2):238-47.

21. Smith's General Urology 16th edition 2004. Tanagho and McAninch, eds. Chapter 13. "Bacterial Infections of the Urinary Tract" Nguyen, Hiep. pp. 203 - 227.

22. Hooten, TM, Scholes, D, Hughes, JP, et al. A Prospective Study of Risk Factors for Symptomatic Urinary Tract Infection in Young Women. NEJM 1996; 335: 468-74

23. Degli Antoni A, Weimer LE, Fragola V, Giacometti A, Sozio F. A Reduction Grade of Lipodystrophy and Limited Side Effects after HAART Regimen with Raltegravir, Lamivudine, Darunavir and Ritonavir in an HIV-1 Infected Patient after Six Years of Antiretroviral Therapy West Indian Med J 2015;64(3).

24. Meduri GU, Headley S, Kohler G, et al: Persistent elevation of inflammatory cytokines predicts a poor outcome in ARDS. Plasma IL-1 beta and IL-6 levels are consistent and efficient predictors of outcome over time. Chest 1995; 107:1062-73

25. Nuntnarumit P, Pinkaew O, Kitiwanwanich S. Predictive values of serial C-reactive protein in neonatal sepsis. J Med Assoc Thai 2002; 85 Suppl 4:S1151-8.