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PROFILE OF SEPTIC WORK UP AMONG PATIENTS ADMITTED INTO THE INTENSIVE CARE UNIT IN UNIVERSITY OF ABUJA TEACHING HOSPITAL GWAGWALADA, ABUJA

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ABSTRACT

Background: Several infectious agents are responsible for sepsis in all age groups presenting with fever which can have devastating consequences if not adequately treated. Sepsis may arise from bacteria, fungi and viral origin but are localized in particular organ or system with systemic affection. Febrile illness is a leading reason for admission to the intensive care unit of hospitals in the tropics and these patients comes mostly from inpatients rather than from outpatients. Diagnostic apparatus needed for sepsis work up are usually not available in most cases and the data regarding septic work up are very scanty. Therefore, this research set out to determine the pattern of isolates from septic work-up among patients admitted to the intensive care unit in Abuja.

Methodology: This was a descriptive cross-sectional study. Sixty-four consecutive patients admitted to the intensive care unit with symptoms such as fever were involved in the study in a view to determine the septic state of the patients. Samples were collected. Blood culturing was performed using the BACTEC 9050® system and biochemical analytical profile index were used for identification and confirmation of bacterial isolates.

Results: The mean age of the patients admitted to ICU was 40.9±3.2 with the highest proportion within the age range of 31-40 years accounting for 31.7% of the patients enrolled and the lowest proportion being 10-20 years group accounting for 5.0%. Out of the 64 patients investigated in the ICU 60 patients had clinical and positive cultures with an overall positive and negative infection rate of 93.8% and 6.3% respectively. From the positive cultures yields 86.7% were bacteremia and 13.3% were fungaemia. Multiple infections were observed among the male patients, Multi-drug resistance bacteria were observed among *Klebsiella pneumoniae*, *E. coli* and *P. aeruginosa* isolates.

Conclusion: Bacterial and fungal isolates were found in this study but increased rate of polymicrobial isolation and nosocomial infections calls for concern.

Key words: Profile of infectious agents, sepsis, fever, septic work up, Abuja

PROFIL DU TRAVAIL SEPTIQUE CHEZ LES PATIENTS ADMIS À L'UNITÉ DE SOINS INTENSIFS DE L'UNIVERSITÉ D'ABOUJA, HÔPITAL D'ENSEIGNEMENT DE GWAGWALADA, ABUJA

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ABSTRAIT

Contexte: Plusieurs agents infectieux sont responsables de la sepsie dans tous les groupes d'âge présentant une fièvre pouvant avoir des conséquences dévastatrices s'ils ne sont pas traités de manière adéquate. La sepsie peut être d'origine bactérienne, fongique ou virale, mais elle est localisée dans un organe ou un système en particulier avec une atteinte systémique. La maladie fébrile est l'une des principales causes d'admission dans les unités de soins intensifs des hôpitaux tropicaux et ces patients proviennent principalement de patients hospitalisés plutôt que de patients externes. Les appareils de diagnostic nécessaires au traitement de la septicémie ne sont généralement pas disponibles dans la plupart des cas et les données concernant le traitement septique sont très rares. Par conséquent, cette recherche visait à déterminer le type d'isolats provenant d'un traitement septique chez des patients admis dans l'unité de soins intensifs d'Abuja

Méthodologie: Il s'agissait d'une étude descriptive transversale. Soixante-quatre patients consécutifs, admis dans l'unité de soins intensifs avec des symptômes tels que fièvre, ont été impliqués dans l'étude afin de déterminer leur état septique. Les échantillons ont été collectés. La culture de sang a été réalisée à l'aide du système BACTEC 9050® et un indice de profil analytique biochimique a été utilisé pour l'identification et la confirmation des isolats bactériens.

Résultats: L'âge moyen des patients admis aux soins intensifs était de $40,9 \pm 3,2$ ans, la proportion la plus élevée des 31 à 40 ans représentant 31,7% des patients inscrits et la plus faible proportion des 10 à 20 ans représentant 5,0%. Sur les 64 patients étudiés en USI, 60 patients avaient des cultures cliniques et positives avec un taux d'infection global positif et négatif de 93,8% et 6,3% respectivement. Parmi les cultures positives, 86,7% étaient des bactériémies et 13,3% des cas de fongémie. Des infections multiples ont été observées chez les patients masculins. Des bactéries multirésistantes ont été observées parmi les isolats de *Klebsiella pneumoniae*, *E. coli* et *P. aeruginosa*.

Conclusion: Des isolats bactériens et fongiques ont été trouvés dans cette étude, mais l'augmentation du taux d'isolement polymicrobien et d'infections nosocomiales est préoccupante.

Mots-clés: profil des agents infectieux, sepsis, fièvre, traitement septique, Abuja

INTRODUCTION

Sepsis which indicates changes in the patient status is a systemic response both to infection and hemodynamic, metabolic and inflammatory derangement, which can present in mild cases as systemic inflammatory response syndrome (SIRS) or progress to severe sepsis and septic shock[1]. Sepsis is a leading cause of morbidity and mortality worldwide and particularly in Africa where awareness is low and resources are limited[2], cause of mortality in about 30% to 65% in the tropics[1,2] but this figure is much more reduced in well developed countries. Therefore, the presence of SIRS with a high laboratory suspicion of positive microbial cultures is considered sepsis. In the Intensive Care Unit (ICU) severe sepsis is defined as a state of sepsis with concomitant organ dysfunction and hypoperfusion which are often than not reversed with appropriate use of antimicrobial agents in the ICU [1-4]

The Intensive Care Unit (ICU) in any developing countries is an epicenter of infectious agents and that of infection control[3]. Therefore any cases of infection in the ICU are capable of triggering sepsis. Patients admitted to the ICU comes with some level of infection and reduced immune systems which means that there must be aggressive means of eradicating the infection patients coming into the ICU and prevention of new nosocomial infection which is important in critical care management of patients

[4,5]. In a study conducted in the tropics, 66.2% had sepsis and blood culture positivity guided therapy in 12.5% [5].

Point prevalence studies in the ICU are the simplest approach to describing the epidemiology of sepsis. For example, 32.8% of 895 patients in 254 Mexican ICUs had sepsis on a single day in 1995 [6-8]. The threshold of eligibility for treatment almost certainly differs by country and levels of sophistication such as availability of ICU beds, varying levels of universal health insurance, and other cultural and economic factors. For instance, only 27.3% and 27.1% of sepsis patients were admitted to the ICU in Brazil and the UK respectively compared to 32% and 51.1% in Spain and the USA respectively [8]. There are several reasons for increase in sepsis in patients admitted to the ICU; workload in the critical care unit and the increase number of tubes such as nasogastric tubes, the oxygen tubes, central line and the intravenous line which are meant to alleviate fluid accumulation that may lead to infections may contribute to multiple site infections [9-11].

The most common infection in the ICU is septicemia but urinary tract infection and gastrointestinal tract infections do exist which may be nosocomial in nature. The hazard of patients acquiring nosocomial infection in the ICU is high [12-13]. There should be a define time for admission to the ICU not transferring patients when every management fails with

deteriorating health of the patients. Physiological host immune state can also determine the progress of sepsis in patients admitted to the ICU, viral and fungi infections flourishes in immune-compromised patients and the elderly [5, 9, 13-14].

Intensive care unit-acquired bloodstream infection was associated with an increased intensive care unit mortality rate [15]. Several studies of bloodstream infections in those admitted to the ICU in African hospitals suggest that the prevalence of bacterial bloodstream infections among patients in the ICU with fever or clinical sepsis exceeds that described in developed countries and bacterial isolates exceed that of fungal infections [2,5,11,12,15-18]. Bacteraemia is a common cause of illness in the ICU in areas of high and low malaria prevalence [19-20]. Gram-negative organisms, especially *Escherichia coli*, exceed Gram-positive organisms such as *Staphylococcus aureus* in importance in several published reports on bloodstream infections in both adults and children from African countries. The use of blood culture to assess septicemia seriously ill patients has hasten the diagnostic process with fast recognition of presence sepsis, quick isolation of the infective agents and resolution of antimicrobial agents [9,11-12,19-21].

Ceftriaxone and levofloxacin are antibiotics with good susceptibility profile against most of the bacteria isolates. Meronem have been used with success in the ICU [12, 21-22]. The uses of antiviral and antifungal have been used with caution but have been associated with good result [22]. Bacterial are well known cause of antibacterial resistance in our environment, resistance such as β -lactamases and extended spectrum β -lactamases were well documented among enterobacteriaceae [21, 23-24]. The aim was to determine the profile of etiology agents resulting from septic work up among patients admitted into the intensive care unit in Abuja.

MATERIALS AND METHODS

Study background

This study was carried out at the Microbiology research laboratory unit, Microbiology and Parasitology department and the Intensive Care Unit (ICU) of University of Abuja Teaching Hospital (UATH) Gwagwalada, Federal Capital Territory (F.C.T). The Hospital is located in Gwagwalada whose geographical coordinates are 8° 56' 29" North and 7° 5' 31" East. It has an area of 1,043 km². The ICU is a 10 bedded care unit. The Federal Capital Territory had a projected population of 1,406,239 inhabitants in the year 2006, of which 157770 (11.22% approximately) inhabitants reside in Gwagwalada [25]. Projected population of Gwagwalada city in 2012 was over 1 million people. The hospital provides

health care services to the inhabitants of Abuja and neighboring states including Niger, Kaduna, Kogi and Nassarawa states.

Study population

Sixty-four consecutive patients admitted to the intensive care unit with symptoms such as fever were involved in the study in a view to determine the septic state of the patients.

Study design

This was a descriptive cross-sectional study conducted from December 2015 to October 2017.

METHODS

Diagnosis was achieved in collaboration with the Intensivist. Patients admitted to the ICU were recruited. The purpose of this study was explained to the subjects and/or with their relatives and consent to participate was sought. Interviewer-administered, structured questionnaires were used as the study tool. The questions outlined in the data forms were explained to the subjects and completed forms which contain information that included the bio-demographic data. Also, provisional diagnosis and laboratory processes, such that the eventual result was noted in the data forms and communicated to the Intensivist and the patients or the relatives.

SPECIMEN COLLECTION, TRANSPORTATION AND PROCESSING

Septic areas were identified especially along the central line and urinary catheter. Specimens were collected from septic areas and blood for blood culture. Each specimen received was examined for quality, in terms of amount, sterility and presence or absence of debris.

The BACTEC culture bottles were inspected and the top of the culture bottle was cleansed with a sterile swab containing ethanol alcohol. With vacutainer needle, about 5mls of blood was moved into the culture bottle and scanned into the BACTEC chamber to await positive alert. Those with positive bacterial and fungal alert were subcultured on Chocolate, Blood, MacConkey and Sabouraud agar plates. After overnight incubation on these agars, the growth characteristics were noted and pure growth was Gram stained. Colonies that were Gram positive were further characterized using the catalase, coagulase and novobiocin disc tests. Those with Gram negative were further characterized using the API^R 20 (Oxoid, 211667 Hampshire, UK). Gram negative identification and iMMVPC test (indole, motility, methyl red, voges-proskauer and citrate) [23]. Culture plates with

positive results were tested for antimicrobial sensitivity using the Kirby-Bauer Diffusion Susceptibility test protocol. Three well-isolated colonies of similar appearance from the isolates and the controls were emulsified in separate 4ml of sterile physiological saline each, labelled, test and controls. The turbidity of the suspensions (both test and controls) was compared to 0.5 Macfalan standards. Muller-Hinton media for both the test and the control were streaked with test suspension and control suspension respectively using sterile swab. After 5mins, sterile forceps was used to place the antibiotics disc, evenly distributed on both plates with similar antibiotics tested in both the test and the controls. Within 20minutes of applying the discs, the plates were incubated at 35°C for 18 to 24 hours. After overnight incubation, the test and the control plates were examined. Using a transparent ruler on the underside of the plates the diameter of each zone were measured in mm. Interpretation; The zone diameter of each antibiotics of control were compared with the CLSI standards, if within the CLSI acceptable limits for Quality control strains, then the zone diameter of each antibiotics of the test were compared with CLSI zone diameter breakpoints and was recorded sensitive, intermediate or resistance. Antibiotics susceptibility pattern was determined using the Muller-Hinton media by the disk diffusion method. Materials used were; Muller-Hinton media, Petri dish, Antibiotics disks (Oxoid, Hantsphire, UK), Macfalan standard, sterile swab stick, control strains (*Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Enterococcus faecalis* ATCC 29212).

DATA

The data obtained was coded on entering and analyzed using Epi Info version 3.5.1 package. Confidence interval was 95% and the p value was 0.05.

RESULTS

This study was carried out among 64 patients who had ICU stay for treatment between the ages of sixteen years and eighty-one years and the outcome of the laboratory results were discussed with the patients/or their relatives before submitting to the Consultant anesthesiologist/intensivist. The mean age of the patients admitted to ICU was 40.9±3.2 with the highest proportion within the age range of 31-40 years accounting for 31.7% of the patients enrolled and the lowest proportion being 10-20 years group accounting for 5.0%. Eleven ICU patients representing 15.0% were within the 31-40 years age group, 10 and 8 patients were from the 61-70 and >70 years age group representing 20.0% and 15.6% respectively. However, this distribution was statistically significant (P <0.05, df=6 Table 1). There were predominantly

female patients 43 (67.2%) admitted to the ICU with male to female ratio of 1:2. The infection rate among the female was 58.2% while the overall infection rate in male was (25) 41.7% of the total patients enrolled with 21 patients had one infection while four male patients had multiple infections. This distribution was statistically significant (P <0.05, Table 11)

Out of the 64 patients investigated in the ICU 60 patients had clinical and positive cultures with an overall positive and negative infection rate of 93.8% and 6.3% respectively. From the positive cultures yields 86.7% were bacteremia and 13.3% were fungaemia. Multiple infections were observed among the male patients, Multi-drug resistance bacteria were observed among *Klebsiella pneumoniae*, *E. coli* and *P. aeruginosa* isolates and polymicrobial isolates was observed in 35.0% of the total patients admitted to the ICU. C-reacting protein and Procalcitonin assay were 100.0% sensitive and positive predictive value for bacteria sepsis using blood culture as standard. Of the 60 isolates obtained from 64 culture positive, 13 were isolated from the 41- 50 years age group giving a prevalence of 51.9%, 10 (61.0%) each from the 31-40 and 61-70 years age group respectively. This was statistically significant (p=0.001, Table 1). Out of the total eight fungi isolates from this study, 6 (75.0%) were candidaemia while 2 (25.0%) were *Cryptococcus neoformans* isolate.

There were colonization of 21(32.8%) urinary catheter, 15(23.4%) intravenous lines, 6 central lines and 9 NG tubes during this study but the infection rate of these materials were 100% for urinary catheter and the central line. This was not statistically significant (p=0.08, Table 11).

Gram negative bacteria were the most isolated bacteria among the patients investigated following blood culture with 28 isolates representing 53.8% while the total Gram positive were 15 bacteria representing 28.8%. There were nine (17.3%) anaerobes and were all bacillus species (Figure 1). Patients with gram negative sepsis had longer ICU stay and were predominantly associated with polymicrobial infection than gram positive sepsis. This relationship was statistically significant (p=0.002; positive spearman correlation= 0.251).

Sixty-four blood culture were analyzed from the ICU which yielded single and multiple isolates characterized using the API system. The following organism were isolated; *Klebsiella pneumoniae* (*K. pneumoniae*), *Escherichia coli* (*E.coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*) as Gram negative bacteria. *Staphylococcus aureus* (*S.aureus*) as Gram positive bacteria (Figure 2). Among the organism isolated, *Escherichia coli* (26.9%) was the most predominant

bacteria recovered, *S. aureus*, *P. aeruginosa* and *Coagulase Negative Staphylococcus* (CONS) isolation rate were 15.4%, 17.3% and 9.6% respectively (Figure 2). The rate of susceptibility of the bacteria isolates were represented in table 4, levofloxacin, augmentin

and meronem had a good susceptibility profile to ICU isolates. Three (33.3%) *P. aeruginosa* isolates were multi-drug resistance while two (40%) *K. pneumoniae* and 4 (28.6%) *E. coli* isolates were Extended spectrum beta Lactamases (ESBL) producers.

TABLE I: DISTRIBUTION OF ISOLATION AMONG AGE GROUP IN ABUJA

Age group Percent (years) Culture(%) (%)	Total	Percent	Positive
10 – 20 51.9	5	15.0	5
21 – 30 61.1	9	20.0	7
31 – 40 35.0	11	31.7	10
41 – 50 47.8	14	12.8	13
51 – 60 21.4	7	15.6	7
61 – 70 55.5	10	5.0	10
>70 55.5	8	5.0	8
Total 100.0	64	100.0	60

df = 6

P = 0.001

TABLE II: DISTRIBUTION OF PATIENTS ADMITTED TO THE ICU IN ABUJA

Gender	Infection Rate (%)	Frequency	Percent (%)
Males	21	32.8	25 (41.7)
Females	43	67.2	35 (58.3)

TABLE III: DISTRIBUTION OF PATIENTS ADMITTED TO THE ICU AND THE SITE OF COLONIZATION

Sites	Colonization Percent	Infection Rate(%)	P-value
Urinary Catheter	21	32.8	100
Intravenous line	15	23.4	93.3
Central Line	6	9.4	100
Feeding Tube	13	20.3	84.6
NG Tube	9	14.1	88.9
Total	64	100.0	

TABLE IV: ANTIBIOTICS SUSCEPTIBILITY PATTERN OF THE ISOLATES FROM ICU PATIENTS IN GWAGWALADA

Bacteria	CLIN	CEFTA	AUG	LEV	CEFTR	MER	GEN	CEFP
<i>K. pneumoniae</i> n=5	100.0	70.0	90.0	100.0	91.8	100.0	60.8	98.0
<i>E. coli</i> n=14	90.0	80.0	90.0	100.0	96.5	100.0	69.8	100.0
<i>P. aeruginosa</i> n=9	44.0	95.0	96.5	50.0	70.5	50.0	33.0	50.0
<i>Bacillus spp</i> n=6	96.0	60.0	82.0	43.0	44.0	100.0	76.3	80.0
<i>S. aureus</i> n=8	50.0	90.0	70.0	100.0	90.0	100.0	30.0	100.0
<i>Acinetobacter</i> n= 5	70.0	80.0	100.0	90.0	90.0	100.0	70.0	80.0
CONS n=5	60.0	80.0	60.0	60.0	60.0	90.0	30.0	30.8

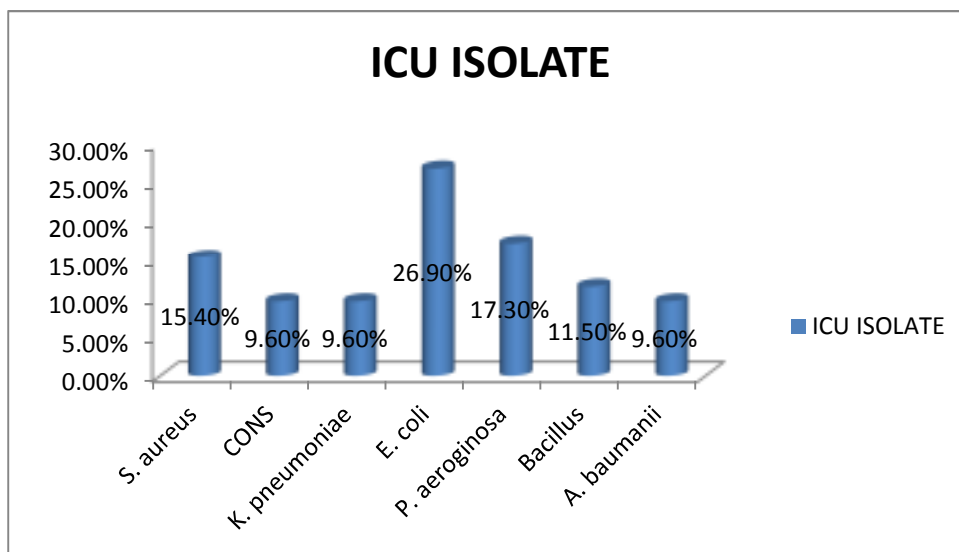


FIGURE 1: DISTRIBUTION OF ISOLATES OBTAINED FROM PATIENTS IN THE ICU

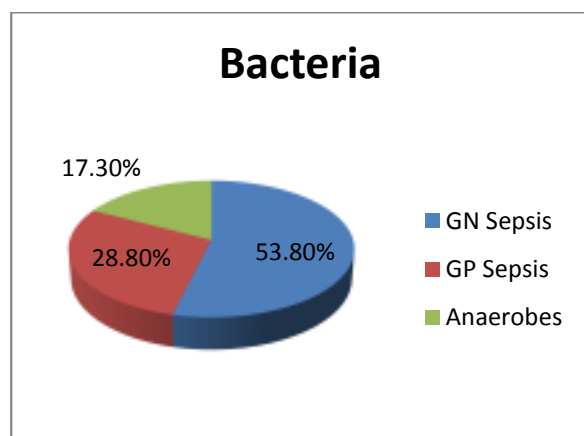


FIGURE 2: DISTRIBUTION OF ISOLATE AMONG PATIENTS ADMITTED TO THE ICU.

DISCUSSION

The infection rate among patients admitted to the ICU in this study was 93.8% and negative culture was 6.3%. This figure varied with findings in Africa [5] and other parts of the world [8,9,13]. The finding of 93.8% in this study was higher than rates of 66.2% in Jos, north-central Nigeria [5], and 27.3% reported in Spain, 51.1% reported in the US, 27.3% in Brazil [8], 20.0% among ICU patients reported by Adria and colleagues in France [9] and 25.4% reported by Stephan [13]. These differences may be due to the methodology employed in our study, invariably the study area and literacy level of the population. The study in Jos [5] expanded the scope of sepsis in relation to those patients with HIV/AIDs in other wards of the hospital. The study in the US, Spain and

France [8, 9] took place in the developed world and are not short of sophisticated equipment's which are lacking in our environment. Therefore, ICU infection rate is low in those studies. Idoko [11] and Alausa [12] had demonstrated that bloodstream sepsis was higher in malaria endemic area of the tropic.

In addition, the high infection rate might be due to the low level of literacy among the populace. Often than not, most patients present late to the hospital with worsen clinical condition. Early presentation may decrease hospital stay and reduce the number of patients for ICU admission. Adria in France [9] established a correlation between workload in the ICU and increase ICU acquired infections. In our setting more patients requires ICU admissions because of late presentation in the hospital.

Age of admission into the ICU have a relationship with rate of ICU acquired infection, in this study infection rate among the older age group was 100.0% (51years to > 70 years) whereas infection rate among the younger age group was lower than 100%. This relationship was statistically significant. The finding was contrary to the knowledge that the older age groups were more predisposed to nosocomial infection because of reduced immunity. Although, Stephan concluded that age >75 years by itself does not appear to be a significant predictor of ICU-acquired nosocomial infection or mortality rate [13]. The finding in this study was contrary to a cohort study by Blot who found that the incidence of bloodstream infection (per 1000 patient days) decreased with age: 8.4 per thousand in middle-aged, 5.5 per thousand in old, and 4.6 per thousand in very old patients [14]. This might be due to differences in

sample size. Female gender predominates in our study with 67.2% and infection rate of 58.3%. This was contrary to study by Alqarni where male predominate with 54% [16] and Sanusi with 62.7% males [27].

In this study, bacteria were more isolated than fungi isolates (81.2% Vs 12.5%) and isolation rate of polymicrobial was 35.0%, this finding was similar to findings by Crowe [17]. The high polymicrobial isolation might be due to the methodology employed in specimen collection and meticulous processing mechanism that minimizes low microbial yield. Urinary catheter was the most colonized in the ICU with highest infection rate while the central line was the least infected in this study. This finding was not supported by Crowe in Nottingham where respiratory tract was the most predominant site of origin of infection with 39.7% of total ICU infections [17].

All the fungal isolates were unicellular yeast cell (*C. albicans* and *C. neoformans*). This might be due to the small samples size. From our study, there were predominant gram negative sepsis than gram positive sepsis (53.8% Vs 28.8%), anaerobes isolated in this study were 17.3%. This findings was similar to 62.2% Vs 46.8% by Florian [8], 47.0% Vs 34.0% isolated by Alqarni [16] and 73.3% Vs 26.7% by Sanusi [27] but contrary to findings by Crowe who got more gram positive [17]. Moreover, Gram negative organisms were frequently isolated from ICU patients. Gram negative bacteria were completely responsible for fever. The distribution was statically significant ($p=0.001$) and correlate positively with high pyrexia and positive Bactec blood culture (spearman correlation=0.408). Gram negative bacteria have potent lipid which has the capacity to induce endotoxic sepsis and consequently increased interleukin 11 and tumor necrotic factor. Increased gram negative isolations might be due to nosocomial infections. The diagnostic mechanism employed was Bactec blood culture which has abundant nutrient for virtually all fast going bacteria to thrive. Notification of culture positivity will lead to prompt diagnosis and reduce patient's hospital stay.

Gram positive sepsis is increasingly becoming common in our environment due to increased rate of antibiotics resistance. Anaerobes isolated in this study

contribute to the rate of polymicrobial isolation in this study.

E. coli was the most frequently isolated among patient in the ICU with 26.9% of the total isolates. This was consistent with other finding [16]. However the findings of 26.9% for *E. coli* was contrary to studies by Florian where *Staphylococcus* predominate with 20.5%, Crowe revealed *Staphylococcus aureus* as most isolated with 22.5% of the total isolates and findings by Sanusi where *Klebsiella pneumonia* Predominates with 26.7%. In our study, there was high isolation rate of *Pseudomonas aeruginosa* and Coagulase negative *Staphylococcus* (CONS) with 17.3% and 9.6% of the total bacteria isolated. The unique nature of *Pseudomonas aeruginosa* will promote its colonization of the various tubes used in the ICU such as IV line and urinary catheter. The difference in the isolation rate of the bacteria might be due its pathogenesis most especially virulence factor rather than differences in their cell wall.

Critical care antibiotics are mainly bactericidal in action and taken into consideration the golden hour Gram negative and Gram positive isolates were sensitive to levofloxacin, augumentin, meronem, ceftriaxone. This is consistent with other studies [21-23] where most of the isolates were sensitive to cell wall acting antibiotics. From this study *E. coli* isolates exhibit significant extended bête lactam resistance while two of the *Pseudomonas aeruginosa* exhibited multidrug resistance and therefore increase the patient's hours of hospital stay. Indiscriminate use of antibiotics, irrational administration of antibiotics and poor administration of drugs may be responsible for this increasing antibiotic resistance.

Conclusion: The nature of Infection in the Intensive Care Unit (ICU) can be used as a predictor of infection in the hospital. Bacterial and fungal isolates were found in this study but increased rate of polymicrobial isolates and nosocomial infections calls for concern. Therefore, increased awareness on hand hygiene among ICU caregivers is necessary to make a big difference.

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