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Prevalence of Multidrug Resistance Gram Negative Bacteria among Patients with Bacteremia in Erbil, Iraq

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The presence of microorganisms in a patient's blood is a critical determinant of the severity of the patient's illness and its complication is one of the main infective causes of mortality and morbidity. Early and prompt antibiotic therapy based on the knowledge of the prevalent microorganisms can help reduce this rate.
Objectives: Our study aimed to carry out prevalence study on bacteremia isolated from blood samples among patients in Erbil city and analyze its antibiotics susceptibility pattern test and multi-drug resistance.
Materials and Methods: A total of 1023 from 2015 until 2021 bacteremia were isolated from patients blood samples attending (Nanakali, Raparin, Maryamana) hospitals and BIO lab from both male and female. Only 57 cases had been identified as bacteremia isolates which were identified by using microscopical, macroscopical identification, cultural, BacT/ALERT and vitek 2 compact system. Also antibiotic susceptibility test was performed by vitek 2 compact on 13 antibiotics.

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Results: Only 57 bacteremia isolates were isolated from 1023 samples from (2015-2021), in our study the percentage of females infected with bacteremia were more than the males, females being 29/1023 (2.84%) and males being 28/1023 (2.74%), about the age groups in (2015-2021) infections by bacteremia were increased in (21-30) age people being 13/57 (22.81%) in total, in (2015-2021) the most common bacteria that cause bacteremia were *Escherichia coli* being 28/57(49.12%) followed by *Klebsiella pneumonia* being 11/57 (19.3%) , *Enterobacter spp.* being 7/57 (12.28%) , *Salmonella typhi* and *Serratia marcescens* both had 1/57 (1.75%) , *Acinetobacter baumanni* had 7/57 (12.3%) and finally *Pseudomonas aeruginosa* had 2/57 (3.5%) . *Escherichia coli* this bacteria mainly found in females 16/28 (57.14%), in (2015-2021), for cancer patients with bacteremia *Escherichia coli* was the most common isolated bacteria being 24/732 (3.30%), bacteremia mostly infected patients with acute myeloid leukemia were 12/38(31.58%) in Nanakali hospital, the bacteria that isolated from patients with bacteremia had resistance to more than three classes of antibiotics they were highly resistance to vancomycin 15 (100%), tetracycline12 (80%) followed by sulfamethoxazole 11 (73.33%) then to erythromycin 9 (60%) and both amoxicillin and clindamycin had 8 (53.33%) antibiotic resistance.

Conclusions: The study showed that the rate of bacteremia increased in last few years in Erbil city especially in cancer patient and those having weak immunity, bacteria acquired resistance to antibiotics and this due to frequent use of antibiotics, morbidity attribute to antibiotic resistant is significant, if prevailing resistance trends continue, high societal and economic costs can be expected. Better management of antibiotic use, and infection control is needed to avoid infections that caused by drug resistant pathogens bacteremia.

Keywords: Gram-negative bacteria; bacteremia; cancer patients; multidrug resistance; age; gender.

1. INTRODUCTION

Most episodes of occult bacteremia spontaneously resolve, and serious sequelae are increasingly uncommon. However, serious bacterial infections occur, including pneumonia, septic arthritis, osteomyelitis, cellulitis, meningitis, brain abscesses, and sepsis, possibly resulting in death [1]. It can occur spontaneously, during certain tissue infections, with use of indwelling genitourinary or intravenous catheters, or after dental, gastrointestinal, genitourinary, wound-care, or other procedures. Bacteremia may cause metastatic infections, including endocarditis, especially in patients with valvular heart abnormalities. Transient bacteremia is often asymptomatic but may cause fever. Development of other symptoms usually suggests more serious infection, such as sepsis or septic shock [2].

Gram negative bacteremia is a devastating public health threat, with high mortality in vulnerable populations and significant costs to the global economy. Concerning, rates of both Gram-negative bacteremia and antimicrobial resistance in the causative species are increasing. Gram negative bacteremia develops in three phases. First, bacteria invade or colonize initial sites of infection. Second, bacteria overcome host barriers, such as immune responses, and disseminate from initial body sites to the bloodstream. Third, bacteria adapt to survive in the blood and blood- filtering organs [3]. Acute myeloid leukemia (AML) represents the hematologic malignancy with the highest risk of bacteremia and invasive fungal infections (IFIs) [4]. Treatment of AML by combination chemotherapy results in persistent neutropenia, which further increases the risk of opportunistic infections [5,6].

Escherichia coli is the gram-negative organism most frequently isolated in adult patients with bacteraemia and in severe cases it may lead to death [7].

Enterobacter spp. is a genus of gram-negative, rod-shaped, facultatively anaerobic bacteria of the *Enterobacteriaceae* family [8].

Pseudomonas aeruginosa has become an important cause of infection, especially in patients with compromised host defense mechanisms. It is the most common pathogen isolated from patients who have been hospitalized longer than 1 week. It is a frequent cause of nosocomial infections such as pneumonia, urinary tract infections, and bacteremia [9].

Salmonella enterica is a major cause of invasive infections worldwide [10].

Acinetobacter baumannii is a Gram-negative rod that can be isolated in nature from water and soil. It is becoming an important cause of resistant nosocomial infections as it was found to be a causative agent in ventilator associated pneumonia, central line associated blood stream infection, catheter associated urinary tract infection and surgical site infection [11].

Klebsiella pneumonia In primary bacteremia, *Klebsiella pneumoniae* directly infects your bloodstream. In secondary bacteremia, *Klebsiella pneumoniae* spreads to your blood from an infection somewhere else in your body [12]. Emergence of resistant *Klebsiella pneumoniae* isolates has been reported widely [13].

Serratia marcescens bacteremia has become ubiquitous recently *Serratia marcescens* bacteremia, either hospital- or community-acquired, can no longer be treated as insignificant [14]. It is recommended that *Pseudomonas spp.* be covered with the initial choice of antibiotics. Most clinicians will empirically treat potential Pseudomonas bacteremia with two drugs from different antibiotic classes. This is due to the fact that *Pseudomonas spp*. can quickly develop beta-lactam resistance. Combination of an anti-pseudomonal β-lactam (piperacillin-tazobactam, imipenem/meropenem or cefepime) plus an aminoglycoside (or anti-pseudomonal quinolone such as ciprofloxacin) would be the initial standard therapy. De-escalation of the initial regimen to a single appropriate antibiotic is recommended once the culture and sensitivity results are available. Combination therapy has also been advocated for bacteremia due to *Enterobacter* and *Klebsiella pneumonia*, especially when there is concern for an extended spectrum beta-lactamase producing species. The emergence of resistant *Enterobacteriae* able to produce *Klebsiella pneumonia* carbapenemases and New Delhi Metallo-beta lactamase is a growing global public health threat. Clinically unstable patients should also receive combination therapy upon the identification of gram negative bacteremia. Penicillin allergic patients may be treated with aztreonam (with or without either an aminoglycoside or ciprofloxacin) [15]. Widespread excessive dispensing and irresponsible use of antibiotics has resulted in the development of resistant strains. Unfortunately, most antibiotics are available over the counter in the developing countries and can be dispensed without prescription; therefore, patients and general public education are crucially needed [16].

2. METHODS

2.1 Sample Collection

A total of (1023) samples were collected from blood from hospitalized patient with bacteremia in (Nanakali, Raparin, Maryamana) hospitals and BIO Lab in Erbil city from January 2015-August 2021. After collection all bacterial isolates were subjected to a series of confirming tests. Selection of a vein for puncture is facilitated by palpation. The area around the intended puncture site should be cleaned with a prepackaged alcohol swab or a gauze pad saturated with 70% isopropanol. Once the skin has been cleansed, it should not be touched until after the venipuncture has been completed. After the skin is cleansed, a tourniquet is applied 4 to 6 inches (10–15 cm) above the intended puncture site to obstruct be return of venous blood to the heart and to distend the veins. Before performing a venipuncture, the phlebotomist should estimate the volume of blood to be drawn and select the appropriate tubes for the plasma or serum tests requested an appropriate needle must also be selected. The most commonly used sizes are gauges 19 to 22 (1.06 – 0.71mm outside diameter) [17]. For isolation of microorganisms, the specimen was directly inoculated on culture media; Blood culture and macConkey agar plates were incubated aerobically at 37°C for (24-48) hours. Pure colonies of isolated microorganisms were identified using morphological, biochemical tests, Species identification and antibiograms for pathogens were performed using Vitek 2 system [18].

2.2 Antimicrobial Susceptibility Test by Vitek 2 Compact System

The system includes an advanced expert system that analyzes minimum inhibitory concentration patterns and detects phenotypes for most organisms tested. This helps optimize laboratory efficiency for lean laboratory management. Rapid results allow clinicians to discontinue empiric therapy and prescribe targeted therapy, resulting in improved patient outcomes and enhanced antibiotic stewardship [19]. With its ability to provide accurate "fingerprint" recognition of bacterial resistance mechanisms and phenotypes, the advanced expert system is a critical component of Vitek2 technology. The Vitek2 card contains 64 microwells. Each well contains identification substrates or antimicrobial. Vitek2 offers a comprehensive menu for the identification and antibiotic susceptibility testing of organisms. The Vitek2 test card is sealed, which minimizes aerosols, spills, and personal contamination. Disposable waste is reduced by more than 80% over micro titer methods [20].

2.3 Statistical Analysis

Data entry and statistical analysis were performed using SPSS v.23 software. Comparisons were made using Pearson Chi-square. A p-value of < 0.05 was considered indicative of a statistically significant difference and p-value < 0.01 was considered indicative of a highly statistically significant difference.

3. RESULTS

Demographic data and clinical characteristics of Gram negative bacteria isolated from patients with bacteremia.

Out of 1023 isolates only (57) were positive from patients as in Table 1. our results according to age group showed that we had nine groups they were (0-10) years had 4(7.02%) mainly seen in males had 3 (5.27%), (11-20) years had 8 (14.04%) mostly found in females 5 (8.77%) , for (21-30) years had 13 (22.81%) in which females percentage were greater they had 7(12.28%) , for (31-40) years had 6 (10.52%) showed that males percentages were greater 4(7.02%), for two groups (41-50) and (51-60) years both had 9(15.80%) and 7(12.28%) respectively both groups mostly seen in females they had 6(10.53%) and 5(8.77%) also for another two groups (61-70) and (71-80) years both had 4(7.02%) mainly seen in males they had 3(5.27%) and lastly for (81-90) years had 2 (3.50%) seen equally in both genders 1(1.75%) as in Table 1.

3.1 Distribution of Bacteremia According to Years

Out of 1023 isolates only (57) were positive between 2015 and 2021 as in Table 2. Results showed that we had 4 (6.45%) positive cases out of 62 in 2015 and 2 (3.63 %) positive Cases out of 55 in 2016 and in 2017 we had 2 (1.71%) positive cases out of 117 and 10(7.14%) positive cases out of 135 in 2018 and in 2019 we had 14 (4.76%) positive cases out of 294 and 10(14.93 %) positive cases out of 67 in 2020 and in 2021 we had 15 (5.12%) positive cases out of 293 Statistical analysis showed that significant correlation between the bacteria and year (P<0.04) as seen in Table 2 and Fig. 1.

Table 1. Demographic data and clinical characteristics of gram negative bacteria isolated from patients with bacteremia

Ages groups	Gender		
	NO (%)	**Male NO (%)**	**Female NO (%)**
0-10	4 (7.02%)	3 (5.27%)	1 (1.75%)
11-20	8 (14.04%)	3 (5.27%)	5 (8.77%)
21-30	13(22.81%)	6 (10.53%)	7 (12.28%)
31-40	6 (10.52%)	4 (7.02%)	2 (3.51%)
41-50	9 (15.80%)	3 (5.27%)	6 (10.53%)
51-60	7 (10.52%)	2 (3.51%)	5 (8.77%)
61-70	4 (7.02%)	3 (5.27%)	1 (1.75%)
71-80	4 (7.02%)	3 (5.27%)	1 (1.75%)
81-90	2 (3.50%)	1 (1.75%)	1 (1.75%)
Total	**57 (100%)**	**28 (49.16%)**	**29 (50.85%)**

No= Number, %=Percentage

Table 2. Distribution of bacteremia according to years

Years	Positive	%	Negative	%	Total	%	P (value)
2015	4	6.45	58	93.55	62	6.06	
2016	2	3.63	53	96.36	55	5.37	
2017	2	1.71	115	98.29	117	11.44	
2018	10	7.41	125	92.59	135	13.2	
2019	14	4.76	280	95.24	294	28.74	
2020	10	14.93	57	85.07	67	6.55	
2021	15	5.12	278	94.88	293	28.64	
Total	**57**	**5.57**	**966**	**94.43**	**1023**	**100**	**P<0.04**

**If P value is less than 0.05 is significant*

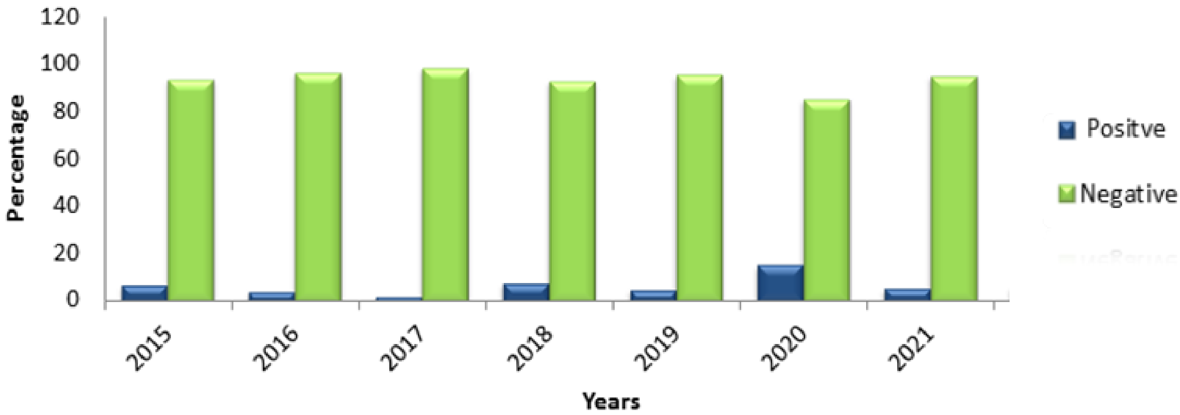

Fig. 1. Distribution of bacteremia according to years

3.2 Distribution of Bacteremia among Genders

In 2015 out of 62 samples the female ratio was less than the male ratio, the males had 3(4.84%) positive cases and 30 (48.39%) negative cases and for the females we had 1 (1.61%) positive cases and 28 (45.16%) negative cases. In 2016 out of 55 samples the female ratio was more than the males we had 28(50.91%) female samples in which 2(3.64%) were positive and 26(47.27%) were negative, for the males we had 27(49.09%) samples in which 0(0%) were positive and 27(49.09%) negative. In 2017 out of 117 samples the female ratio was more than the male ratio, the females had 2(1.71%) positive cases and 60(51.28%) negative cases and for the males we had 0 (0%) positive cases and 55(47.00%) negative cases. In 2018 out of 135 samples the female ratio was less than the males we had 45(33.33%) female samples in which 8(5.92%) were positive and 37(27.41%) were negative, for the males we had 90(66.67%) samples in which 2(1.48%) were positive and 88 (65.19%) negative. In 2019 out of 294 samples the male ratio was exceeded to the female ratio , the males had 8 (2.72%) positive cases and 153 (52.04%) negative cases and for the females we had 6 (2.04%) positive cases and 127(43.20%) negative cases, As for 2020 and 2021, in 2020 we had 67 samples and 2021 we had 293 samples, males ratio exceeding females, for 2020 females we had 29(43.28%) samples 4(5.97%) positive 25(37.31%) negative and the males had 38(56.72%) samples 6(8.96%) were positive and 32(47.76%) negative, as for 2021 we had 124(42.32%) female samples and 169(57.68%) male ones for the females 6 (2.05%) were positive and 118(40.27%) negative as for males 9 (3.07%) were positive and 160 (54.61%) negative. Statistical analysis showed that non-significant correlation (P<0.17) as in Table 3 and Fig. 2.

3.3 The Relation between Bacteremia and Ages

The distribution of bacteremia. In 2015 was seen mostly among the (21-30) having 2/4 (50%) meanwhile in 2016 it was different it was seen among two age groups as same (21-30), (51-60) all of them having 1/2 (50%) , in 2017 it was seen among two age groups as same (21- 30) and (61- 70) having 1/2 (50%) , in 2018 was seen mostly among (21-30) having 4/10 (40%) and other two age groups as same (11-20) and (41-50) that having 2/10 (20%) also in 2019 was mostly seen in (31-40) that have 4/14 (28.57%). In 2020 most of age groups approximately have same ratio but mostly seen (41-50), (51-60) and (81-90) having 2/10 (20%) and lastly in 2021 also the majority whom were infected were between (21-30), (61-70) and (71-80) years having 3/15 (20%). Statistical analysis showed that is non- significant correlation between bacteria and age (P< 0.87) as in Table 4.

3.4 Distribution of Gram Negative Bacteria Isolated from Patients with Bacteremia According to Years

Our result showed that out of 57 Positive samples that were isolated , *Escherichia coli* was mainly seen in 2015 and 2016 with 3/28 (10.71%) and 2/28 (7.14%) respectively, *Escherichia coli*, *Klebsiella pneumonia* and *Enterobacter* were mainly seen in 2017 with 1/28

(3.57 %), 1/11(9.09 %) and 1/7 (14.3 %) respectively, in 2018 *Escherichia coli*, *Klebsiella pneumonia* and *Acinetobacter* were mainly seen with 9/28 (32.14 %) , 1/11 (9.09 %) and 1/7 (14.3 %) respectively, in 2019 *Escherichia coli* , *Klebsiella pneumonia* , *Enterobacter* and *Salmonella typhi* were mostly seen having 4/28 (14.3 %) , 2/11 (18.18 %) ,6/7 (85.7 %) and 1/1 (100%) respectively. In 2020 *Escherichia coli* was mostly seen having 5/28 (17.85%) also *Klebsiella pneumonia* and *Serratia marcescens* having 3/11 (27.27%) and 1/1 (100 %) respectively, while in 2021 *Escherichia coli* , *Klebsiella pneumonia* , *Acinetobacter* and *Pseudomonas aeruginosa* were mainly seen having 4/28 (14.3%), 3/11 (27.27%), 6/7 (85.7%) and 2/2 (100 %) respectively . Statistical analysis showed that is non- significant correlation between bacteria and years (P <0.64) as in Table 5.

3.5 Distribution of Gram-negative Bacteria Isolated from Patients with Bacteremia According to Gender

The number of isolated *Escherichia coli* was high in female 15 (53.57%) compared with 13 (46.43%) in male and for *Klebsiella pneumonia* was 7 (63.64%) in female and 4 (36.36%) in male , while for *Enterobacter* was higher in males than females 5 (71.43 %) in male 2 (28.57 %) in female , in both *Salmonella typhi* and *Serratia marcescens* were 0 (0%) in female and 1 (100%) in male, while for *Acinetobacter* was 4 (57.14%) in female and 3 (42.86%) in male and *Pseudomonas aeruginosa* were 1 (50%) in female and 1(50%) in male for as in Table 6. Statistical analysis showed that is non- significant correlation (P< 0.33) between different species and gender.

Table 3. Distribution of bacteremia among genders

Years	Male		Female		Total	P (value)
	P (NO%)	N (NO%)	P (NO%)	N (NO%)		
2015	3 (4.84%)	30 (48.39%)	1 (1.61%)	28 (45.16%)	62 (6.06%)	
2016	0 (0%)	27 (49.09%)	2 (3.64%)	26 (47.27%)	55 (5.37%)	
2017	0 (0%)	55 (47.00%)	2 (1.71%)	60 (51.28%)	117 (11.45%)	
2018	2 (1.48%)	88 (65.19%)	8 (5.92%)	37 (27.41%)	135 (13.19%)	
2019	8 (2.72%)	153 (52.04%)	6 (2.04%)	127 (43.20%)	294 (28.74%)	
2020	6 (8.96%)	32 (47.76%)	4 (5.97%)	25 (37.31%)	67 (6.55%)	
2021	9 (3.07%)	160 (54.61%)	6 (2.05%)	118 (40.27%)	293 (28.64%)	
Total	**28 (2.74%)**	**545 (53.27%)**	**29 (2.84%)**	**421 (41.15%)**	**1023 (100%)**	**P <0.17**

P= Positive, N= Negative, No= Number, %=Percentage
**If P value is less than 0.05 is significant*

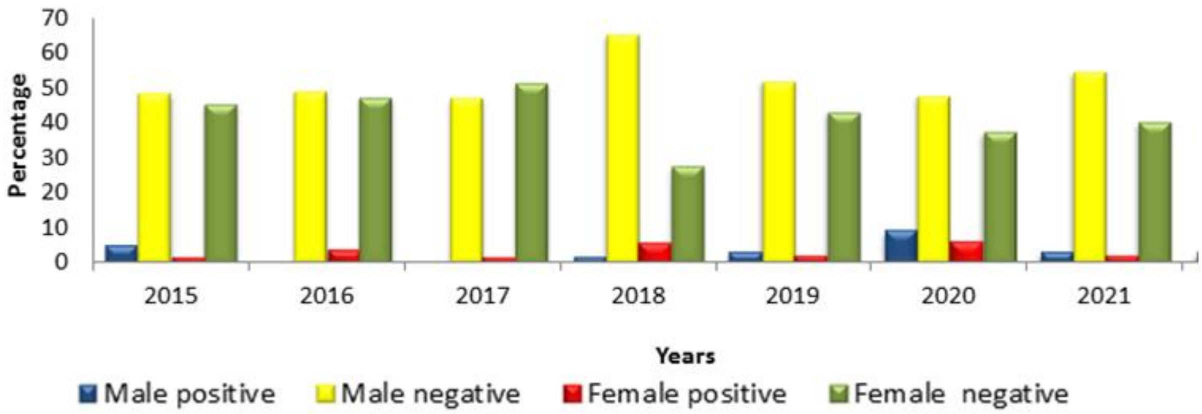

Fig. 2. Distribution of bacteremia among genders

Table 4. The relation between bacteremia and ages

Years	Ages									Pvalue
	0 – 10 N0%	**11-20No%**	**21 30No%**	**31-40No%**	**41-50No%**	**51- 60No%**	**61 -70No%**	**71 -80 No%**	**81-90No%**	**Total No %**	
2015	0 0%	1 25%	2 50%	0 0%	1 25%	0 %	0 0%	0 0%	0 0%	4 7.02%	
2016	0 0%	0 0%	1 50%	0 0%	0 0%	1 50%	0 0%	0 0%	0 0%	2 3.51%	
2017	0 0%	0 0%	1 50%	0 0%	0 0%	0 0%	1 50%	0 0%	0 0%	2 3.51%	
2018	1 10%	2 20%	4 40%	0 0%	2 20%	1 10%	0 0%	0 0%	0 0%	10 17.54%	
2019	2 14.28%	2 14.28%	2 14.28%	4 28.57%	3 21.43%	1 7.14%	0 0%	0 0%	0 0%	14 24.56%	
2020	1 10%	1 10%	0 0%	1 10%	2 20%	2 20%	0 0%	1 10%	2 20%	10 17.54%	
2021	0 0%	2 13.33%	3 20%	1 6.67%	1 6.67%	2 13.33%	3 20 %	3 20%	0 0%	15 26.32%	
Total	**4 7.02%**	**8 14.04%**	**13 22.81%**	**6 10.5%**	**9 15.8%**	**7 12.28%**	**4 7.02%**	**4 7.02%**	**2 3.50%**	**57 100%**	**P< 0.87**

*No= Number, %= Percentage *If P value is less than 0.05 is significant*

Table 5. Distribution of gram negative bacteria isolation from patients with bacteremia among years

Isolated bacteria	Years								P value
	2015 No(%)	2016 No(%)	2017 No(%)	2018 No (%)	2019 No (%)	2020 No (%)	2021 No (%)	Total No (%)	
Escherichia coli	3 10.71%	2 7.14%	1 3.57%	9 32.14%	4 14.3%	5 17.85%	4 14.3%	28 49.12%	
Klebsiella pneumonia	1 9.09%	0 0%	1 9.09%	1 9.09%	2 18.18%	3 27.27%	3 27.27%	11 19.3%	
Enterobacter spp.	0 0%	0 0%	1 14.3%	0 0%	6 85.7%	0 0%	0 0%	7 12.28%	
Salmonella typhi	0 0%	0 0%	0 0%	0 0%	1 100%	0 0%	0 0%	1 1.75%	
Serratia marcescens	0 0%	0 0%	0 0%	0 0%	0 0%	1 100%	0 0%	1 1.75%	
Acinetobacter baumanni	0 0%	0 0%	0 0%	1 14.3%	0 0%	0 0%	6 85.7%	7 12.3%	
Pseudomonas aeruginosa	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	2 100%	2 3.5%	
Total	**4** **7.01%**	**2** **3.5%**	**3** **5.26%**	**11** **19.3%**	**13** **22.81%**	**9** **15.8%**	**15** **26.32%**	**57** **100%**	**P<0.64**

*No= Number of bacteria, %=Percentage *If P value is less than 0.05 is significant*

Table 6. Distribution of gram-negative bacteria isolates from patients according to gender

Isolated bacteria	Gender						P (value)
	Female		Male		Total		
	NO	%	NO	%	NO	%	
Escherichia coli	15	53.57 %	13	46.43%	28	49.12%	
Klebsiella pneumonia	7	63.64 %	3	36.36%	11	19.3%	
Enterobacter spp.	2	28.57 %	5	71.43%	7	12.28%	
Salmonella typhi	0	0%	1	100%	1	1.75%	
Serratia marcescens	0	0%	1	100%	1	1.75%	
Acinetobacter baumanni	4	57.14 %	3	42.86%	7	12.28%	
Pseudomona aeruginosa	1	50%	1	50%	2	3.81%	
Total	**29**	**50.85 %**	**28**	**49.16%**	**57**	**100%**	**P<0.33**

*No= Number of bacteria, %=Percentage *If P value is less than 0.05 is significant*

3.6 Distribution of Gram Negative Bacteria Isolated from Patients with Bacteremia from Cancer Patients

Out of 732 samples collected 38 (5.19%) identified as Gram negative bacteria isolated from patients with bacteremia as in Table 7. Results showed that *Escherichia coli* isolates are the most frequent encountered 24(3.30%) followed by *Klebsiella pneumonia*, *Enterobacter* 6 (0.82%) and *Acinetobacter baumanni* 2(0.27%). Statistical analysis showed that is non-significant correlation (P< 0.32) between different species isolated from cancer patients.

3.7 Types of cancer among Gram negative in nanakali hospital

Out of 732 samples of bacteremia collected 38 (5.19%) samples were positive from cancer patients according to our Table 8, in 2015 acute myeloid leukemia was present mostly in patients 2/4(50%) . In 2016 and 2017 acute myeloid leukemia and acute lymphocytic leukemia were present in patients 1/2 (50%) respectively. In 2018 acute lymphocytic leukemia was present mostly in patients 8/18 (44.44%) and second mostly present was acute myeloid leukemia 3/10 (30%). In 2019 acute myeloid leukemia was present mostly in patients 6/13 (46.15%) and in 2020 multiple myeloma was mostly present 2/6 (33.33) lastly in 2021 bacteremia occurred the mostly in patients with non hodgkin lymphoma 1/1(100%). Statistical analysis showed that is non-significant correlation (P < 0.66) between types of cancer and bacteremia as in Table 8.

3.8 Antibiotic Susceptibility Patterns Tests for Gram Negative Bacteria in Patients with Bacteremia

Out of 15 (5.12%) cases were positive isolates of Gram-negative bacteria in 2021 were screened for their antibiotic susceptibility to thirteen antibiotics, widely used antibiotics. the results were interpreted according to standard value by clinical and laboratory standard of antimicrobial sensitivity testing. It is obvious that Gram negative bacteria isolates showed high resistance (100%) to Vancomycin (80%) to Tetracycline , On the other hand, the lowest resistance were (20%) to Tigecycline, (33.33%) to Rifampin, (26.67%) to Gentamicin and (40%) to ciprofloxacin and levofloxacin as in Table 9. Statistical analysis showed that is non- significant correlation (P< 0.61) between Gram negative bacteria and different types of Antibiotics.

Table 7. Distribution of gram negative bacteria isolated from patients with bacteremia from cancer patients for (2015-2021) years in nanakali hospital

Isolated bacteria	NO + ve	% +ve	NO - ve	% -ve	Total	P (value)
Escherichia coli	24	3.30%	708	96.70%	732	
Klebsiella pneumonia	6	0.82%	726	99.18%	732	
Enterobacter spp.	6	0.82%	726	99.18%	732	
Acinetobacter baumanni	2	0.27%	730	99.73%	732	
Total	**38**	**5.2%**	**694**	**94.8%**	**732**	**P<0.32**

*No= Number of bacteria, %=Percentage *If P value is less than 0.05 is significant*

Table 8. Types of cancer among bacteremia in nanakali hospital for (2015-2021) years

Types of cancer	**Years**								
	2015 NO %	**2016 NO %**	**2017 NO %**	**2018 NO %**	**2019 NO %**	**2020 NO %**	**2021 NO %**	**Total NO %**	**P (value)**
Chronic myeloid leukemia	1 25%	/	/	1 10%	/	1 16.67%	/	3 7.89%	
Non- Hodgkin lymphoma	/	/	/	1 10%	2 15.35%	1 16.67%	1 100%	5 13.16%	
Acute myeloid leukemia	2 50%	1 50%	1 50%	2 20%	6 46.15%	/	/	12 31.58%	
Acute lymphocytic Leukemia	/	1 50%	1 50%	3 30%	1 7.67%	/	/	6 15.79%	
Breast	/	/	/	/	/	1 16.67%	/	1 2.63%	
Colon	/	/	/	/	4 30.77%	1 16.67%	/	5 13.1%	
Myelodysplastic syndrome	/	/	/	1 100%	/	/	/	1 2.63%	
Multiple myeloma	1 25%	/	/	2 20%	/	2 33.33%	/	5 2.63%	
Total	**4 100%**	**2 100%**	**2 100%**	**10 100%**	**13 100%**	**6 100%**	**1 100%**	**38 100%**	**P< 0.66**

(Total number of cancer patients =38)

*NO= number, % = percentage *If P value is less than 0.05 is significant*

Table 9. Antibiotic susceptibility patterns tests for (15) gram negative bacteria in patients with bacteremia in 2021

Antibiotics	Resistance		Intermediate		Susceptible		P value
	NO	%	NO	%	NO	%	
Ampicillin	7	46.67%	3	20%	5	33.33%	
Ciprofloxacin	6	40%	/		9	60%	
Clindamycin	8	53.33%	7	46.67%	/		
Ceftriaxone	7	46.66%	4	26.67%	4	26.67%	
Erythromycin	9	60%	5	33.33%	1	6.67%	
Gentamicin	4	26.67%	3	20%	8	53.33%	
levofloxacin	6	40%	4	26.67%	5	33.33%	
Amoxicillin	8	53.33%	7	46.67%	/		
Rifampin	5	33.33%	10	66.67%	/		
Sulfamethoxazole	11	73.33%	/		4	26.67%	
Tetracycline	12	80%	3	20%	/		
Tigecycline	3	20%	3	20%	9	60%	
Vancomycin	15	100%	/		/		P<0.61

*No = Number, % = Percentage *If P value is less than 0.05 is significant*

Table 10. Percentage of multidrug resistance among gram negative bacteria isolated from patients with bacteremia in 2021

Isolated bacteria	Number of antibiotics resistance (total number of antibiotics = 13)
Escherichia coli	7 (53.85%)
Klebsiella pneumonia	9 (69.23%)
Pseudomonas aeruginosa	5 (38.46%)
Acinetobacter baumanni	11 (84.62%)

Table 11. Resistance rate of gram-negative bacteria isolates from patients with bacteremia in 2021

Antibiotics	**No of Resistance % of Gram negative in 2021**			
	***Acinetobacter baumanni* (6)**	***Escherichia coli* (4)**	***Klebsiella pneumonia* (3)**	***Pseudomonas aeruginosa* (2)**
Ampicillin	1 16.67%	1 25%	2 66.67%	/
Cefazolin	1 16.67%	1 25%	2 66.67%	/
Ceftriaxone	3 50%	1 25%	1 33.33%	/
Cefexime	2 33.33%	/	/	/
Aztreonam	/	4 100%	1 50%	2 100%
Pipracillin	4 66.67%	4 100%	3 100%	2 100%
Ceftazidime	3 50%	/	3 100%	/
Imipenem	2 33.33%	/	1 33.33%	2 100%
Gentamicin	3 50%	/	/	2 100%
Ciprofloxacin	2 33.33%	2 50%	1 33.33%	2 100%
Levofloxacin	2 33.33%	/	1 33.33%	/
Erythromycin	3 50%	3 75%	/	/
Rifampin	/	/	/	/

Multidrug resistance among Gram negative bacteria isolated from patients with bacteremia in 2021. In 2021 out of 293 samples 15 were positive and 13 antibiotics were used and antibiotics susceptibility test was made for the all isolates and results showed that the bacteria were resistance to the most of antibiotics as seen in Table 10. *Acinetobacter baumanni* had highest number of antibiotic resistance was 11 (84.62%) followed by *Klebsiella pneumonia* which had 9 (69.23%) antibiotic resistance then *Escherichia coli* that had 7 (53.85%) and finally *Pseudomonas aeruginosa* had lowest number of antibiotic resistance had 5 (38.46%) resistance, they had resistance to more than three classes of antibiotics mostly (62%) of isolates and the range rate for resistance between (5-11) antibiotics.

3.9 Resistance Rate of Gram-negative Bacteria Isolates from Patients with Bacteremia

Our result in Table 11 showed that *Acinetobacter baumanni* mainly resistance to Pipracillin 4/6 (6.67%) followed by Ceftriaxone , Ceftazidime, Gentamicin and Erythromycin 3/6 (50%) , for *Escherichia coli* showed resistance to Aztreonam and Pipracillin 4/4 (100%) then followed by Erythromycin 3/4 (50%) , for *Klebsiella pneumonia* showed highly resistance to Pipracillin and Ceftazidime percentage of resistance 3/3 (100%) followed by Ampicilin and Cefazolin 2/3 (66.67%) and lastly for *Pseudomonas aeruginosa* showed resistance to Aztreonam.

4. DISCUSSION AND CONCLUSION

Pipracillin, Imipenem, Gentamicin and Ciprofloxacin have percentage of resistance 2/2 (100%). as in Table 11.

Bacteremia is a major complication of infection by *Enterobacreriaceae* as it can lead to severe sepsis with acute organ failure and septic shock [21]. Bacteremia is the presence of bacteria in bloodstream, among the health care-associated infections, bacteremia accounts for maximum cases of mortality and morbidity, despite the fast improvement in diagnostic techniques, blood culture remains the gold standard for the diagnosis [22].

And we also observed that the number of cases in 2020 are lower than the year before and this due to many factors one of them I presume is due to the quarantine in Erbil because of coronavirus outbreak so the number of patients those visited the government hospitals were less. Our results 2018 showed that in 10/135 (7.14%) isolates of Gram-negative bacteremia were more than the results recorded by [22], that were 6265 samples in total and about 316 (5.04%) were positive with Gram-negative Bacteria were isolated at tertiary care center in Delhi, India. On other hand from 2017 to 2019 we had 26/546 (4.76%) isolates of Gram-negative bacteremia which were less to Huttner et al. [23] study, which out of 2345 total samples 504 (21.49%) were positive at 3 tertiary care hospitals in Geneva, Lausanne, and St Gallen, Switzerland.

Bacteremia were more than females but was higher than ours a total of 165 patients infected with bacteremia 101 (61.21%) were males and 64 (38.79%) females conducted from January 2017 to September 2017 in Al-Sader teaching hospital in Amara city in Iraq, and agreed also with results reported by Daga et al. [24] who founded that total of 48 bacteremia positive patients 27 (56.2%) were males in study conducted from 2015 to 2017 in University hospital of Londaria. The sex distribution of patients in our study is consistent with those of other reported studies, showing predominance of males .Moreover, there is a gender gap found in susceptibility to some infectious agents and in the adaptive immune response, which has in part physiological basis in reproductive hormone modulation of immune defense, bacterial virulence and cell physiology [25]. Statistical analysis showed that non-significant correlation ($p<0.17$) between bacteria and gender from patients with bacteremia.

According to the age category in Fann university hospital in Dakar, Senegal had shown that the distribution of bacteremia between the years 2013 and 2014 in reported by Lakhe et al., [26] was more found in the age groups (2-40 years) and (40-60 years) with respectively (38%) and (40.5%), while in our study the distribution of bacteremia among the years (2015-2021) was higher between the age groups (21-30 years) and (41-50 years) with 13/57 (22.81%) and 9/57 (15.8%) respectively, therefore the most representative age group of patient with bacteremia in our study was (21-30) years old (22.81%) whereas in Fann hospital the most representative age group was (40-60) years old (40.5%). Otherwise, children aged (0-10 years) infected with bacteremia between the years (2018-2020) in our study was low with 1/10

(10%), 2/14 (14.28%) and 1/10 (10%) respectively in comparison to the study conducted at Emergency pediatric unit of Aminu Kano teaching hospital in 2013 with result reported by (Idris et al., 2018) who founded that the distribution of bacteremia was higher (33.3%) in children aged 24 months or younger compared to (12.3%) among older children, this may be attributed to the immature immune system. Another plausible reason is that children under 24 months of age constituted the majority of the study population, statistical analysis showed that non-significant correlation (p<0.87) between bacteria and age from patients with bacteremia.

In our study, it showed that from our samples that we collected from 2015 to 2021 *Escherichia coli* 28/57(49.12%) was most common isolates, followed by *Klebsilla pneumonia* 11/57(19.3%), *Enterobacter* 7/57(12.28%) and *Acinetobacter baumannii* 7/57(12.3%) , this disagreed with results recorded by Bajaj et al. [22] which demonstrates that from blood samples were received in the microbiology department of Govind Ballabh Pant Hospital from India most infections caused by *Klebsiella pneumonia* 98/316 (31.01%) followed by *Escherichia coli* 21/316 (6.64%) and *Enterobacter* 15/316 (4.74%). Statistical analysis showed that non-significant correlation between bloodstream infections by Gram-negative bacteria and years (P <0.64).

Our data from 2015-2021 recorded that out of 732 samples that collected from Nanakali hospital showed the most frequent cause of Gram negative bacteremia was *Escherichia coli* 24 (3.30%), this result is disagreed with study by Muhammad et al. [27] in Baghdad city which shows that out of 33 positive blood cultures the most common species was *Enterobacter spp.*12/33 (36.4%), statistical analysis showed that non-significant correlation (P<0.32) between bacteremia and cancer.

The most frightening yet preventable complication in critical care units is bloodstream infection. High incidence of multidrug-resistant bacteria leads to increased staying in hospital, rise in financial burden on the patients, and in many instances, loss of life, it is often associated with hospitalization, insertion of foreign bodies such as catheters into blood vessels, and other predisposing factors like staying in intensive care unit, lapses in hand washing, and non-adherence to infection control practices by medical staff. Genitourinary tract, intra-abdominal foci, and respiratory tract are the frequent sources of blood stream infections [22]. Our result in Tables 3-10 showed that *Acinetobacter baumanni* mainly resistance to Pipracilin 4/6 (66.67%), for *Escherichia coli* showed high resistance to Aztreonam and Pipracilin percentage of resistance 4/4 (100%), (100%) for *Pseudomonas aeruginosa* showed high resistance to Aztreonam, Pipracilin, Gentamicin, Imipenem and Ciprofloxacin had percentage of resistance 2/2 (100%). Isolated *Klebsiella pneumonia* showed complete resistance (100%) to pipracilin and ceftazidime, (33.33%) for ciprofloxacin, and showed no resistance to gentamicin. Our finding is different from study done by (Lakhe et al.,2018) who recorded that isolated *Klebsiella* showed complete resistance (100%) to amoxicillin-clavulanic acid, 80% for cotrimoxazole and 60% for gentamicin and ciprofloxacin. And also in his study showed that only one patient has resistance to pipracillin (14.3%), and *Acinetobacter* has high resistance to Gentamicin (42.8%). Whenever in our study *Acinetobacter* was high resistance to pipracillin (66.67%), and one patient showed resistance to ampicillin (16.67%). Other authors believe that the degree of antibiotic resistance does not significantly influence the risk of death, which mainly occurs as a result of the severity of the underlying disease, the initial status of the patient and the type of antibiotic treatment used. Inappropriate antibiotic treatment seems to be the main reason associated with a high mortality [28].

ETHICAL APPROVAL AND CONSENT

The bacterial strains used in this study were isolated from the routine clinical specimens and consent was obtained from the patients. This study was approved by the Scientific and Research Ethics Committee at the College of Health Sciences/ Hawler Medical University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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