Impact the antibiotic resistance for Staphylococcus aureus in hospitalized cancer patients in Erbil Governate/Iraq

Abstract

Background: Infection is a continuous problem in cancer patients, especially in developing ~~country~~countries. Multidrug-resistant Staphylococcus aureus ~~are~~ is among the most frequent complication in immunocompromised cancer patients and poses the greatest risk to immunocompromised cancer patients.

Objectives: Our study aimed to carry out a study on isolated *Staphylococcus aureus* from various clinical samples among cancer patients in Erbil city and analyze its epidemiology and antibiotics susceptibility pattern test and multi-drug resistance.

Materials and Methods: A total of 865 from 2016 until 2020 were isolated Staphylococcus aureus from 6 clinical samples (Urine, Sputum, Wound swab, ~~and~~ Nasal swab, Blood, and Stool) from patients attending Nanakaly Hospital and from both males and females. Only 100 cases had been identified as isolates of *S.aureus* which was identified by using macroscopical, microscopical, biochemical tests and Vitek 2 compact system. Also, antibiotic susceptibility tests were performed by Vitek 2 compact on 19 antibiotics.

Results: Only 100 S.aureus isolates were isolated from 865 samples ~~distribution~~ distributed according to their source of isolation in the cancer patient, urinary tract infection is the most our specimen followed by wound infection, respiratory tract infection, blood infection, and gastrointestinal infection. Breast cancer is the most common in our study followed by Colon cancer and Multiple myeloma, with the percentage of females infected with *S.aureus* more than the males, with females being 74/865(8.5%) and males being 28/865(3.2%), after 2016 infections by *S.aureus* was increased in young and middle-aged people being 52/100(52%) in total, from 2016-2020 *S.aureus* infected patients with breast cancer was 47/100(47%), the colon was 27/100(27%) and multiple myeloma was 26/100(26%). Although (Aztreoman, Ertapenem, Ticarcillin-clavulanic acid) can be considered ~~as~~ effective agents ~~toward~~ for MDR strains for empirical antibiotic therapy in cancer patients. *S.aureus* isolates had resistance to more than six antibiotics.

Conclusions: The study findings showed a significant distribution of MDR *S.aureus* which may increase the burden of healthcare-associated infections in cancer patients. Moreover, mechanisms of resistance should also be investigated for better characterization of the multi-drug resistance of S.aureus isolates.

Keywords: S. aureus, age, gender, cancer patient, multidrug resistant.

Introduction

The relation between bacteria and cancer Tumor growth and metastasis are a complicated biological process that involves a subset ~~or~~ ofindividual cancer cells detaching from the primary tumor, migrating to the blood/lymph, and colonizing distant organs or tissues (Zhang et al.,2014).Neutrophils are the first line of defense in the host immune system against pathogen infection and act as a double-edged sword in the processes of cancer occurrence and development (Coffelt et al.,2016).Cancer metastasis is one of the leading causes of ~~cancer~~ cancer-related mortality worldwide, and approximately 13% of all tumor-related deaths are related to metastasis. Currently, surgical treatment is one of the most effective strategies for cancer patients, and most cancer patients receive at least one surgical procedure as part of their treatment (Wyld et al.,2015).Colorectal cancer (CRC) is one of the most common malignancies and among the leading causes of death in the industrialized world (Coffelt et al.,2016).when clinically suspected, diagnostic workup includes cultures and imaging, and treatment includes ~~broad~~ broad-spectrum antibiotics and drainage (Abreu et al.,2011). Lung cancer is the leading cause of cancer-related death in the western hemisphere (Siegel et al.,2014). Nosocomial infections caused by CoNS (Coagulase Negative Staphylococci) are more likely to occur among patients with malignancy especially those who develop chemotherapy-induced damage to mucosal surfaces and neutropenia (Boyce,2004). S. aureus is also reported to be the second most common cause of bloodstream infection after coagulase-negative Staphylococcus in patients with the neoplastic disease(Wisplinghoff et al.,2003).SABIs (Staphylococcus aureus Bloodstream Infections) in cancer patients are a significant cause of morbidity and mortality in both neutropenic and non-neutropenic patients (González-Barca et al.,2001).Infections triggered by S. aureus are a primary source of sickness predominantly among ~~the~~ immunosuppressive cancer patients (Brook and Frizier,1998). In addition, *S. aureus* is a common cause of SSI (Surgical Site Infection) after breast operations. Studies found that *S. aureus* caused 19% and 40%, respectively, of SSIs following breast cancer operations (Omar and Al-Mousa,2013). Gram-positive bacteria account for at least half of all microbiologically documented infections in cancer patients (Mikulska et al.,2014). In addition, S. aureus infection mediates the enhancement of non-small cell lung cancer cell metastasis due to upregulation of the TLR4/MyD88 pathway (Toll-like receptor/Myeloid differentiation primary response 88) pathway (An et al.,2016). Although the prevalence of *S. aureus* as a cause of infection in cancer patients varies widely depending on the specific population, the type of infection studied, and geographic location, S.aureus has a major clinical impact on patients with malignancy (Bodro et al.,2014).National surveillance reports have shown that S.aureus is the second leading cause of CLABSI (Central Line-associated Bloodstream

Infection) (Sievert et al.,2013).The mortality rate in cancer patients with S. aureus-CLABSI is 25%–30% and more than 50% of patients develop hematogenous complications (Ghanem et al.,2007).In this context, bacterial pathogenicity factors may play a decisive role by stimulating cancer cell growth. while a strong proliferative effect has been described for LPS(Lipopolysaccharide), the endotoxin of Gram-negative bacteria, in the lung, liver, ovarian, gastric, and breast cancer (Wang et al.,2015).

Although the most common pathogens found in NSCLC (Non-small lung cell cancer) are of Gram-negative origin, Gram-positive germs such as S. aureus and Streptococcus pneumoniae account for about 25% of pulmonary infections in lung cancer patients and are the leading cause of septicemia in lung cancer (Berghmans et al.,2003). Pulmonary bacterial infections are frequently found in advanced stages of lung cancer and may contribute to the progression of this disease (Berghmans et al.,2003). The influenza virus is known to increase the susceptibility to pneumonia caused by S. aureus. Furthermore, this latter caused 4% of sepsis among hospitalized patients with cancer (Torres et al.,2015).

Invasive methicillin-susceptible *Staphylococcus aureus* (MSSA) infections should be treated with an anti-staphylococcal beta-lactam such as cefazolin or nafcillin. In a matched ~~case~~ case-control study in which approximately 40% of patients had cancer, treatment of MSSA bacteremia with vancomycin, as opposed to ~~a~~ beta-lactam, was associated with higher mortality (Kim et al.,2008). Multidrug-resistant (MDR) *Staphylococcus aureus* is a gram-positive, common pathogen for nosocomial bacteria that induces pneumonia, sepsis, and bacteremia, especially among intensive care unit patients (Jang,2016). The percentage of S. aureus isolates among cancer patients that are methicillin-resistant varies geographically but broadly appears to be on the rise (Montassier et al.,2013). Since 2000, multiple cases of hospital and ~~community~~ community-acquired MRSA prostatic abscesses have been reported (Sukhal et al.,2013). *S. aureus* infection has been recognized as one of the most urgent public health threats not only because it is resistant to all commonly used antibiotics (Recker et al.,2017). Vancomycin remains the mainstay of treatment for MRSA; however, high vancomycin failure rates among patients with cancer and MRSA bloodstream infection have been reported (Mahajan et al.,2012). Many strategies have been advocated to prevent MRSA infection with variable degree of evidence based, including search and destroy policy, restrictive antibiotic prescribing policy (Watters et al.,2000).

Methods

Sample collection:A total of (865) samples were collected from cancer patients with 3 main types ~~from~~ hospitalized patients with cancer(Breast cancer, Colon cancer, Multiple myeloma). Six different sources (Urine, Sputum, Wound and Nasal swabs, Blood, Stool). After collection, all bacterial isolates were subjected to a series of confirming tests. Clinical samples were collected from patients attending Nanakali hospital in Erbil city during the period 2020. Clean-Catch midstream urine of the patients was collected in a sterile tube (4-5ml) and immediately transported to the laboratory. Guidelines for proper specimen collection were given to all patients.

Vitek2 compact system

The redesigned colorimetric Vitek2 compact system, with an updated advanced expert system (AES) (bioMerieux, Marcy l'Etoile, France) was evaluated for its accuracy and rapidity to identify clinical isolates and to detect several antimicrobial resistance(Nakasone et al.,2007). Principles of the Vitek2 is an automated microbiology system utilizing growth-based technology. This system accommodates the colorimetric reagent cards that are incubated and interpreted automatically. Overall, the Vitek2 gave 95.8% of compatibility with the reference API strips (bioMerieux) in the identifications (ID) s of the Gram- positive cocci (GPC), Gram-negative rods (GNR), and yeasts. The accuracy was finally estimated to be 98.3% through additional confirmatory tests. Also, >90% of identifications of GPC and GNR were obtained within 7 hours of incubation. The most resistant isolates were identified within 12 hours of incubation. In conclusion, the new colorimetric Vitek2. Identified within 12 hours of incubation. In conclusion, the new colorimetric Vitek 2 compact system with AES greatlyimproved its accuracy in species identification and detection of antimicrobial resistances, and it will be highly acceptable to clinical microbiology laboratory function (Kaase et al., 2009) The Vitek2 has everything health care laboratories need for fast, accurate microbial identification, and antibiotic susceptibility testing.

RESULTS

Out of 865 isolates only (100) were positive for*Staphylococcus aureus* from cancer patients between 2016 and 2020 as in Table (1). Results showed that we had 40(27%) positive cases out of 150 in 2016 and 16(8%) positive cases out of 200 in 2017 and ~~in~~ 2018 we had 25(11%) positive cases out of 225 and 12(5%) positive cases out of 232 in 2019 and in 2020 we had 7(12%) positive cases out of 58 statistical analysis showed that non-significant correlation between the bacteria and years (P >0.05) as seen in Table (1).

Comment [SYZE1]: Title of table 1 not present

Years	*Staphylococcus aureus*						
	Positive	**%**	**Negative**	**%**	**Total**	**%**	**P-value**
2016	40	27	110	73	150	100	
2017	16	8	184	92	200	100	
2018	25	11	200	89	225	100	
2019	12	5	220	95	232	100	
2020	7	12	51	88	58	100	
Total	100	11.5	765	88	865	100	0.0961

~~Table 1.~~

Incidence of *Staphylococcus aureus* amonggenders

In 2016 out of **150** samples the female ratio was more than the male~~s~~, the males had **8**(**5.3**%) positive cases and **25**(**16.6%**) negative cases and for the females we had **32**(**21 %**) positive cases and **85**(**57%**) negative cases. In 2017 out of **200** samples the female ratio exceeded the males we had **140(70%)** female samples ~~in~~ ofwhich **10(5%)** were positive and **130(65%)** were negative, for the males we had **60(30%)** samples in which **6(3%)** were positive and **54(27%)** negative.Asfor2018and2019,in2018wehad**225**samples,andin 2019**232**samples,female~~'s~~ratio exceeding male's, for 2018 females we had **183(81%)** samples **18(8%)** positive, **165(73.3%)** negative and the males had **42(18.6%)** samples **7(3.1%)** were positive and **35(15.5%)** negative, as for 2019 we had **158(68%)** female samples and **76(33.6%)** male ones for the females were **8(3.4%)** positive and **150(64.6%)** negative as for males 10(3.3%) were positive and 130(43.3%) negative,In2020femalehad**6(10%)**positivecasesand**42(72%)**negativecasesandformales,we had **1(1.7%)** positive ~~casas~~ cases and **9(15%)** negative cases. Statistical analysis showed that non-significant correlation between ***S.aureus***and gender (P >0.05) as in **Table (2).**

Table (2): Incidence of *Staphylococcus aureus* among genders.

Year	**Male**		**Female**		**Total**	**P value**
	P(No%)	**N(No%)**	**P(No%)**	**N(No%)**	**No(%)**	
2016	8(5.3)	25(16.6)	32(21)	85(57)	150(100)	
2017	6(3)	54(27)	10(5)	130(65)	200(100)	

2018	7(3.1)	35(15.5)	18(8)	165(73.3)	225(100)	
2019	6(2.6)	70(30)	8(3.4)	150(64.6)	232(100)	
2020	1(1.7)	9(15)	6(10)	42(72)	58(100)	
Total	28(3.2)	193(22)	74(8.5)	572(66)	865(100)	0.0589

P=Positive ,N=Negative ,No=Number,%=percentage

Distribution of *Staphylococcus aureus* in different clinicalsamples

From 2016 until 2020 ***S. aureus*** were isolated from **6** clinical samples (Urine, Sputum, Wound, and Nasal swabs, Blood, and Stool) in 2016 urine was the major source of ***S.aureus*24/150** that's **16%,**and wound swab second **9/150** meaning **6%**, sputum, and blood were the least of the samples **7/150** meaning **4.6%**, we didn't have any stool samples. In 2017 urine **6/200(3%)** being the most and wound swab **4/200(2%)** being the second, sputum **3/200(1.5%)** being third and blood **2/200(1%)** and stool **1/200(0.5%)**. In 2018 urine **10/225(4.4%)** being the most, wound swab **5/225(2.22%)** being the second most, blood **4/225(1.7%)** and stool **4/225 (1.7%),** sputum **2/225(0.8%)**. In 2019 urine also was the major source being **5/232(2.1%)** and blood ~~being~~ wasthe second most **4/232(1.7%)**, wound swabs **2/232(0.9%)** stool ~~being~~ wasthe last having **1/300(0.3%)** and didn**'**t have any blood samples. In 2020 urine remained the main source being **4/58(7%)** and wound swabs **2/58(3.4%)** and blood **1/58(1.72%)** and didn**'**t have sputum and stool specimens. Statistical analysis showed that significant correlation between ***S. aureus*** and different clinical samples (P >0.05) as in **Table (3)andFigure(1).**

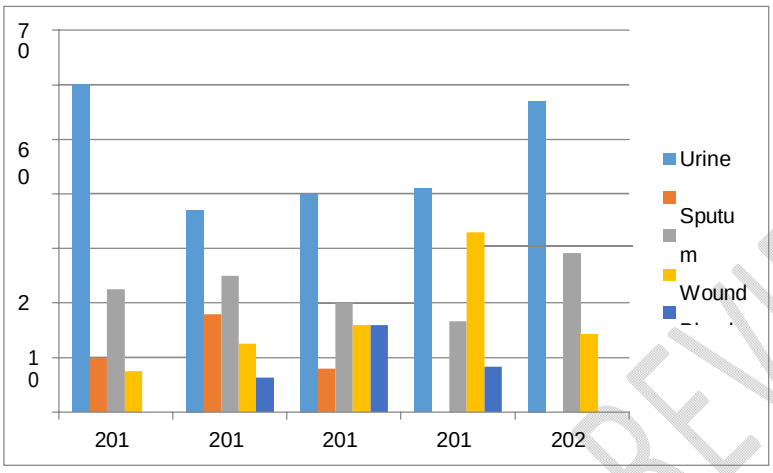
Table (3) Distribution of *Staphylococcus aureus* in different clinical samples.

Years		**Urine**	**Sputum**	**Wound Swab**	**Blood**	**Stool**	**Total**	**P- value**
		N(%)	**N(%)**	**N(%)**	**N(%)**	**N(%)**	**N(%)**	
2016	Positive	24(60%)	4(10%)	9(22.5%)	3(7.5%)	-	40(6.4%)	
	Negative	60(54%)	10(9%)	25(22.4%)	15(13%)	-	110(13%	
2017	Positive	6(37%)	3(18%)	4(25%)	2(12.5%)	1(6.25%)	16(9%)	
	Negative	110(60%)	17(9%)	46(25%)	6(2.3%)	5(2.7%)	184(21%)	
2018	Positive	10(40%)	2(8%)	5(20%)	4(16%)	4(16%)	25(3%)	
	Negative	125(62%)	30(15%)	20(10%)	13(6.5%)	12(6%)	200(23%)	
2019	Positive	5(41%)	-	2(16.6%)	4(33%)	1(8.3%)	12(1%)	
	Negative	108(49%)	-	54(24.5%)	43(19.5%)	15(7%)	220(25%)	
2020	positive	4(57%)	-	2(29%)	1(14.3%)	-	7(0.8%)	
	Negative	30(59%)	-	15(29%)	2(4%)	-	51(6%)	
Total		486(57%)	128(15%)	182(21%)	75(8.8%)	38(4.4%)	865	0.0340

N=Number of samples %=Percentage

Figure (1) Distribution of *S.aureus*in different clinical samples

Comment [SYZE2]: Title below in figures



Incidence of Staphylococcu aureus amongages

The incidence of S.aureus in 2016 was seen mostly among youngadults and people younger than 60 years old (19-59) having 24/40(60%), meanwhile, in 2017 it was different it was seen mostly among the elderly (60 or older) having 9/16 (56%). In 2018 also it was seen mostly between the ages 19 to 59 providing 13/25(52%) and in 2019 also the majority who~~m~~ were infected were between 19 and 59 years old having 7/12(58%), lastly in 2020 also mostly between the ages19 and 59 years having 4/7(57%). Statistical analysis showed that significant correlation between bacteria and age ($P < 0.05$) as in Table (4)**Figure (2).**

Table (4) The relation between S.aureus and ages.

Years	≤18 No.(%)	19-59 No.(%)	60≤ No.(%)	Total No.(%)	P-value
2016	5(12.5%)	24(60%)	11(27.5%)	40(100%)	
2017	3(18.75%)	4(25%)	9(56.25%)	16(100%)	
2018	7(28%)	13(52%)	5(20%)	25(100%)	
2019	2(16.6%)	7(58%)	3(25%)	12(100%)	
2020	1(14.28%)	4(57%)	2(28.6%)	7(100%)	
Total	18(18%)	52(52%)	30(30%)	100(100%)	<0.0001

No.= number ofpositivepatients %=percentage

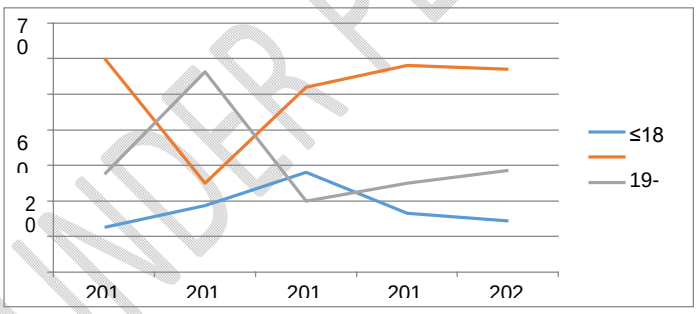


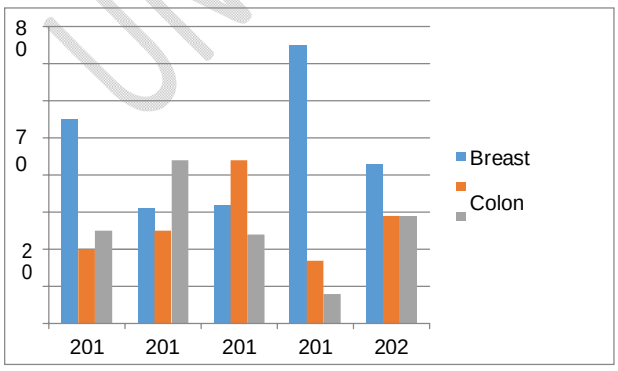
Figure (2) The relation between *S.aureus*and ages.

Types of cancer among patients infected with *Staphylococcusaureus*

In 2016 *S.aureus*was present mostly in patients with breast cancer being**22/40(55%)**, multiple myeloma **10/40(25%),**and colon cancer being **8/40(20%)**. In 2017 *S.aureus*was present mostly in patients with multiple myeloma type being **7/16(44%)** breast cancer being second and colon cancer being the least. In 2018 out of **25** patients with *S.aureus***11** were colon cancer being **(44%)** while ~~in~~ breast cancer ~~being~~ **8/25(32%)** and lastly in multiple myeloma ~~being~~ was the least having **6/25(24%)**. In 2019 out of **12** patients with *S.aureus***9** were breast cancer being **(75%)** while ~~in~~ colon cancer ~~being~~ **2(17%)** and lastly in multiple myeloma **1(8%)**. Lastly in 2020 mostly ~~being~~ breast cancer **3/7(43%)**. Multiple myeloma and colon cancer ~~being~~ are**2/7(29%)** for each. Statistical analysis showed that significant correlation between types of cancer and *S. aureus* ($P < 0.05$) as in **Table (5)** and **Figure(3)**.

Table (5) Types of cancer among patients infected with infected *S.aureus*

Type	Breast	Colon	Multiple Myeloma	Total	P-value
	No(%)	No(%)	No(%)	No(%)	
2016	22(55%)	8(20%)	10(25%)	40(100)	
2017	5(31%)	4(25%)	7(44%)	16(100)	
2018	8(32%)	11(44%)	6(24%)	25(100)	
2019	9(75%)	2(17%)	1(8%)	12(100)	
2020	3(43%)	2(29%)	2(29%)	7(100)	
Total	47(47%)	27(27%)	26(26%)	100(100)	<0.0001



No: number of patients, %: Percentage

Figure(3) Types of cancer among patients infected with infected*S.aureus.*

Number and percentage of antimicrobials resistance among*Staphylococcusaureus*The antibiotics resistance pattern of **(100)**isolatesof *S.aureus*were screenedfortheir resistancetonineteenwidelyusedantibioticsfrom2016until2020,in2016themostrésistance~~were~~was to(Tigecycline**31/40(77.5%)**,Piperacillin**30/40(75%)**,Aztreonam**28/40(70%)**andlastly Vancomycin**27/40(67.5%)**andweresensitivetoAmikacin**28/40(70%)**,in2017mostresistance weretoAmoxicillin**13/16(81%)**andAztreonambeing**14/16(87%))**andsensitivityto CiprofloxacinandTicarcillin-clavulanicacidbeing**7/16(43.7%)**.In2018themostresistancewasto Ciprofloxacin being **19/25(76%)** and the least resistance to Imipenem **9/25(36%)** andin2019 themostresistancewastoCeftriaxoneandErtapenem**10/12(83%)**and the leastresistanceto Gentamycin **5/12 (42%).** In 2020 the most resistancewasto Ampicillin, Amoxicillin,Cefepime,Tigecycline, and Vancomycin being 6/7(86%) as in **Table (6).**

Table (3-6) Number and percentage of antimicrobials resistance among *S.aureus*

	2017 (N=16)			2018 (N=25)			2019 (N=12)			2020(=7) N		
ANTIBIOTICS	**R N(%)**	**I N(%)**	**S N(%)**	**R N(%)**	**I N(%)**	**S N(%)**	**R N(%)**	**I N(%)**	**S N(%)**	**R N(%)**	**I N(%)**	**S N%**
Ampicillin	26(65%)	4(10%)	10(25%)	11(68%)	1(6.2%)	5(31%)	16(64%)	3(12%)	6(24%)	9(75%)	1(8.3%)	2(16.6%)	6(86%)	-	1(14.3%)
Amoxicillin	21(52.5%)	5(12.5%)	14(34%)	13(81%)	-	3(18.7%)	14(56%)	2(8%)	9(36%)	8(66%)	-	4(33%)	6(86%)	-	1(14.3%)
Amoxiclav	19(47.5%)	3(0.07%)	18(45%)	10(62%)	-	6(37.5%)	15(60%)	1(4%)	9(36%)	9(75%)	-	3(25%)	4(57%)	1(14.3%)	2(28.6%)
Ceftriaxone	15(37.5%)	1(0.02%)	24(60%)	12(75%)	-	4(25%)	13(52%)	4(16%)	8(32%)	10(83%)	-	2(16.6%)	5(71%)	-	2(28.6%)
Aztreonam	28(70%)	1(0.02%)	11(27%)	14(87%)	1(6.2%)	1(6.2%)	17(68%)	2(8%)	6(24%)	7(58%)	2(16.6%)	3(25%)	4(57%)	-	3(43%)
Piperacillin	30(75%)	4(10%)	6(15	11(68	2(12.5%)	3(18.7	12(48	3(12	10(40%	8(66%	1(8.3%	3(25%)	4(57	1(14.3	2(28.6

			%)	%)		%)	%)	%)	)	)	)		%)	%)	%)	
Nitrofuranton	6(15%)	10(25%)	24(60%)	8(50%)	4(25%)	4(25%)	12(48%)	4(16%)	9(36%)	6(50%)	2(16.6%)	4(33%)	3(43%)	2(28.6%)	2(28.6%)	
Ertapenem	5(12.5%)	8(20%)	27(67%)	11(68%)	2(12.5%)	3(18.7%)	15(60%)	3(12%)	7(28%)	10(83%)	-	2(16.6%)	4(57%)	-	3(43%)	
Amikacin	12(30%)	-	28(70%)	7(43%)	3 (18.7%)	6(37.5%)	15(60%)	5(20%)	5(20%)	8(66%)	1(8.3%)	3(25%)	5(71%)	-	2(28.6%)	
Gentamycin	10(25%)	7(17.5%)	23(57%)	9(56%)	3(18.7%)	4(25%)	17(68%)	3(12%)	4(16%)	5(42%)	3(25%)	4(33%)	5(71%)	1(14.3%)	1(14.3%)	
Levofloxacin	16(40%)	-	24(60%)	10(62%)	2(12.5%)	4(25%)	14(56%)	5(20%)	6(24%)	6(50%)	1(8.3%)	5(41%)	4(57%)	1(14.3%)	2(28.6%)	
Cefepime	13(32.5%)	9(22.5%)	18(45%)	6(37%)	5(31%)	5(31%)	13(52%)	5(20%)	6(24%)	9(75%)	-	3(25%)	6(86%)	-	1(14.3%)	
Tobramycin	24(60%)	2(0.05%)	14(35%)	12(75%)	1(6.2%)	3(18.7%)	16(64%)	4(16%)	5(20%)	7(58%)	1(8.3%)	4(33%)	5(71%)	-	2(28.6%)	
Tigecycline	31(77.5%)	-	9(22%)	9(56%)	3(18.7%)	4(25%)	10(40%)	5(20%)	10(40%)	8(66%)	-	4(33%)	6(86%)	-	1(14.3%)	
Imipenem	11(27.5%)	8(20%)	21(52%)	9(56%)	2(12.5%)	5(31%)	9(36%)	3(12%)	13(52%)	7(58%)	-	5(41%)	4(57%)	1(14.3%)	2(28.6%)	
Ciprofloxacin	25(62.5)	6(15%)	9(22%)	8(50%)	1(6.2%)	7(43.7%)	19(76%)	1(4%)	5(20%)	6(50%)	1(8.3%)	5(41%)	5(71%)	-	2(28.6%)	
Vancomycin	27(67.5%)	1(0.02%)	12(30%)	10(62%)	2(12.5%)	4(25%)	14(56%)	2(8%)	9(36%)	7(58%)	-	5(41%)	6(86%)	-	1(14.3%)	
Doripinem	-	13(32%)	27(67%)	7(43%)	3(18.7%)	6(37.5%)	13(52%)	5(20%)	7(28%)	8(66%)	-	4(33%)	4(57%)	-	3(43%)	
Ticarcillin-clavulanic acid	-	11(27%)	29(72.5%)	5(31%)	4(25%)	7(43.7%)	11(44%)	4(16%)	10(40%)	9(75%)	-	3(25%)	5(71%)	-	2(28.6%)	

R=resistance, I= intermediate , S= sensitive, N=number of patients, %= percentage

MDR among *Staphylococcus aureus* in2020

In 2020 out of 58 samples 7 were positive and an antibiotics susceptibility test was made for ~~the~~ all isolates ~~and~~ the results showed that the bacterium was resistant to ~~the~~ most antibiotics as seen in Table (7) they had resistance to more than three classes and most isolates resistance to more than **6** antibiotics as in table.

Table (7) Percentage of MDR among *S.aureus*in 2020

Antibiotics	No.(percentage)(N total=7)
Ampicillin (10mcg)	6(86%)
Amoxicillin (20mcg)	6(86%)
Amoxiclav (30mcg)	4(57%)
Ceftriaxone (30mcg)	5(71%)
Aztreonam (30mcg)	4(57%)
Piperacillin (100mcg)	4(57%)
Nitrofurantoin (300 mcg)	3(43%)
Ertapenem (10mcg)	4(57%)
Amikacin (10mcg)	5(71%)
Gentamycin(10mcg)	5(71%)
Levofloxacin(10mcg)	4(57%)
Cefepime (30mcg)	6(86%)
Tobramycin (10mcg)	5(71%)
Tigecycline (15mcg)	6(86%)
Imipenem (10 mcg)	4(57%)
Ciprofloxacin(5 mcg)	5(71%)
Vancomycin (30 mcg)	6(86%)
Doripinem (10mcg)	4(57%)
Ticarcillin-clavulanic acid (75mcg)	5(71%)

No.(N)=number of patients

Discussion

Gram-positive bacteria account for at least half of all microbiologically documented infections in cancer patients (Mikulska et al., 2014), S. aureus infection incidence may be increasing, at least in some regions (Asgeirsson et al., 2011), probably due to higher numbers of invasive procedures and/or at-risk situations. Due to surgery, long-term stay intravenous catheters, repeated radiotherapy, and chemotherapy, cancer patients that suffer from inhibited bone marrow function, neutropenia, and mucosal barrier damage can be easily infected with Gram-positive bacteria (Holland et al., 2014). A total of (865) samples were collected from six sources (Urine, Wound, and Nasal swabs, Sputum, Blood, and Stool) from hospitalized patients with cancer (Breast, Colon, Multiple Myeloma) in Nanakali hospital in Erbil city from January 2016 to November 2020. After collection, all bacterial isolates were subjected to a series of confirming tests.

From 2016 to 2020 the percentage of female infected with S. aureus were more than the males, female being 74/865(8.5%) and males being 28/865(3. 2%) from 2019 to 2020 the percentage of females infected with S. aureus were more than the males, females being 74/865(8.5%) and males being 28/865(3.2%).Our results disagreed with that reported by (Smit et al.,2017) who foundded that male

infected with Staphylococcus were more than females a total of 2638 patients infected with S. aureus 1022(38.7%) were females and 1616(61.3%) were males in (Northern Denmark).

The incidence of Staphylococcus aureus in 2016 was seen mostly among youngadults and people younger than 60 years old (19-59) having 24/40(60%), meanwhile, in 2017 it was different it was seen mostly among the elderly (60 or older) having 9/16 (56%). In 2018 also it was seen mostly between the ages 19 to 59 providing 13/25(52%) and in 2019 also the majority whom were infected were between 19 and 59 years old having 7/12(58%), lastly in 2020 also mostly between the ages19 and 59 years having 4/7(57%). Statistical analysis showed that significant correlation between bacteria and age. From 2016-2019 the total Staphylococcus aureus infected patients with breast cancer was 47/100(47%), colon cancer was 27/100(27%),and multiple myeloma was 26/100(26%) this rise in breast cancer is due to the high number of females infected with Breast cancer and colon cancer for males which were more predominant in 2016 than multiple myeloma, our result agrees with the results recorded by (Bai et al.,2018) in which total of 214 cancer patients 40/214(19%) were breast cancer and 23/214(11%) gastric cancer and the least multiple myeloma having 3/214(1.4%), but our result disagrees with the results reported by (Espersen et al.,1987) in which (71%) multiple myeloma and (28%) acute lymphatic leukemia and (4.4) which is endocarditis. In the developing world, cancer is projected to increase by 70% over the next 20–25 years. Breast cancer represents 20–30% of cancer among women and is likely to account for a major part of that increase. These expectations are anticipated because the populations of developing countries are ageing and cancer is largely a disease of older people. Lifestyle changes are likely to contribute (Majid et al.,2017) In both the MiddleEast and the West, carcinoma of the breast is the most common malignancy of women. In the West, there is a cultural tendency toward late marriages and limited childbearing. In this setting, multiparity and breastfeeding are protective against breast cancers that are predominantly found after the menopause. In the MiddleEast, breast cancer is frequently seen during the childbearing years (Majid et al.,2009)

The extensive emergence of Multidrug-resistant (MDR) bacteria has increased the burden of morbidity and mortality among cancer patients with BSI (Marín et al., 2014). In recent decades, antimicrobial resistance in S. aureus isolates has emerged worldwide. Multi-drug resistance in S. aureus is defined by the existence of methicillin resistance or lack of susceptibility to greater than or equal to one active agent in greater than or equal to three antimicrobial categories (Magiorakos et al., 2012). In 2020 out of 58 samples 7 were positive and an antibiotics susceptibility test was made for the all isolates and the results showed that the bacterium was resistant to the most antibiotics as seen in Table (3-7) they had resistance to more than three classes of antibiotics mostly (86%) of isolates, our finding is higher than the study done by (Bai et al., 2018) who recorded that out of 214 isolates (14.5%) were found to be multi-drug resistance and also with the study done by (Zhouqi et al.,2021), who recorded that the prevalence of MRSA was (44%) among S. aureus bacteremia in cancer patients. Our results showed that the most effective antibiotics were (Nitrofurantoin, Amoxiclav, Aztreonam, piperacillin, Ertapenem, Levofloxacin, Imipenem, Doripinem) showing sensitivity to more than (40%) to ofthese 8 antibiotics as seen in Table (3-7). S. aureus is one of the 'ESKAPE' organisms that are responsible for the majority of bacterial infections in patients with malignancy (EJ,2013). Cancer patients are highly susceptible to bloodstream infection (BSI) due to frequent hospital admissions, cytotoxic chemotherapy, use of invasive procedures, and exposure to broad-spectrum antibiotics (Walshe et al., 2002). Accordingly, they witnessed a more significant increase in the incidence of BSI, and a higher mortality rate than noncancer patients in recent years (Hsieh et al., 2019), with prevalence ranging from 11 to 38% and the mortality rate around 40% (Macedo et al., 2019).Monitoring cancer occurrence in young adults, often under 50 years, is informative because it often reflects relatively recent changes in exposure to

carcinogenic factors. Younger generations worldwide are experiencing ~~an~~ earlier and ~~longer~~ longer-lasting exposure to excess adiposity over their lifetime than previous generations. Numerous cancers are associated with excess bodyweight, and evidence from experimental studies from murine models suggests that obesity and an obesogenic diet accelerate the multistage transition from normal tissue to invasive malignancy and metastatic disease (Sung et al.,2019). So, the rise in cancer between ages 18 and 60 maybe due to obesity and smoking.

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Comment [SYZE3]: Why no numbers in references??

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