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An Observational Study to Determine the Organism/ Organisms That Colonize the Central Lines and To Study the Sensitivity of Those Organisms

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Sanjith Saseedharan*[1], Roopa Karanam[2], Vaijyanti Kadam[2], Dnayeshwar Diwane[3], Elizabeth J Mathew[3], Bikky Chaurasia[3]

[1]HEAD OF CRITICAL CARE DEPARTMENT, [2]CRITICAL CARE CONSULTANT, [3]ICU REGISTRAR, S.L. RAHEJA HOSPITAL, (A FORTIS ASSOCIATE), MUMBAI, INDIA

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ABSTRACT

Aims and objectives: This is the first time that 100% of central lines inserted in a hospital setup have been studied for colonization. This study aimed to determine organism/organisms that colonize the central lines, to study the temporal relationship of the identification of the colonizers, and to study the relationship to variables like antibiotic use and Acute Physiology and Chronic Health Evaluation II score. ***Materials and methods:*** This is a prospective observational study conducted on 200 patients in whom central lines were inserted at S. L. Raheja Hospital (A Fortis Associate), Mumbai. Tips of all central lines that were removed were cultured. Simultaneous blood cultures were also done. Patient demographics, Acute Physiology and Chronic Health Evaluation II score scores, and length of stay were noted to ascertain the relationship between severity of illness, length of stay in ICU, and colonization of central line. ***Results:*** The rate of colonization as per the results of our study was 29%. Gram-positive organisms make 43.1%, gram-negative 41.7%, and fungus in 13.7% of cases. There was no relationship to severity of illness, duration of the length of central line days, or comorbidities with the rate of colonization. ***Conclusion:*** Very few studies exist regarding the colonization rate of central lines. The data of true colonization rate from our single-center reveal that central lines do get colonized with gram-positive and gram-negative organisms in almost equal proportion. This data also seems to suggest that comorbidities, the severity of illness, or the length of time that the catheter is in situ does not change the colonization rate. This data may thus help us to make protocols for clinical management and in devising materials for making catheters.

INTRODUCTION

Intravascular catheters are frequently used in modern-day medical practice mainly to assess and monitor critically ill patients. It is used primarily to monitor central venous pressure or to administer fluid, medications, or total parenteral nutrition, or obtain blood samples.

Central venous catheters (CVC) act as a portal of entry of bacteria that colonize the skin adjacent to the entry point or may serve as foreign bodies that harbour micro colonies leading to multiple complications[1].

Approximately 87% of bloodstream infections are associated with the presence of some type of intravascular device[2]. Catheter-Related Blood-Stream Infections (CRBSI) is the most life-threatening of all healthcare-acquired infections[2].

The use of central venous catheters puts patients at risk for local and systemic infectious complications. It includes local site infection, CRBSI, septic thrombophlebitis, endocarditis, and other metastatic infections (e.g., lung abscess, brain abscess, osteomyelitis, and endophthalmitis)[3].

Infections associated with the use of intravascular catheters represent around 10-20% of all nosocomial infections and cause substantial morbidity and mortality[4;5]. More than 250,000 intravascular catheter-related bacteremias and fungemia occur annually in developed countries like the USA with an attributable mortality of 12-25%[4].

Microbial contamination leads to the development of complex fungal or bacterial biofilm communities which are a potential source of BSI[6]. The most problematic feature of mature biofilms in case of catheter-related infection is an increased ability of biofilm cells to survive antimicrobial agents and the host immune system[7].

Central venous catheter infections most commonly occur in one of three ways: colonization of the catheter tip during insertion, contamination at the catheter hub with routine use, and infection from another source within the body that spreads through the bloodstream and attaches to the lumen. Rarely CVCs can become infected from contaminated infusions[8].

CVC contamination causes an increase in hospitalization costs, morbidity, mortality, and duration of hospitalization; thus, prevention of these infections can be effective in reducing these outcomes[9].

CVC-related bloodstream infections also prolong hospitalization by an average of 6.5 days[10].

Increased mortality rates may also be attributed to the effects of CVC infections. Probably the most significant problem created by a central venous catheter infection is the negative impact one can have on a patient's quality of life and leads to an economical burden[11].

To overcome these problems, there is a need for a study regarding colonization patterns and factors affecting colonization.

Furthermore, determining which antibiotic is appropriate for the treatment of a CRBSI can be quite difficult. Antibiotic resistance is becoming increasingly more common creating a barrier to successful eradication of the organism causing the infection. Hence, studying the antibiotic sensitivity profile of the particular organism will decrease morbidity resulting in better patient management.

Thus, data obtained from the study will have a huge impact on the future both on patient management and guiding the catheter manufacturing industry, particularly in the Indian scenario.

MATERIALS AND METHODS

After receiving written approval from a properly constituted Ethics Committee (EC), a prospective observational study was conducted on 200 patients in whom central lines were inserted at S. L. Raheja Hospital (A Fortis Associate), Mumbai.

Inclusion criteria:

1. Patients older than 14 years, in whom Central line (multi-lumen/single /Hemodialysis line/jugular sheath insertion) needs to be removed unrelated to the central line-associated infection.

2. Those patients where there was suspicion of Central Line-Associated Blood Stream Infections (CLABSI), and the line is removed for that purpose.

3. All patients with other sources of infection who had central lines inserted.

Exclusion criteria:

1. Patients who were admitted to SL Raheja hospital with central lines inserted outside.

2. Central lines accidentally removed,

3. Proven cases of CLABSI and/or cases in which the central line bundle was not followed were excluded.

Central line insertion had been carried out by the trained ICU registrar after all aseptic precautions and has been audited by infection control nurse/assistants. The central line had been removed by the researcher himself for this purpose.

At the time of removal of the central line, the terminal 5 cm of the central line had been cut and taken for culture using an aseptic technique and put in a sterile container. The labelling of the container included giving a serial number from 1 to 200. It had been written down in the format "CLS/2017/SLRH/Sr. no.' with the hospital ID of the patient and the patient initials. Then the sample was transferred to the microbiology laboratory by the infection control nurse and personally handed over to the microbiology technician to ensure processing within 2 hours of removal of line.

In CLABSI suspected cases as per standard protocol, simultaneous central line and peripheral blood cultures were taken and catheters were not removed for such purposes.[3, 16]

Cultures had been processed as per standard methods and observations had been done by both Maki's method and subculture method of the lumen. Then the colony counts were determined.[3] the readings and interpretation had been taken by the microbiologist. Processing had been done by microbiology technicians under the guidance of a technical supervisor.

The growth of ≥1 microorganism in a quantitative or semiquantitative culture of the catheter tip, had been defined as colonization.[3] All organisms isolated had been tested for sensitivity to study epidemiology. Organism isolation and susceptibility testing had been done as per CLSI (Clinical And Laboratory Standard Institute) guidelines 2017. The disposal and sample retention policy of the study material has been as per SLRH Laboratory policy. Statistical analysis was carried out by using IBM SPSS software version 2015.

Ethical policies: Hospital Ethics committee approval was taken before the start of the study.

Ethical Guidelines: NA

Humane considerations: - NA

Conflict of interests–NIL

Funding - NIL

RESULTS

The study involved a total of 200 patients of which 125 (62.5%) of the cases were males and 75 (37.5%) were females. The ages of the cases were ranging from 15.00–91.00 years with the average age being 60.79 years. The mean Acute Physiology and Chronic Health Evaluation II score (APACHE) score was 13.57. The mean duration of the central line in situ was 9.66 days. (as shown in Table 1)

Table No. 1: 1Demographical Data

Parameters	
No. of Cases	**200**
Age (yrs) Mean SD Range	60.79 15.44 15.00 – 91.00 yrs
Sex (%) Male Female	125(62.5) 075(37.5)
Mean APACHE Score	13.57
Mean Duration of Central Line in Situ	9.66

The total no. of cases with catheter colonization was 58(29%). Out of which 24% patients showed growth in Makis method and 26% patients showed growth in the subculture method (Table 2).

The analysis shown in Table 3 and Graph 1 states that 27.7% of the cases had colonization that belongs to Apache Score < 15 which was comparable with 31.4% of the cases with Apache Score >15. 28.2% of the cases had colonization that belongs to Nutrition Risk Score (NRS 2002) < 4 which was comparable with 30.0% of the cases with NRS (2002) > 4 (Table 4, Graph 2). 28.5% of the cases had colonization that belongs to Nutric Score < 5 which was comparable with 31.4% of the cases with Nutric Score >5(Table 5, Graph 3). 42.9% of the cases had colonization that belongs to Neutropenia (< 4000) which was more as compared to 29.1% of the cases with Leucocytes (> 11000) (Table 6, Graph 4). According to Table 7 and

Graph 5, 23.1% of the cases had colonization that belongs to Duration of Central Line < 7 which was less as compared to 33.9% of the cases with Duration of Central Line > 7.

However, the differences observed between the two groups studies among the above-stated variables as the APACHE score, NRS, Nutric Score, Leucocyte status, duration of the central line in situ were not found statistically significant.

Table No. 2: Profile of Organisms Colonized among Study Cases

Organisms	**No. of Cases (N = 200)**	**Percentage**
Total No. of Cases with Colonized	58	29.0
Makis	48	24.0
Subculture	26	13.0

Table No. 3: Association Between Apache Score and Colonization

Apache Score	**No. of Cases**	**Cases with colonization No. %**
≤ 15	130	36 27.7
> 15	070	22 31.4

By Chi Square Test P > 0.05 Not Significant

Graph 1

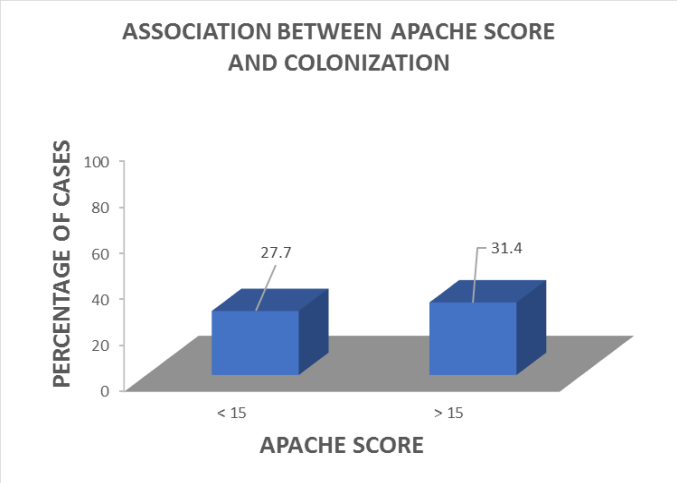


Table No. 4: Association Between Nrs (2002) and Colonization

NRS (2002)	No. of Cases	Cases with colonization No. %
≤ 4	110	31 28.2
> 4	090	27 30.0

By Chi Square Test P > 0.05 Not Significant

Graph 2

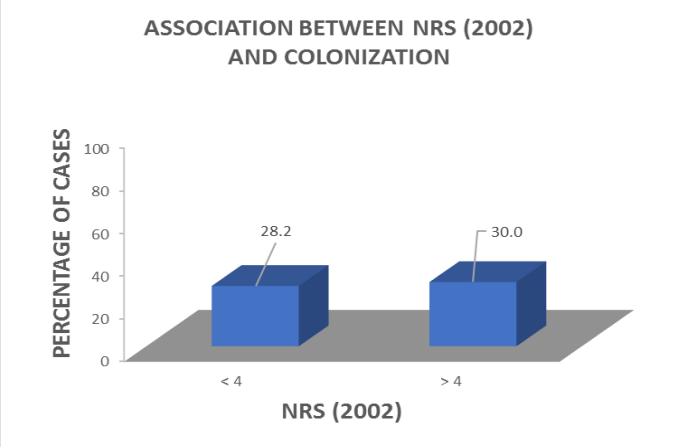


Table No. 5: Association Between Nutric Score and Colonization

Nutric Score	No. of Cases	Cases with colonization No. %
≤ 5	165	47 28.5
> 5	035	11 31.4

By Chi Square Test P > 0.05 Not Significant

Graph 3

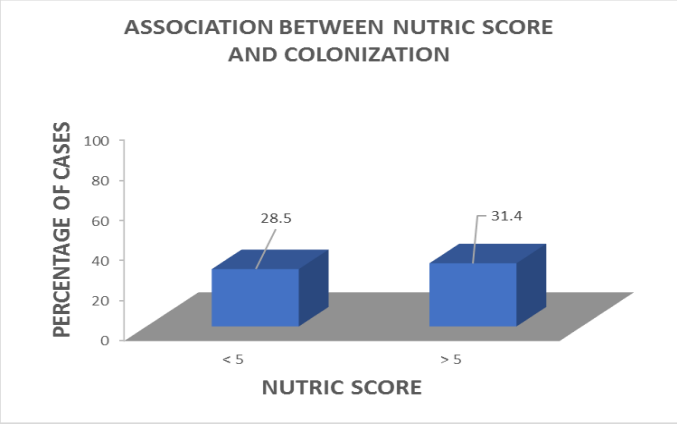


Table No. 6: Association Between Wbc Count and Colonization

WBC Count	No. of Cases	Cases withColonization No. %
Neutropenia (≤ 4000)	007	03 42.9
Normal (4000 – 11000)	081	21 25.9
Leucocytes (≥ 11000)	110	32 29.1

By Chi Square Test P > 0.05 Not Significan

Graph 4

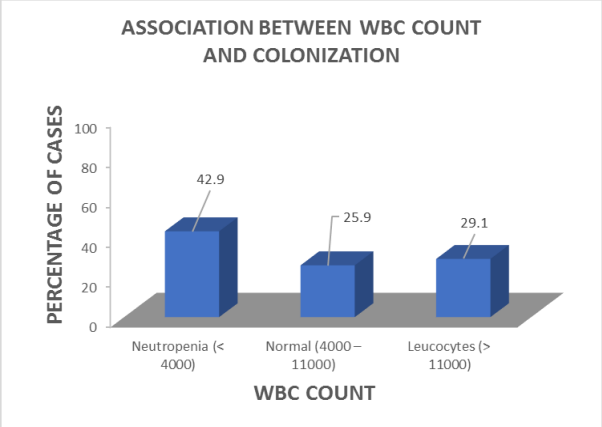
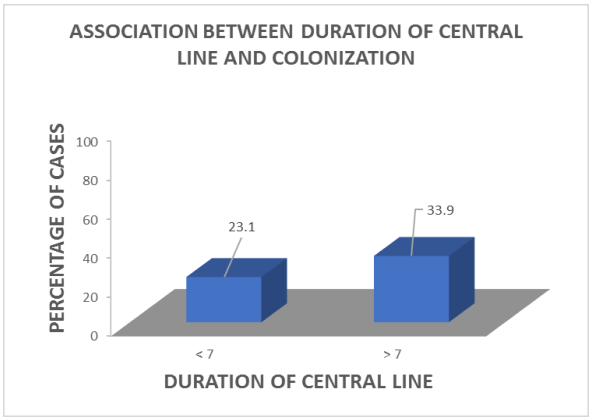


Table No. 7: Association Between Duration of Central Line and Colonization

Duration of central line	No. of Cases	Cases with colonization No. %
≤ 7	091	21 23.1
> 7	109	37 33.9

By Chi Square Test P > 0.05 Not Significant

Graph 5



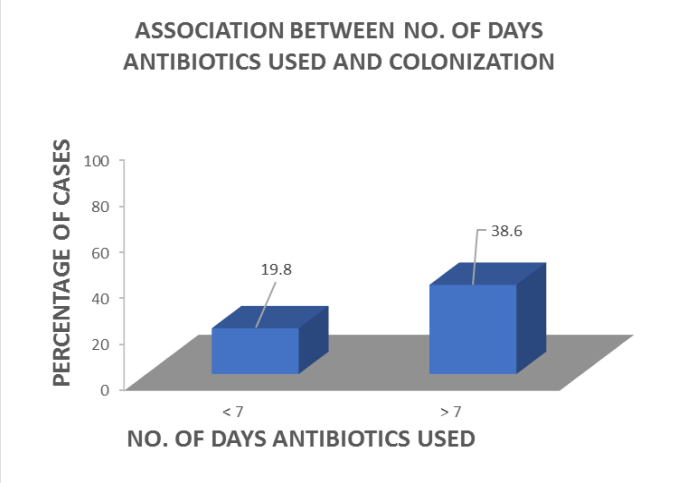
According to Table 8 and Graph 6, 19.8% of the cases that had colonization used Antibiotics for < 7 days which was significantly less as compared to 38.6% of the cases that used Antibiotics > 7 days.

Table No. 8: Association Between No. of Days Antibiotics Used and Colonization

No. of Days Antibiotics Used	No. of Cases	Cases with colonization No. %
≤ 7	096	*19 19.8
> 7	101	39 38.6

By Chi Square Test *P < 0.05Significant

Graph 6



Out of 200 processed catheters, 58 of them showed significant growth. Out of which 27 showed growth of gram-positive organisms, 24 showed growth of gram-negative organisms, 9 cases showed fungal growth.

Among gram-positive organisms, the most observed growth was Staphylococcus Epidermis (24.1%) followed by Staphylococcus Aureus (6.9%) followed by Enterococcus Faecalis (5.2%). The growth of all three organisms i.e. Enterococcus Cloacae and Enterococcus Faecium and Staphylococcus Lentus were reported to be 1.7%. Other Enterococcal species showed a total growth of 5.2% (Table 9, Graph 7). Among gram-negative organisms, Pseudomonas and Klebsiella pneumonia showed maximum growth in 13.8% cases each. Serratia and Acinetobacter showed growth in 5.2% and 3.4% cases respectively. Proteus

species, Enterobacter aerogenes, and Burkholderiacepecia showed growth in 1.7% cases each (Table 10, Graph 8). Most common fungus grown was Candida Albicans (6.9%) followed by Candida tropicalis (3.4%). Candida Auris and Candida ciferri showed growth of 1.7% cases each. (Table 11, Graph 9)

Table No. 9: Total Number of Organism Colonized (*Gram +Ve*)

Organisms	**No. of Cases Colonized (N = 58)**	
	No. of Cases	**Percentage**
Staphylococcus Aureus	04	06.9
Staphylococcus Epidermis	14	24.1
Staphylococcus Lentus	01	01.7
Enterococcus Sp.	03	05.2
Enterococcus Cloacae	01	01.7
Enterococcus Faecium	01	01.7
Enterococcus Faecalis	03	05.2

Graph 7

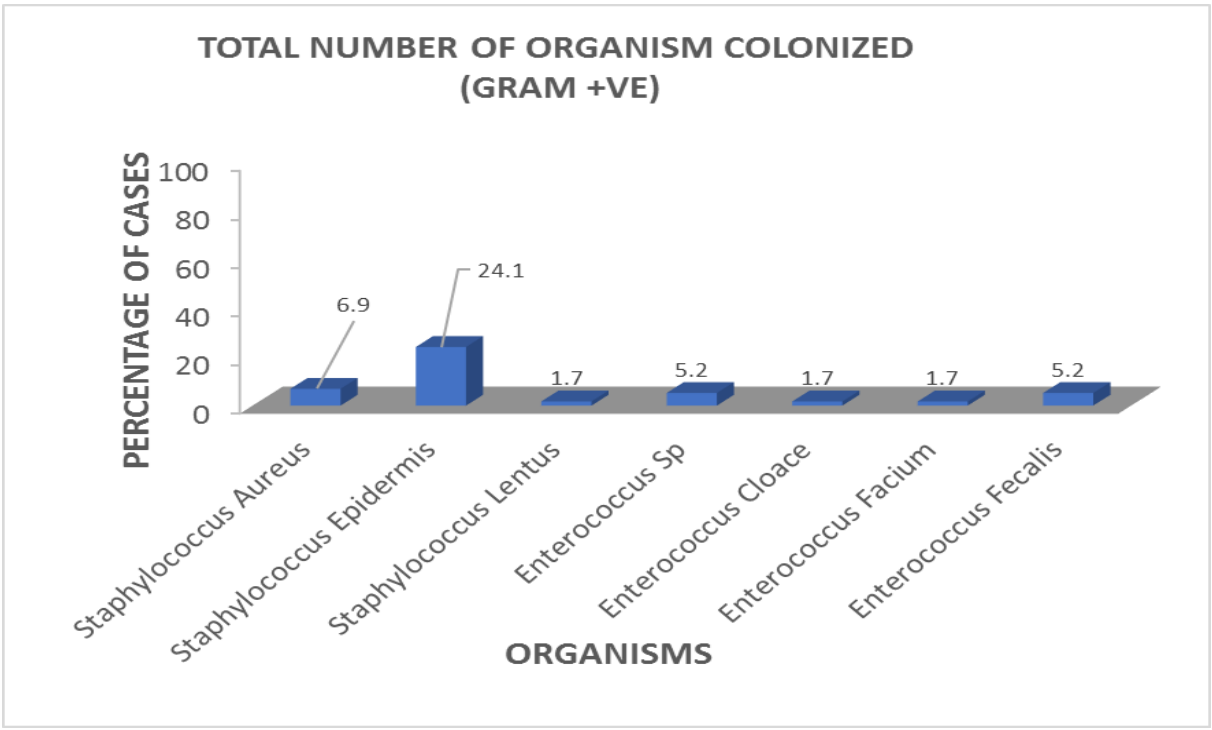


Table No. 10: Total Number of Organism Colonized (Gram -Ve)

Organisms	No. of Cases Colonized (N = 58)	
	No. of Cases	Percentage
Pseudomonas	08	13.8
Serratia	03	05.2
Proteus	01	01.7
Klebsiella Pneumoniae	08	13.8
Enterobacter aerogenes	01	01.7
Acinectobacter	02	03.4
Burkholderiacepecia	02	03.4

Graph 8

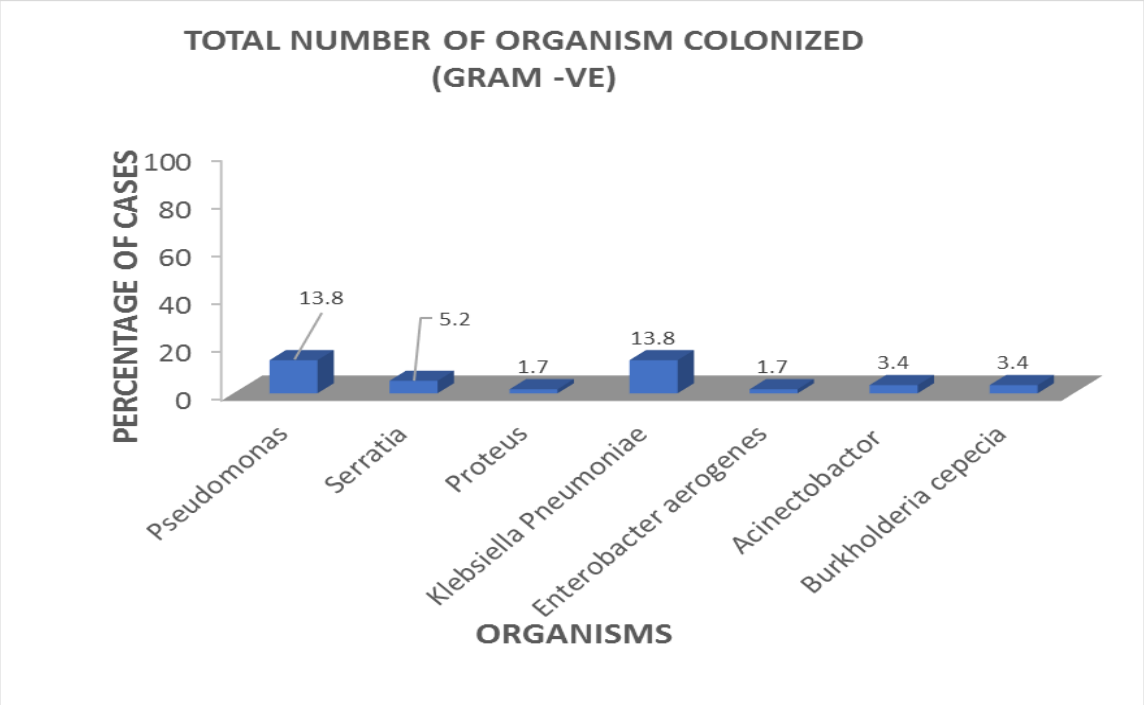
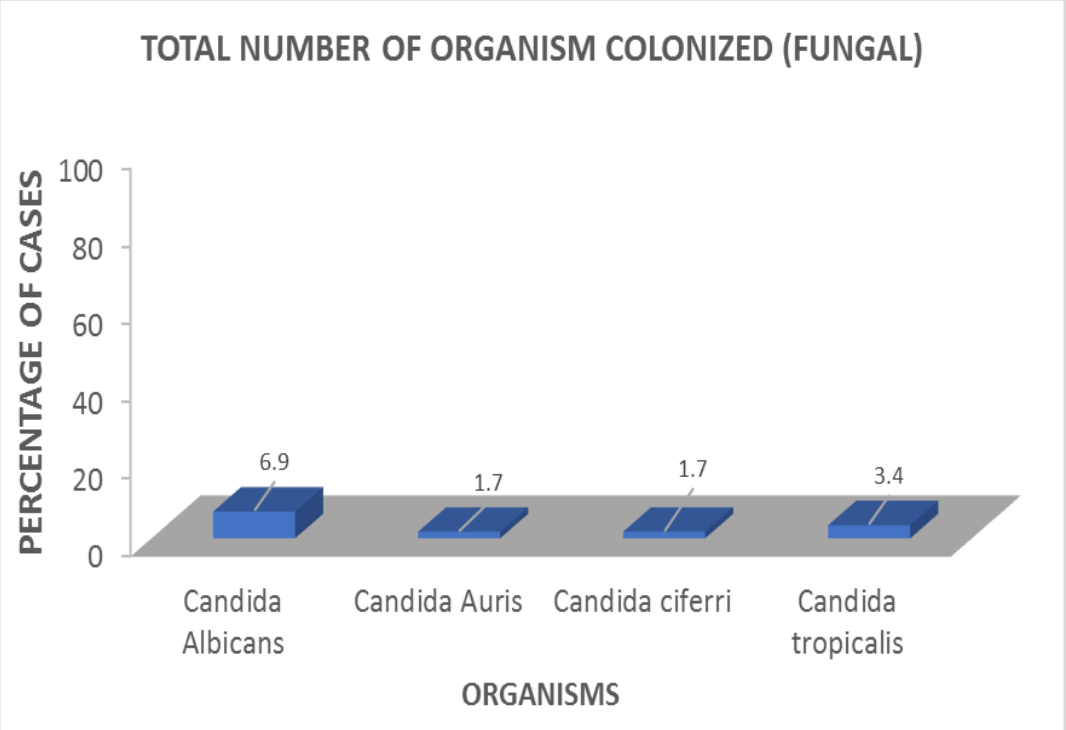


Table No. 11: Total Number of Organism Colonized (Fungal)

Organisms	No. of Cases Colonized (N = 58)	
	No. of Cases	Percentage
Candida Albicans	04	06.9
Candida Auris	01	01.7
Candida ciferri	01	01.7
Candida tropicalis	02	03.4

Graph 9

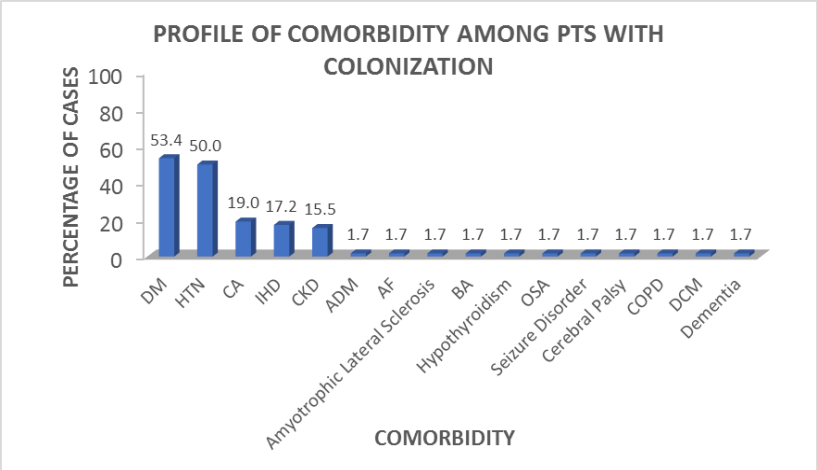


Cases with Diabetes and Hypertension had colonization of 50.0 -53.4% and 19.0% for cancer patients. (Table 12, Graph 10)

Table No. 12: Profile of Comorbidity Among Pts With Colonization

Comorbidity	Cases with Colonization (N = 58)	
	No. of Cases	Percentage
DM	31	53.4
HTN	29	50.0
CA	11	19.0
IHD	10	17.2
CKD	09	15.5
CVA	01	01.7
AF	01	01.7
Amyotrophic Lateral Sclerosis	01	01.7
BA	01	01.7
Hypothyroidism	01	01.7
OSA	01	01.7
Seizure Disorder	01	01.7
Cerebral Palsy	01	01.7
COPD	01	01.7
DCM	01	01.7
Dementia	01	01.7

Graph 10



According to Table 13 and Graph, 11,89.5% of colonized cases with Staphylococcus were sensitive for antibiotics like Linezolid, 84.2% for Vancomycin and Teicoplanin whereas 78.9% of colonized cases with Staphylococcus were resistant to antibiotics like Penicillin, 52.6% for Levofloxacin, and 21.5% for Cotrimoxazole and Tetracycline. Among the colonized cases with Enterococcus, 87.5% were sensitive to antibiotics like Teicoplanin, 75.0% for Linezolid, Vancomycin, and Tigecycline whereas 50.0% of colonized cases with Enterococcus were resistant to antibiotics like Penicillin and Levofloxacin and 25.0% for Tetracycline. (Table14, Graph12)

According to Table 15 and Graph 13, 64.0% of colonized cases with Gram-negative were sensitive for antibiotics like Colistin and Minocycline, 56.0% for Amikacin whereas 44.0% of colonized cases with Gram-negative were resistant to antibiotics like Ciprofloxacin, 40.0% for Meropenem and Piperacillin/Tazobactam. 87.5% of colonized cases with Fungal were sensitive for antibiotics like Caspofungin and Micafungin, 37.5% for Flucytosine whereas 75.0% of colonized cases with Fungal were resistant to antibiotics like Voriconazole, 62.5% for Amphotericin – B and Fluconazole. (Table 16, Graph 14)

The cases with 4 co-morbidity had colonization of 10.0% which was less as compared to 34.7% cases with 3 co-morbidity, 20.0% cases with 2 co-morbidity, and 37.3% cases with 1 co-morbidity but the difference was statistically insignificant. (Table 17, Graph 15)

Table No. 13: Antibiotic Sensitivity for Staphylococcus Cases

Antibiotics	**No. of Cases Sensitive/Resistant cases (N = 19)**			
	No. of Sensitive Cases	**Percentage**	**No. of Resistant Cases**	**Percentage**
Penicillin	02	10.5	15	78.9
Cotrimoxazole	13	68.4	04	21.5
Levofloxacin	09	47.4	10	52.6
Clindamycin	13	68.4	04	21.1
Linezolid	17	89.5	-	-
Vancomycin	16	84.2	01	05.3
Tigecyclin	15	78.9	-	-
Teicoplanin	16	84.2	-	-
Tetracyclin	11	57.9	04	21.5
Daptomycin	13	68.4	-	-

Graph 11

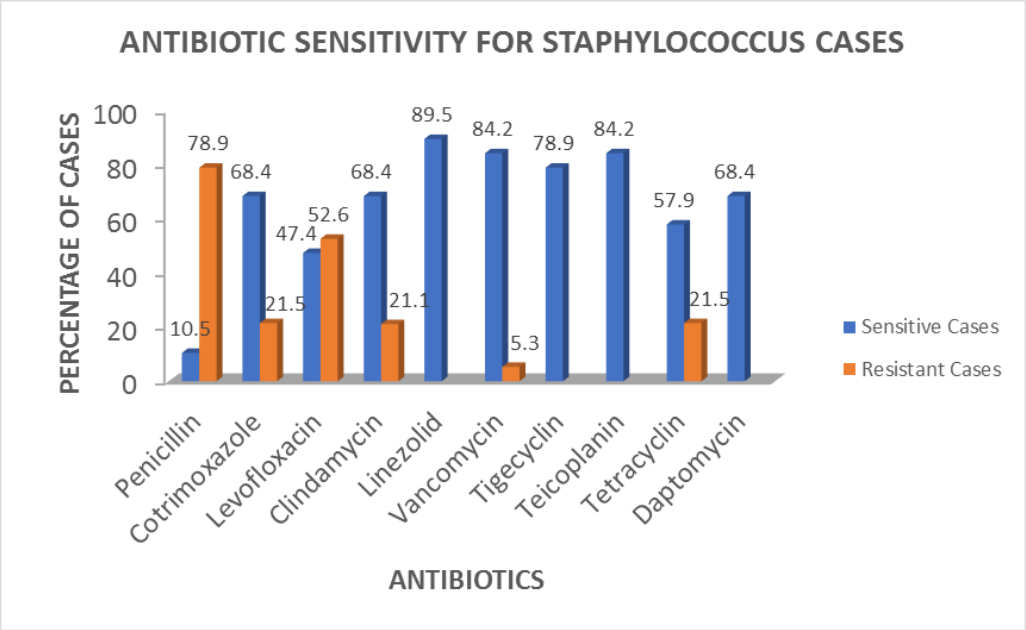


Table No. 14: Antibiotic Sensitivity for Enterococcus Cases

Antibiotics	**No. of Cases Sensitive/Resistant cases (N = 8)**			
	No. of Sensitive Cases	**Percentage**	**No. of Resistant Cases**	**Percentage**
Penicillin	03	37.5	04	50.0
Cotrimoxazole	02	25.0	-	-
Levofloxacin	01	12.5	04	50.0
Clindamycin	-	-	-	-
Linezolid	06	75.0	-	-
Vancomycin	06	75.0	-	-
Tigecyclin	06	75.0	-	-
Teicoplanin	07	87.5	-	-
Tetracyclin	02	25.0	02	25.0
Daptomycin	03	37.5	-	-

Graph 12

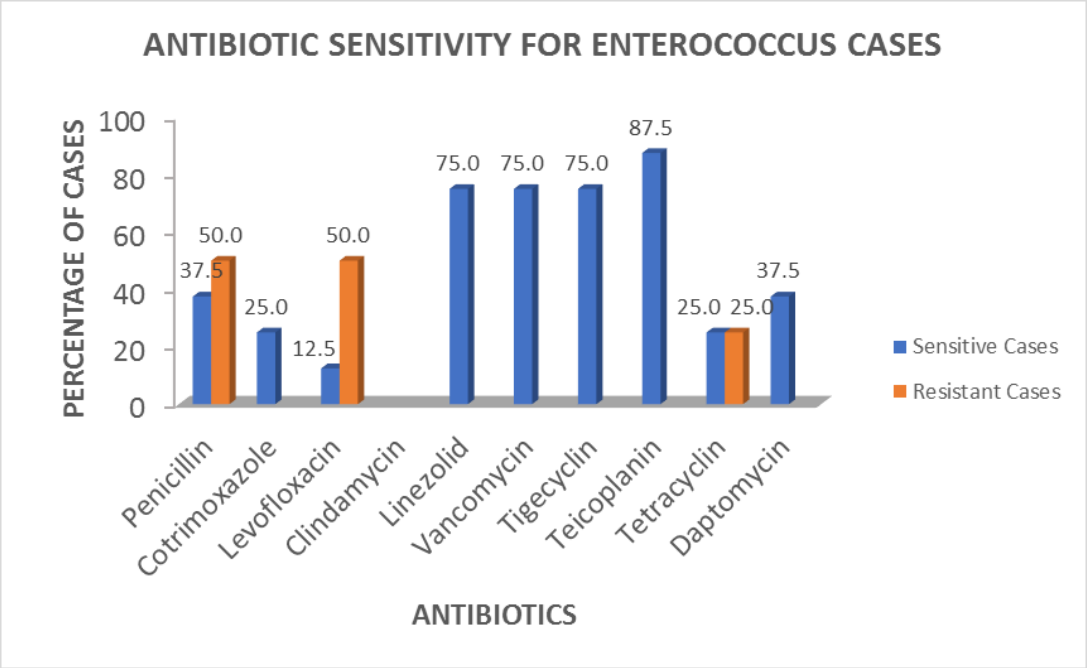


Table No. 15: Antibiotic Sensitivity for Gram Negative Cases

Antibiotics	**No. of Cases Sensitive/Resistant cases (N = 25)**			
	No. of Sensitive Cases	**Percentage**	**No. of Resistant Cases**	**Percentage**
Amikacin	14	56.0	08	32.0
Amoxycillin/Clavulanic Acid	04	16.0	08	32.0
Cefepime	10	40.0	09	36.0
Cefoperazone + Sulbactam	11	44.0	06	24.0
Ceftriaxone/Sulbactam/EDTA	20	80.0	-	-
Ciprofloxacin	11	44.0	11	44.0
Colistin	16	64.0	-	-
Cotrimoxazole	12	48.0	05	20.0
Imipenem/Cilastatin	09	36.0	07	28.0
Meropenem	12	48.0	10	40.0
Minocycline	16	64.0	02	8.0
Piperacillin/Tazobactam	09	36.0	10	40.0
Tigecycline	10	40.0	08	32.0

Graph 13

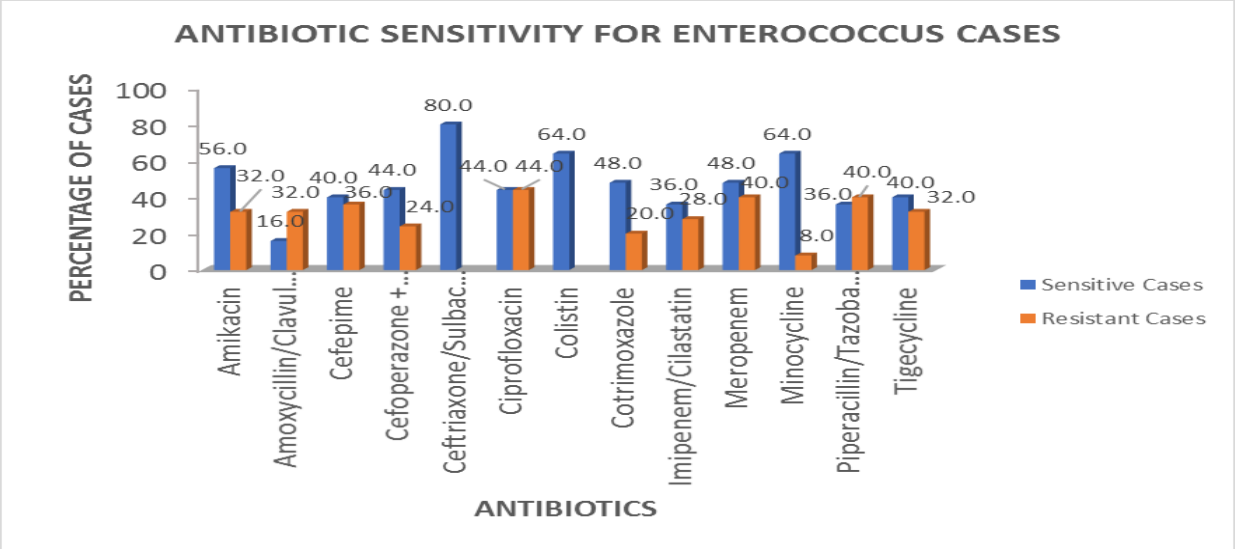


Table No. 16: Antibiotic Sensitivity for Fungal Cases

Antibiotics	**No. of Cases Sensitive/Resistant cases (N = 8)**			
	No. of Sensitive Cases	**Percentage**	**No. of Resistant Cases**	**Percentage**
Amphotericin – B	02	25.0	05	62.5
Fluconazole	02	25.0	05	62.5
Flucytosine	03	37.5	04	50.0
Voriconazole	02	25.0	06	75.0
Caspofungin	07	87.5	-	-
Micafungin	07	87.5	-	-

Graph 14

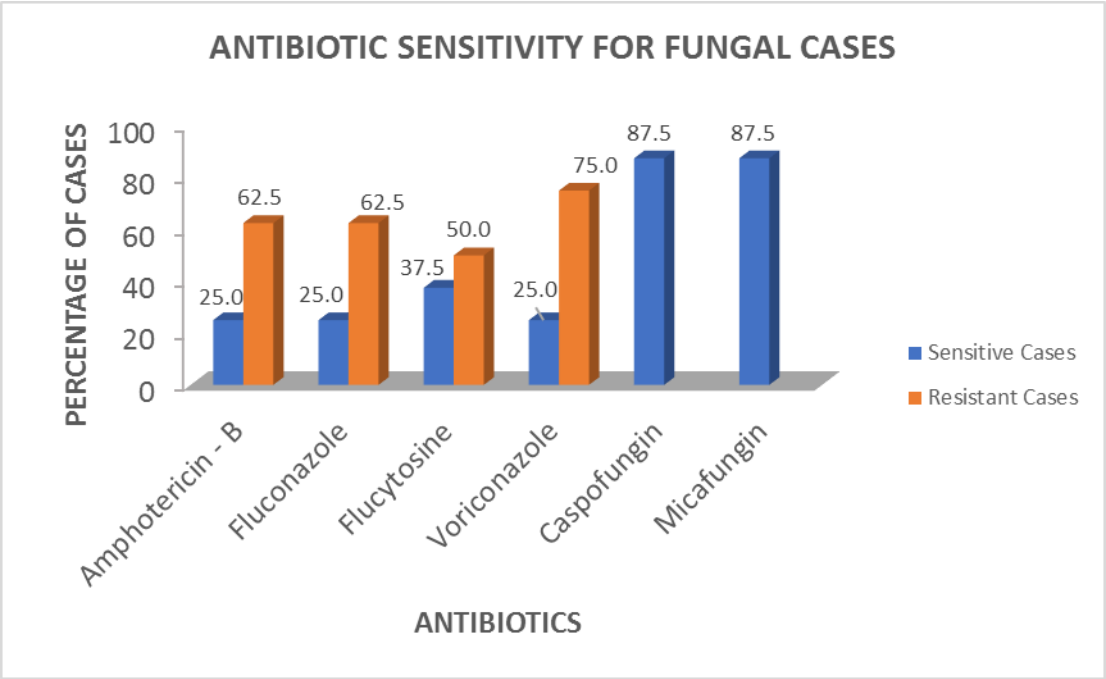
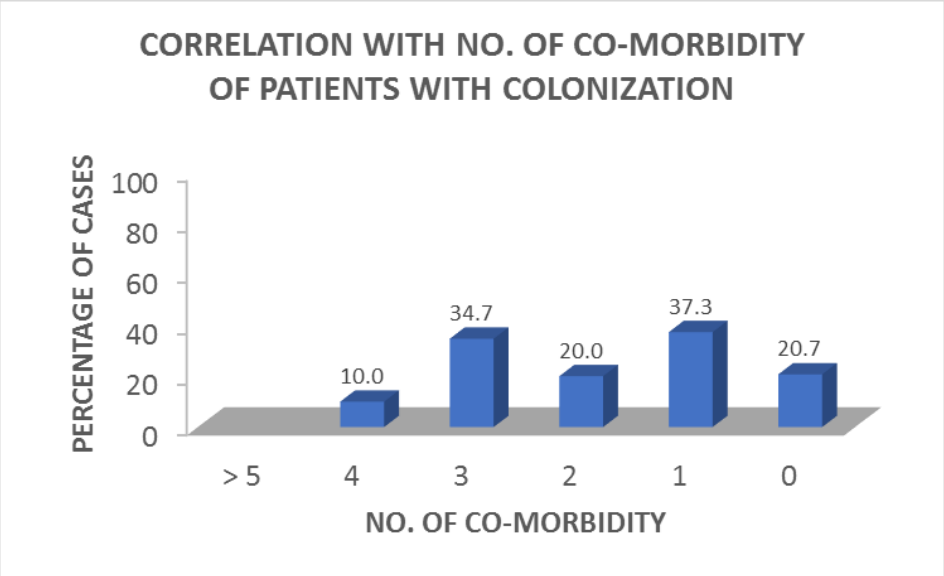


Table No. 17: Correlation With No. Of Co-Morbidity Of Patients With Colonization

No. of Co-Morbidity	No. of Cases	Cases with colonization No. %
> 5	-	- -
4	10	01 10.0
3	49	17 34.7
2	45	09 20.0
1	67	25 37.3
0	29	06 20.7

By Chi Square Test P > 0.05 Not Significant

Graph 15



DISCUSSION

Central venous catheters (CVCs) though indispensable in current medical and intensive care treatment, also puts patients at risk of a catheter-related infection (CRI) resulting in increased morbidity and mortality. The rate of CVC-BSI across Indian hospitals ranges from 4.01/1000 catheter days to 9.26/1000 catheter days. CVC-associated complications like CLABSI, sepsis, septic thrombophlebitis, endocarditis result in significant morbidity, increased duration of hospitalization, and additional medical costs. Catheter colonization precedes catheter-related infections. Hence, there is a necessity of citing the organisms colonizing the catheter in critically ill patients and governing the antibiotic policies for effective management. The study was conducted on 200 patients admitted to SLR hospital fulfilling all inclusion and exclusion criteria. The mean age of the patients included in the study was 60.79 years with male predominance i.e. 62.5%. The total duration of catheter days was 1930. In the present study, out of 200 patients with a central line, 58 showed colonization with the incidence of colonization being 29%. The colonization rate in our study was found to be 30.03 per 1000 catheter days. The incidence rate of central line catheter colonization ranges from 18.3% to 78% in different studies[150-154]. According to MaríaJesúset al, colonization was found in 18.3% cases[155]. According to Hagau N *et al*, colonization was found in 25.88% cases[156] which was similar to the observations found in our study. Patil *et al* reported the colonization rate of 31.34 per 1000 catheter-days[158]. Gahlot et al reported a colonization rate of 36.4 per 1000 catheter days[157]. These findings support the findings in our study. Organisms were

identified by the semiquantitative method i.e. Makis method for extraluminal growth and by the quantitative method for intraluminal growth. 24% of catheter tip cultures displayed colonization by the Makis method, and 13% colonization was displayed by the subculture method. The Makis method was used for tip culture by various studies including Harshal Shah *et al* [159], Gahlot *et al*[157], Patil *et al* [158]. In our study, to define the severity of disease, the APACHE score was used as a parameter. THE mean APACHE score was 13.57. It was found that 27.7% of the cases had colonization with a reported Apache Score of < 15 which was comparable with 31.4% of the cases with an Apache Score of> 15. The difference found was not statistically significant. A similar finding was reported in a study conducted by Soni *et al* in which there was no relationship between APACHE Score and risk of catheter infection[160]. Deliberato RO *et al* observed that the APACHE II mean value ± standard deviation score was 15.43±4.52 and there was no correlation between APACHE score and bloodstream infection[161]. Both these studies support observations made by our study.

Malnutrition is associated with increased mortality and morbidity, extends hospital length of stay, reduces the quality of life, and increases healthcare costs. Systematic screening at hospital admission by using the Nutritional Risk Screening-2002 score is recommended to detect patients at nutritional risk. In the present study, an attempt was made to correlate the Nutritional Risk Screening-2002 score with catheter colonization. It was found that 28.2% of the colonized cases had NRS (2002) < 4 which was comparable with 30.0% of the cases with NRS (2002) > 4 and the difference was not statistically significant. Thibault R *et al* observed that the proportion of patients at nutritional risk (Nutritional Risk Screening-2002 score >3) was not significantly different between patients with HCAI and non-infected patients and hence even though the Nutritional Risk Screening-2002 score is a validated nutritional screening tool, but its validity to identify patients at risk of HCAI remains to be determined in prospective studies[162]. However, this aspect lacks sufficient data and should be further investigated.

The Nutrition Risk in Critically ill (NUTRIC Score) is designed to quantify the risk of critically ill patients developing adverse events that may be modified by aggressive nutrition therapy. In the present study, an attempt was made to correlate the NUTRIC score with catheter colonization. It was found that 28.5% of the colonized cases had a NUTRIC score less than or equal to 5 which was comparable with 31.4% of the cases with a NUTRIC score >5and the difference was not statistically significant. There is a paucity of studies in which

correlation between NUTRIC score and no. of colonizers was established and needs further investigation.

In our study, out of 200 patients, 7 patients were neutropenic, and leukocytosis was present in 110 patients. Out of 7 neutropenic patients, 3 (42.9%) cases developed colonization of catheter and out of 110 leukocytosis patients, 32 (29.1%) patients developed colonization. The rate of colonization in Neutropenic patients was more as compared to 29.1% of the cases with Leukocytosis but the difference was not statistically significant. There is a paucity of studies in which correlation between abnormal WBC count and no. of colonizers was established and needs further investigation.

In the present study, the mean duration of the central catheter was 9.66 days[109]. Catheters were placed for≥7 days, out of which 37 showed positive organisms comprising 33.9% of the total. Of the 91 catheters placed for less than 7 days, 21 (23.1%) showed biofilm formation. Although this difference was not statistically significant there is a clinical relationship between the duration of the central line *in situ* and the colonization. Thus, this may also indicate the increase in the number of cases of CLABSI with the increased duration of catheterization. Gil *et al* 1983 observed that in 220 central venous catheters in ICU patients, found that the incidence of sepsis rose from 1.5 to 10% when the duration of catheterization exceeded 6 days[163]. Collignon *et al*. (1988) examined 780 catheters to determine the association between different insertion sites, duration of catheter insertion, and catheter-related sepsis[164]. Richet H *et al* 1990 observed that central venous catheterization longer than five to seven days was associated with a higher risk of catheter-related infection[165].

In our study, a benchmark of 7 days is selected because according to few studies those catheters that are inserted for a short period (7 days) are usually colonized intraluminally (contamination of the hubs). 7 days catheterization was also used as a reference in a study by Sadoyma *et al*[166].

Out of 200 patients, 197 received antibiotics. 96 patients received antibiotics for <7 days and 101 patients received antibiotics for >7 days. 19.8% of the cases that had colonization used Antibiotics for < 7 days which was significantly less as compared to 38.6% of the cases that used Antibiotics > 7 days.

Thus, this may indicate that a longer duration of treatment received by the patient indicates a grave prognosis which might explain the increased incidence of catheter colonization in such

critically ill patients. Since there is a paucity of studies regarding the correlation between the duration of antibiotics received by patients and no. catheter colonization, the establishment of correlation needs more research.

There was no temporal relationship between the presence of comorbidities and the colonization of the central line tip. In this study, the occurrence of comorbidities in the colonized samples was Diabetes (53.4%), hypertension (50%), carcinoma(19%), IHD (17.2%), and Chronic Kidney Disease (15.5%) with no clinically and statistically significant difference. Until now there has been no study highlighting the relationship between the colonization rate and the underlying disease.

In our study, out of 200 processed catheters, 58 showed significant growth. Out of which 27 (46.55%) showed growth of gram-positive organisms. which complies with a study done in Manipal[81] where 42.16% of the pathogens causing tip colonization were due to Gram-positive. In our study, among gram-positive organisms, the most commonly observed growth was Staphylococcus Epidermis (24.1%) followed by Staphylococcus Aureus (6.9%) followed by Enterococcus Faecalis(5.2%). Wisplinghoff *et al* [167] showed that the commonest isolates were CONS (31%) followed by S. aureus (20%). Subba Rao *et al* [168] showed that the commonest isolates in ICU patients were CONS (32.4%). Both these studies support observations found in our study. Patil et al 2011 observed that CONS were the most common organisms responsible for culture-positive catheter colonization and among CONS, Staphylococcus Epidermis was the most common organism isolated i.e. 45% and Staphylococcus aureus accounted for 15% growth[170]. Richet *et al*. in 1990 isolated S. aureus as the second most common microorganism from both central and peripheral venous catheters, accounting for 19.9% of all isolates[165].

In our study, the growth of all three organisms i.e. Enterococcus Cloaace and Enterococcus Faecium, and Staphylococcus Lentus were reported to be 1.7%. Other Enterococcal species showed a total growth of 5.2%.

In our study, out of 200 processed catheters, 58 showed significant growth.

Out of which 24 (41.37%) showed growth of gram-negative organisms. According to a study was done in Manipal 81,57.84% of the pathogens causing tip colonization were due to Gram-negative organisms. Among gram-negative organisms, Pseudomonas and Klebsiella pneumonia showed maximum growth in 13.8% cases each.

According to the done in Manipal[81], P. aeruginosa was the most common gram-negative organism isolated (16.67%). According to a study conducted in AIIMS Delhi, Klebsiella pneumonia was found to be the most common gram-negative organism isolated from catheter tip colonization i.e. 11%[171].

Both these studies support observations found in our study. In the study of Almuneef *et al* (2006), the most common organisms isolated were Klebsiella pneumonia 16%, coagulase-negative staphylococci 14%, and Pseudomonas aeruginosa 11%[172].In the present study, Serratia and Acinetobacter showed growth in 5.2% and 3.4% cases respectively. Proteus species, Enterobacter aerogenes, and Burkholderiacepecia showed growth in 1.7% cases each.

In the present study, out of 200 processed catheters, 58 showed significant growth. Out of which, 9 (15.51%) cases showed fungal growth. The most common fungus grown was Candida Albicans (6.9%) followed by Candida tropicalis (3.4%). Candida Auris and Candida ciferri showed growth of 1.7% cases each. In the study of Ramanathan Parameswaran *et al*., (2011) 16% of infectious agents were Candida species[134]. According to Pawar *et al*., (2008) fungal pathogen isolated from CVC was Candida 11.7%[173.]

These findings were similar to the findings of our study. In one study, Patil et al isolated C. Albicans from a single catheter tip (5%)[158]. Haslett et al found that 3% of the catheters were infected due to C. tropicalis[174] which is similar to observations of our study.

In the present study colonized cases with staphylococcus, most of which are staphylococcus epidermis (CONS) showed maximum susceptibility to Linezolid (89.5%), followed by Vancomycin and Teicoplanin. Whereas 78.9% of colonized cases with staphylococcus were resistant to antibiotics like Penicillin, 52.6% for Levofloxacin, and 21.5% for Cotrimoxazole, and Tetracyclin. which was similar to that in a study done by Khanna et al.[81] where 100% sensitivity was seen to Linezolid.

The majority of the isolates causing colonization were resistant to Penicillin G, and all were sensitive to Vancomycin in this study. This was similar to studies done in Manipal, study done by Parameswaran *et al*[134.]

Resistance to penicillin can be attributed to the fact that this is a tertiary care center in which patients are referred from smaller centers causing selection pressure exerted by extensive use of antibiotics and may be due to transmission of resistant clones between the patients.

This study showed that 87.5% of colonized cases with Enterococcus sp. were sensitive to antibiotics like Teicoplanin which is the most common antibiotic used in our hospital. Other antibiotics sensitivity pattern is 75.0% for Linezolid, Vancomycin, and Tigecycline whereas 50.0% of colonized cases with Enterococcus were resistant to antibiotics like Penicillin and Levofloxacin and 25.0% for Tetracyclin. Which was in concordance with a study done by Deliberato *et al* [161.]

Multiple drug resistance was found in gram-negative organisms. However, it should be noted that 80.0% of colonized cases with Gram-negative were sensitive for antibiotics Ceftriaxone/Sulbactam/EDTA, whereas no resistance was found for Ceftriaxone/Sulbactam/EDTA.

Among the other antibiotics gram-negative bacilli having a sensitivity of 64.0% for Colistin and Minocycline, 56.0% for Amikacin. 44.0% of colonized cases with Gram-negative were resistant to antibiotics like Ciprofloxacin, 40.0% for Meropenem and Piperacillin/Tazobactam.

This was similar to a study by Amin *et al*., which showed 50%gram-negative isolates being resistant to Piperacillin-Tazobactam and meropenem, and 33% being resistant to imipenem[175].

Fungal colonization which predominantly grown Candida albicans shown that 87.5% of colonized cases with Fungal were sensitive for antibiotics like Caspofungin and Micafungin, 37.5% for Flucytosine whereas 75.0% of colonized cases with Fungal were resistant to antibiotics like Voriconazole, 62.5% for Amphotericin – B and Fluconazole.

CONCLUSION

There have been very few studies regarding the colonization rate of central lines. The data of true colonization rate from our single-center reveal that central lines almost equally get colonized with gram-positive and gram-negative organisms. This data also seems to suggest that comorbidities, severity of illness, or length of time that the catheter is in situ do not

change the colonization rate. This data may thus help us to make protocols for clinical management and in devising materials for making catheters.

Limitations:

1. Single-center study 2. Central lines were removed when indicated.

Clinical Significance:

This is the first study looking at the actual colonization rate as the authors have sampled every single line that was inserted during the study period. Data derived from this study will help to set protocols and device new catheter materials in the future.

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Image *Author -1*	**1.DR. SANJITH SASEEDHARAN** ***– Corresponding Author*** S.L RAHEJA HOSPITAL (A FORTIS ASSOCIATE)
Image *Author -2*	**2.DR.ROOPA KARANAM** CRITICAL CARE CONSULTANT S.L RAHEJA HOSPITAL (A FORTIS ASSOCIATE)
Image *Author -3*	**3.DR.VAIJAYANTI KADAM** CRITICAL CARE CONSULTANT S.L RAHEJA HOSPITAL (A FORTIS ASSOCIATE)
Image *Author -4*	**4.DR.DNAYESHWAR DIWANE** ICU REGISTRAR S.L RAHEJA HOSPITAL (A FORTIS ASSOCIATE)
Image *Author -5*	**5.DR.ELIZABETH J MATHEW** ICU REGISTRAR S.L RAHEJA HOSPITAL (A FORTIS ASSOCIATE)
Author -6	**6.DR.BIKKY CHAURASIA** ICU REGISTRAR S.L RAHEJA HOSPITAL (A FORTIS ASSOCIATE)