

Original Research Article

Bacteriological profile and antibiogram of cancer patients admitted in intensive care unit of a tertiary care cancer hospital in central Kerala

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ABSTRACT

Background: Opportunistic bacterial infections remain a serious morbidity among cancer patients. This study was aimed to determine the bacteriological and antibiotic profile of cancer patients admitted to the ICU of a tertiary care centre.

Methods: Cross sectional study was done among cancer patients admitted in the Oncology neutropenic ICU during the period from August 2017 to July 2019. All patients admitted with a proven diagnosis of cancer for whom at least one bacterial culture was sent from any site were included in the study. Laboratory on culture reports were obtained from patient files and analysed.

Results: A total of 278 samples from 256 patients (60±11.6 years) were analysed. Among the 111/278 positive cultures, 29 were blood samples and 1 was a pleural fluid sample. Gram negative organisms were 62.1% with *Escherichia coli* (25, 36.2%) as prevalent. Among the 37.8% gram positives, *Staphylococcus aureus* (18, 42.8%) was prevalent. Most of the *E. coli* strains showed highest resistance to ceftazidime (96%) and highest sensitivity to amikacin. The commonest gram-positive organism, *Staphylococcus* species were 100 % sensitive to vancomycin and linezolid and 100 % resistance to penicillin.

Conclusions: *E. coli* (gram negative) showed highest resistance to ceftazidime and sensitivity to amikacin. *S. aureus* (gram positive) was sensitive to vancomycin and linezolid and resistance to penicillin. An antibiogram for cancer patients helps the clinician to initiate an appropriate empirical antibiotic therapy to reduce mortality and morbidity.

Keywords: Antibiogram, Bacterial infections, Gram positives, Gram negative, Myelo-suppression, Neutropenia

INTRODUCTION

The seriatim of myelo-suppression and bacterial infections is one of the serious causes for morbidity among cancer patients and a perplexity for clinicians. This can be generally ascribed to immunosuppression in cancer patient which results from multiple factors. The underlying disease and the chemotherapy are the paramount factors that act concomitantly or sequentially in the causation of immunosuppression. Most of the patients undergoing chemotherapy may get opportunistic bacterial infections which remains as a serious cause for morbidity.¹⁻⁴ Thus, an empirical therapeutic regimen has significance in the management of opportunistic bacterial

infections in cancer patients prior to receive the culture report. With the advent of new cancer treatments and antibiotic prophylaxis, bacteriological profile of infections changes and new resistance mechanisms arise.⁵

A recent study by done in New Delhi, India in 2019, showed that 76.6 % of the total cultures were positive for bacterial growth.⁶ Members of enterobacteriaceae group (gram-negative bacteria) such as *Escherichia coli* and *Klebsiella pneumonia* are the major organism found to produce antibiotic resistance in the Indian setting.⁷ Kumar et al., in the recent review concluded an increase burden of antimicrobial resistance in India.⁸ This emphasizes the need for antibiotic policy in every

hospital to control the infection and improvement in antibiotic use.⁹ Population wise study on antibiogram among cancer patients admitted in ICU will help the clinician to initiate an appropriate empirical antibiotic therapy which can significantly reduce mortality and morbidity. Studies in South Indian population are scant. This study was aimed at providing a comprehensive data on bacterial cultures sent for patients admitted in the ICU. The antibiotic profile of the bacterial cultures those are positive for growth and the associated factors were also included in the study. This can pave way to better treatment strategies, prevent rampant use of antibiotics and reduce the number of hospitalizations.

METHODS

Study design and population

Cross sectional study was designed among cancer patients admitted to the Oncology neutropenic intensive care unit (ICU) of Amala Institute of Medical Sciences, Thrissur, Kerala, India during the period from August 2017 to July 2019. All patients admitted to the oncology neutropenic ICU with a proven diagnosis of cancer for whom at least one bacterial culture was sent from any site were included in the study. Patients admitted with other unrelated causes of infection, cases with non-availability of patient records or non-consignment of cultures were excluded from the study. Informed consent was obtained from participant for selecting their data for the study. The study was conducted after getting clearance from institutional research committee and institutional ethics committee (IEC/20/AIMS-17). Using the 5% significance level (α), 32.1% prevalence (p) of bacteremia in cancer patients admitted in ICU.¹⁰ and relative precision (d) of 20% of p , the sample size was calculated as 210 using the equation $Z_{1-\alpha/2} pq/d^2$.

Study procedure

The list of patients admitted to the oncology neutropenic ICU was obtained from the ICU registry. Patients were examined clinically. The history such as age, gender, primary site of cancer and treatment history were obtained from the patient files accessed from the Medical records department of the institution. Laboratory culture reports were obtained from patient files as well. Patients for whom culture reports were not available, the same were procured from the Microbiology lab. Neutropenic patient was defined as patients who showed absolute neutrophil count <1000 cells/mm³ at the time of admission to the ICU. Vasopressors were administered in hypotensive patients (BP $\leq 80/50$ mmHg).

Statistical analysis

The data was entered in MS excel worksheet and analyzed using SPSS software. Qualitative data were presented in percentages and analyzed using Chi-square test $P < 0.05$ considered significant.

RESULTS

A total of 500 patients were admitted to the oncology neutropenic ICU during the study period. Out of the total cases, 228 patients and 16 patients were excluded due to non-consignment of cultures and non-availability of patient records, respectively. Finally, a total of 256 patients were included in the study. The mean age of the study participants was 60 ± 11.6 years (Table 1). Out of the 256 cases, 135 (52.7%) were females and 121 (47.3%) were males (Figure 1). Among the study population, recruitment of patients from different clinical settings revealed that 37.1% of them were from outpatient clinic, 36.3% from ward, 25% from emergency department and 1.6 % from other ICUs. There was no statistical association noted with gender, patient setting and type of cancer.

Table 1: Distribution of age.

Age (in years)	Frequency (n)	%
≤ 30	5	2.0
31-40	12	4.7
41-50	25	9.8
51-60	73	28.5
61-70	94	36.7
71-80	42	16.4
≥ 81	5	2.0
Total	256	100

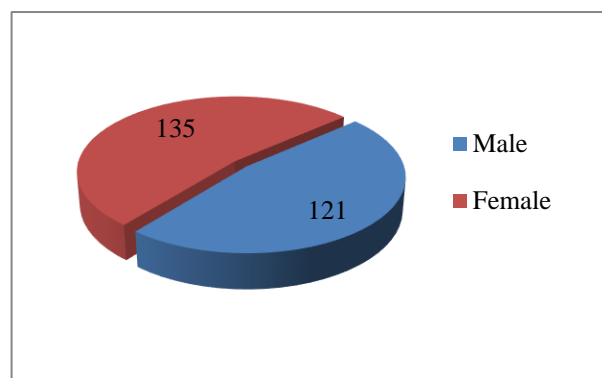


Figure 1: Distribution of gender.

Among the study population, 189 (73.8%) had solid tumour, out of which breast cancer was the highest (45, 17.6 %) followed by lung cancer (33, 12.9%) and colon cancer (24, 9.4 %). Among the haematological tumours (67, 26.2%), multiple myeloma and NHL were the highest. Each being 24 and 9.4 %, respectively (Table 2). No significant difference in the numbers was evidenced ($p > 0.05$). Of these, the frequent modality of treatment was chemotherapy (227, 88.7%) either alone or in combination with surgery / radiotherapy. Among the total patients, 119 (46.5%) patients reported history of febrile illness prior to admission and 41 (16%) patients were hypotensive at the time of admission. Majority of the patients (217, 84.8 %) succumbed to death at the time of

discharge and progressive disease (25, 64.1 %) being the most common cause of death.

Table 2: Distribution of type of cancer and their primary site.

Variables	Frequency (n)	%
Type of cancer		
Solid	189	73.8
Hematological	67	26.2
Primary site of cancer		
Brain	4	1.6
Oral cavity +Tongue	7	2.7
Larynx+Vocal cord+Esophagus	7	2.7
Breast	45	17.6
Lung	33	12.9
Stomach	16	6.3
Pancreaticobiliary system	11	4.3
Colon	24	9.4
Ovary	15	5.9
Endometrium	5	2.0
Cervix	1	0.4
Urinary bladder	2	0.8
Prostate	8	3.1
Multiple myeloma	24	9.4
Myelodysplastic syndrome	3	1.2
Non-Hodgkin's Lymphoma	24	9.4
Hodgkin's Lymphoma	2	0.8
Neuro endocrine tumour	1	0.4
Soft tissue tumour	2	0.8
Germ cell tumour	4	1.6
Unknown primary	4	1.6
Chronic lymphocytic leukemia	2	0.8
Acute myeloid leukemia	12	4.7

Chi-square=0.830; p=0.362 No significant difference was found between major solid tumors and haematological malignancies.

Bacteriological profile and site of isolation

A total of 278 samples were sent from 256 patients admitted in the ICU during the study period. Among this, 111 (39.7%) samples were cultures positive for growth (Figure 2). Out of the 111 positive cultures, 29 were blood samples, 29 were urine samples, 18 were sputum

samples, 15 were throat swabs, 4 were stool samples, 15 were pus samples and 1 was a pleural fluid sample. In the positive cultures, 62.1% (69/111) were Gram negatives and 37.8 % (42/111) Gram positives. Among the Gram negatives, most prevalent organisms were *Escherichia coli* (25, 36.2%), *Klebsiella sp* (18, 26%) and *Pseudomonas aeruginosa* (11, 15.9%). Among the gram positives, the most prevalent were *Staphylococcus aureus* (18, 42.8%) and Enterococci (11, 26.1%) (Table 3). The most frequent organisms encountered in blood samples were Coagulase negative *Staphylococcus* and *Escherichia coli* (each 24%, 7/29) and in urine samples, *E. coli* (34.4%, 10/29) followed by *Klebsiella* species (24%, 7/29). Sputum samples showed highest frequency of *Klebsiella* species (33.3%, 6/18) and throat swab showed highest frequency in *Pseudomonas aeruginosa* and *Staphylococcus aureus* (each 26.6%, 4/15). Pus samples showed highest frequency in *S. aureus* (33.3%, 5/15). Hundred percent of the stool samples showed growth of Non typhoidal salmonella.

The antibiotic resistance pattern in common gram-negative isolates has been shown in the figure 3. Majority of *E. coli* strains showed highest resistance in ceftazidime (96%) and norfloxacin (92%) and highest sensitivity in amikacin (20%). 83-88% of *Klebsiella* species showed resistance to cefazolin and 3rd generation cephalosporins. The highest sensitivity of *Klebsiella* species were found to gentamicin, cotrimoxazole (each 50%) and amikacin (44.4%). Majority of *P. aeruginosa* strains showed sensitivity to amikacin (90.9%). *Burkholderia cepacia* constituting 4.5% (5/111) of the positive cultures were found to have 100% resistance to ceftazidime and 100% sensitive to cotrimoxazole, ciprofloxacin and meropenem.

Non-typhoidal salmonella accounted for 100% of the positive stool cultures, which accounted for 3.6% (4/111) of the total positive cultures. The positive cultures found to have 75% and 50% resistance to ciprofloxacin and ampicillin, respectively. They were found to have 100% sensitivity to 3rd generation cephalosporins and cotrimoxazole. *Acinetobacter baumannii* was constituted 1.8% (2/111) of the positive samples. It showed 50% resistance to 3rd generation cephalosporins, gentamicin and amikacin, and 100% sensitive to cotrimoxazole, ciprofloxacin, piperacillin and tazobactam, cefaperazone and sulbactam and carbapenems.

Table 3: Distribution of type of samples and isolated organisms.

Organism	Blood	Urine	Sputum	Throat	Pus/wound	Pleural fluid	Stool	Total
Gram positive cocci								
<i>Staphylococcus aureus</i>	3	2	4	4	5			18
<i>Coagulase negative staphylococcus</i>	7							7
<i>Streptococci</i>			1	3				4
<i>Enterococci</i>	1	5		2	3			11

Continued.

Organism	Blood	Urine	Sputum	Throat	Pus/wound	Pleural fluid	Stool	Total
Gram positive bacilli								
<i>Bacillus sp</i>	1							1
<i>Diphtheroids</i>			1					1
Gram negative bacilli								
<i>Pseudomonas aeruginosa</i>	1	4	1	4	1			11
<i>Burkholderiacepacion</i>	4		1					5
<i>Acinetobacter baumannii</i>	1		1					2
<i>Stenotrophomonas maltophilia</i>	1							1
Enterobacteriaceae								
<i>Escherichia coli</i>	7	10	3	1	3	1		25
<i>Klebsiella sp</i>	3	7	6	1	1			18
<i>Proteus sp</i>		1			1			2
<i>Non typhoidal salmonella</i>							4	4
<i>Morganella Morgagni</i>					1			1
Total	29	29	18	15	15	4	1	111

Chi-square=0.111, p=0.739. No significant difference was found between gram positive and negative organisms.

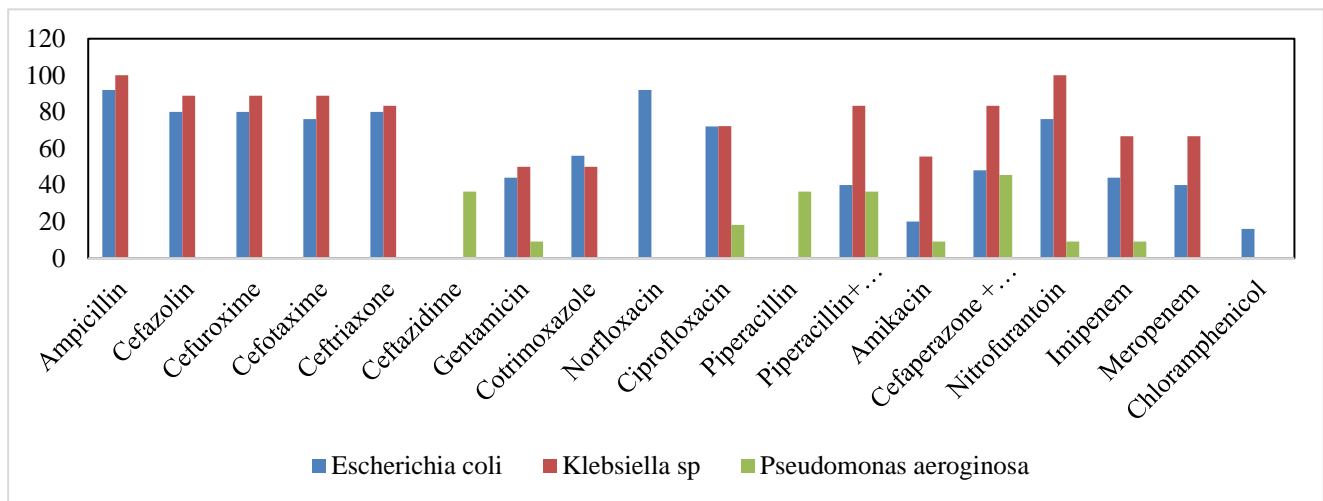


Figure 3: Antibiotic resistance pattern in common gram-negative isolates.

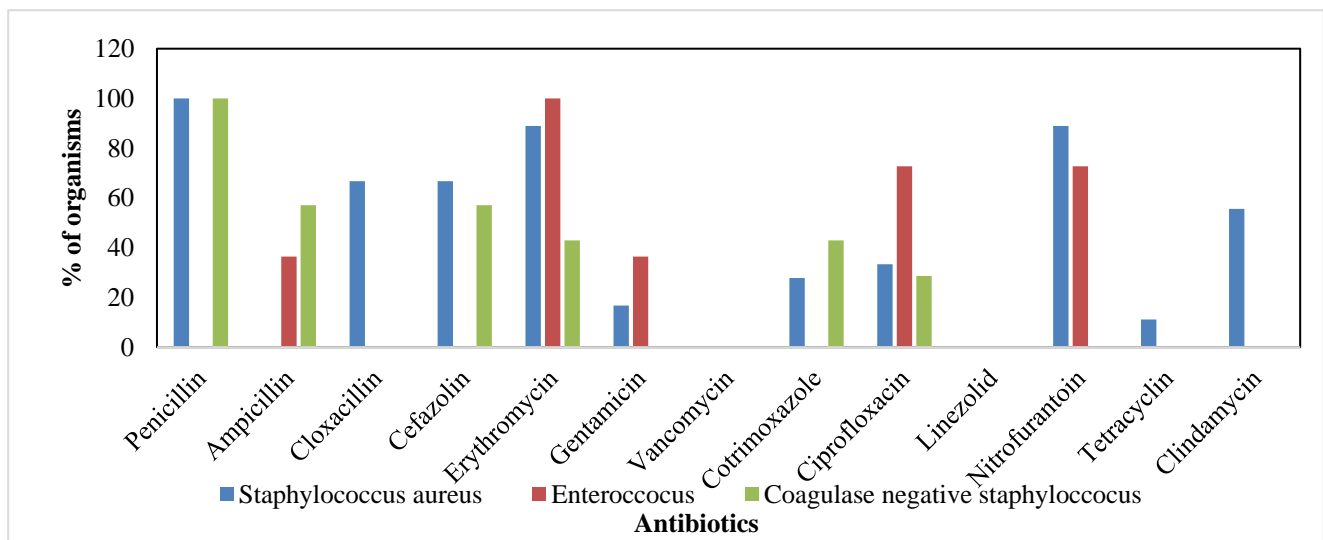


Figure 4: Antibiotic resistance pattern in common gram-positive isolates.

The antibiotic resistance among common gram-positive organisms has been shown in the (Figure 4). The commonest gram-positive organisms were 100 % sensitive to vancomycin and linezolid, and staphylococcus species showed 100% resistance to Penicillin. Majority of Staph. aureus strains displayed highest resistance in nitrofurantoin (88.9%) and erythromycin (88.9%) and highest sensitivity in Tetracycline (88.9%). cloxacillin resistance in *S. aureus* species accounted 66.7%. Enterococcus species showed 100% resistance to erythromycin and highest sensitivity to ampicillin and gentamicin (63.6%). Coagulative negative staphylococcus strains showed 100% sensitivity to gentamicin and highest resistance to ceftazidime (57.1%).

Organisms like diphtheroids, bacillus species, *Stenotrophomonas maltophilia*, *Morganella morgagni* were each found in 0.9% of all positive cultures.

DISCUSSION

A In this observational study on cancer patients, positive cultures were obtained from 39.7% of the total study population and the isolates predominantly showed Gram-negative bacteria (62.1%). The high prevalence of Gram-negative bacteria was reported by various other studies conducted in India and also around the world. In recent years, there has been shift in culture positivity from gram positive to being gram negative, as described in Viscoli et al.¹⁵ in our study, the prevalence of organisms was as follows: *E. coli* (22.5%), *S. aureus* and *Klebsiella sp* (16.2 % each), Enterococci and *Pseudomonas aeruginosa* (9.9% each) and coagulase negative staphylococci (6.3%). Among gram negatives, the predominant organisms were *E. coli* (36.2%), *Klebsiella sp* (26%) and *Pseudomonas aeruginosa* (15.9 %). Previous study done among the cancer patients at Oncology Units in University Hospital, Riyadh, Saudi Arabia showed *Escherichia coli* (*E. coli*) (29.5%) followed by *Acinetobacter baumannii* (18%) were the most predominant pathogen.¹⁰

Similar findings were obtained by Nazneen et al.¹² Among gram positives, where most prevalent were *Staphylococcus aureus* (42.8%) followed by Enterococci (26.1%). Most of the *E. coli* and *Klebsiella* organisms were resistant to 3rd generation cephalosporins. The same was observed in Garg et al.⁶ Previous study reported that cephalosporins showed a widespread resistance to Enterobacteriaceae.¹³

Majority of the *Klebsiella sp* were found to be resistant to amikacin (55.6%) and to beta lactams/beta-lactamase combination (83.3%). Carbapenem resistance in gram negative organisms were tested and the highest resistance was noted with *Klebsiella sp* (66.7 %) followed by *E. coli* (44%) and *Pseudomonas* (9.1%). The study also encountered organisms like diphtheroids, Bacillus species, *Stenotrophomonas maltophilia*, *Morganella*

morgagni each accounting for 0.9% of all positive cultures, which was different from most other studies. We did not encounter resistance to vancomycin and linezolid in *Staphylococcus aureus*. Associations of culture positivity with various factors were analysed and it was found that there was significant association with primary site of cancer and patient setting.

Higher risk for infection was found during cancer chemotherapy and patients with leukemias and solid tumors such as those of the breast, lung, and colon.¹⁴ Despite multiple factors that contribute the immunosuppression many cancers can induce the proliferation of regulatory T cells which are potent inhibitors of the immune system, resulting their accumulation in the periphery and tumor beds.¹⁵ Associations of culture positivity with various factors were analysed in this study and found that there was significant association with primary site of cancer (P=0.003) and patient setting (P=0.021). Forty-one percent of patients with a diagnosis of Multiple myeloma were found to have positive cultures. None of the socio-demographic characteristics, duration of illness, type of cancer, stage of cancer, modality of treatment, hypotension, absolute neutrophil count, duration of stay, showed significant association with culture positivity.

Limitations

Major limitations are 1) The study being a cross sectional study, could not establish causality, 2) Study was conducted in single institution and could not reveal the epidemiology in other centres/geographical areas and 3) The data regarding the timing of cultures sent from different sites with respect to the initiation of antibiotics could not be obtained.

CONCLUSION

An antibiogram for cancer patients admitted in the oncology neutropenic ICU, that sheds light on the local susceptibility pattern of organisms isolated from cultures obtained from various sites. This helps the clinician in initiating an appropriate empirical antibiotic therapy for the patient and reduces mortality and morbidity. Genetic analysis of carbapenem resistance in gram negative organisms is warranted and antibiotic stewardship program is required to improve outcomes.

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REFERENCES

1. Whimbey E, Goodrich J, Bodey GP. Pneumonia in cancer patients. *Cancer Treat Res.* 1995;79:185-210.
2. Evans SE, Ost DE. Pneumonia in the neutropenic cancer patient. *Curr Opin Pulm Med.* 2015;21(3):260-71.
3. Safdar A, Armstrong D. Infectious morbidity in critically ill patients with cancer. *Crit Care Clin.* 2001;17(3):531-70.
4. Yoo SS, Cha SI, Shin KM, Lee SY, Kim CH, Park JY, Jung TH. Bacterial pneumonia following cytotoxic chemotherapy for lung cancer: clinical features, treatment outcome and prognostic factors. *Scand J Infect Dis.* 2010;42(10):734-40.
5. Frost I, Van Boeckel TP, Pires J, Craig J, Laxminarayan R. Global geographic trends in antimicrobial resistance: the role of international travel. *J Travel Med.* 2019;26(8):36.
6. Garg VK, Mishra S, Gupta N, Garg R, Sachidanand B, Vinod K, et al. Microbial and Antibiotic Susceptibility Profile among Isolates of Clinical Samples of Cancer Patients Admitted in the Intensive Care Unit at Regional Tertiary Care Cancer Center: A Retrospective Observational Study. *Indian J Critical Care Med.* 2019;23(2):67-72.
7. Dixit A, Kumar N, Kumar S, Trigun V. Antimicrobial Resistance: Progress in the Decade since Emergence of New Delhi Metallo- β -Lactamase in India. *Indian J Community Med.* 2019;44(1):4-8.
8. Kumar SG, Adithan C, Harish BN, Sujatha S, Roy G, Malini A. Antimicrobial resistance in India: A review. *J Nat Sci Biol Med.* 2013;4(2):286-91.
9. Agrawal V, Shrivastava TP, Adusumilli PK, Vivekanandan K, Thota P, Bhushan S. Pivotal role of Pharmacovigilance Programme of India in containment of antimicrobial resistance in India. *Perspect Clin Res.* 2019;10(3):140-4.
10. Al-Otaibi FE, Bukhari EE, Badr M, Alrabiaa AA. Prevalence and risk factors of Gram-negative bacilli causing blood stream infection in patients with malignancy. *Saudi Med J.* 2016;37(9):979-84.
11. Viscoli C, Varnier O, Machetti M. Infections in Patients with Febrile Neutropenia: Epidemiology, Microbiology, and Risk Stratification. *Clinic Infect Dis.* 2005;40:S240-5.
12. Nazneen S, Mukta K, Santosh C, Borde A. Bacteriological trends and antibiotic susceptibility patterns of clinical isolates at Government Cancer Hospital, Marathwada. *Ind J Canc.* 2016;53(4), 583.
13. Rudresh SM, Nagarathnamma T. Extended spectrum β -lactamase producing Enterobacteriaceae & antibiotic co-resistance. *Indian J Med Res.* 2011;133:116-8.
14. Heather L. Preventing infection in immunocompromised cancer patients: latest recommendations. *Oncol Tim.* 2008;30(18):25-8.
15. Kalathil SG, Thanavala Y. High immunosuppressive burden in cancer patients: a major hurdle for cancer immunotherapy. *Canc Immunol Immunother.* 2016;65(7):813-9.

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