Research Article

THE CRITICALLY-ILL CANCER PATIENT: EPIDEMIOLOGY, MANAGEMENT, AND OUTCOME OF ADMISSIONS TO INTENSIVE CARE UNIT (ICU) IN MEDICAL ONCOLOGY DEPARTMENT AT GUJARAT CANCER AND RESEARCH INSTITUTE (GCRI)

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Abstract :

In a six month retrospective study of patients having admission in medical ICU at Gujarat cancer and research institute (GCRI) from November 2013 to April 2014, 132 admissions were documented, out of these 108 patients were eligible for data analysis. Paediatric age group comprised 18(16.66%), adults 82(75.92%) and geriatric 8(7.4%). The haematological malignancies were 66.66%, solid malignancies 33.33%. The intent of therapy in 67.59% patients was curative and in 32.4% patients it was palliative. Mean duration of ICU stay was 3.57 days(range upto 23 days). The most common reason for ICU admission was pneumonia and other major reasons were neurologic dysfunction, airway compression, septicemic shock, renal dysfunction, differentiation syndrome, cardiac failure, and tumour lysis syndrome. The ventilatory support was required in 56.48% patients. Inotropic support was required in 31.48% patients and both inotropic support and ventilation was required in 24.07%. Culture positivity was documented in 29.62%. Out of total 108 patients, effective ICU mortality was 37% and effective ICU beneficiary were 63%. The factors associated with mortality were haematological malignancies, certain reasons for admission to ICU, requirement of either ventilation or inotrope.

Key words: Medical oncology, Intensive care unit

INTRODUCTION

The management and outcome of cancer patients has been improved over last few years. Also the admission to intensive care unit which was controversial is now becoming a more accepted practice as a part of advanced care. GCRI has a dedicated ICU for medical and paediatric oncology department.

MATERIALS AND METHODS

Aims and objectives: The objective was to categorise the reasons for ICU transfer, to assess the outcome of patients, to stratify risk factors for mortality,to study the demography and duration of ICU stayof the critically ill patient with cancer, to study use of various organ support strategies(e.g. inotropes, ventilation), to find out the organisms grown in various cultures and to compare with the institution's previous outcome evaluations and the worldwide statistics.

Design: Retrospective review of all admissions to the medical ICU at GCRI from November 2013 to April 2014 was done. Total 132 admissions counted. For data analysis the inclusion and exclusion criteria were defined as follows.

Inclusion criteria: 1. Patients admitted to medical ICU in GCRI in study duration.

Exclusion criteria: 1. Those patients whose medical records not available at the time of evaluation. 2. Patients died within 4 hours of medical ICU admission(< 4 hour ICU stay excluded in accordance with APACHE III-j algorithm).This is very short time for management. 3. Non-neoplastic admissions

RESULTS

Admissions in medical ICUduring the study period counted 132, those who had less than 4 hours ICU stay were 23, and 1 was noncancer admission. These patients were excluded from evaluation. Medical records were available in all patients.

Demography: Out of 108 females were 42 (38.88%), males were 66 (61.11%). The diagnosis was haematological malignancy in 72 (66.66%) and solid malignancy in 36 (33.33%). Prechemotherapy patients counted 26 (24.07%) while post chemotherapy patients counted 82 (75.92%).

According to aetiology the major diseases were (Table 1)acute myeloid leukemia (AML) 39 (36.11%) out of that non-promyelocytic AML (non M3) were 23 (21.3%) and Acute promyelocytic leukaemia(APML/M3) were 16(14.8%), ALL 20(18.5%), breast cancer 7(6.5%), lung cancer 6(5.6%), others counted 36(33.33%).

Major reasons for ICU admission(Table2)included pneumonia 29(26.85%), neurological dysfunction 23(21.3%), airway compression 10(9.3%), septicemic shock 10 (9.3%), differentiation syndrome 6(5.6%), renal dysfunction 5(4.6%).

At the time of ICU admission 73(67.59%) patients were on treatment with curativeintent and 35 (32.4%) patients were on palliative treatment. Relapsed/refractory malignancies were on palliative treatment.

Outcome:Total deaths were 56(51.85%) while 40(37.03%) patients transferred out and 12 (11.11%) patients left the hospital against medical advice. There were 2(1.85%) readmissions.

Effective mortality : This was calculated as (in percentage):
Mortality in compliant patients with curative intent of treatment $\times$ 100
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Total number of evaluable patients

Mortality in compliant patients was calculated by subtracting those who left against medical advice (n=12) and deaths in palliative patients(n=15) from total number of evaluable patients(n=108) i.e 81. Mortality in these patients was 41. Thus according to above equation effective mortality was 41$\times$ 100/ 108=37%. Hence the effective ICU beneficiaries were rest 63%.In palliative patients the aim of ICU admission wasat least the 'end of life care.'

Out of 12 patients who left against medical advice five were being treated on curative intent and seven were being treated on palliative intent.

Mean duration of medical ICU stay was 3.57 days(maximum-23day). Ventilation required to 61(56.48%) patients [NIV i.e.non-invasiveventilation in 28 (25.92%) and invasive ventilation in 33 (30.55%)] while 47(43.51%) were managed without ventilator support. Inotropic support was received by 34(31.48%) patients and both ventilation with inotrope were received by 26(24.07%) patients. Culture positivity from any site (blood/urine/sputum/stools) was 32(29.62%).

The factors associated with mortality were haematological malignancies(p=0.029),the reasons for ICU admissionbeing neurological dysfunction, lung metastasis, septicemic shock, differentiation syndrome, tumour lysis syndrome, DIC(disseminated intravascular coagulation) (P<0.05), requirement of either ventilation(p=0.000) or inotrope(p=0.000) or both(p=0.000).

Factors which were evaluated but were found not to be associated with outcome (P>0.05)were age, sex, histopathologicaldiagnosis of cancer, culture positivity, prechemotherapy/post chemotherapy status, intent of therapy, and hospitalisation duration.

The organisms grown in cultures were E.coli(n-11), Klebsiella-5, Acinetobacter -5,Methicilin resistant staphylococcus aureus (MRSA)-3,Staphylococcus hemolyticus-2, E.cloacae-1, Klebsiella ozenae-1, Stenotrophomonas-1, P. aeruginosa-1, Enterococci-1, Coagulase negative staphylococci-1, Fungi-3.Extended spectrum B lactamase (ESBL) positive organisms were documented in 13 patients and carbapenamase positive organisms in 9 patients.
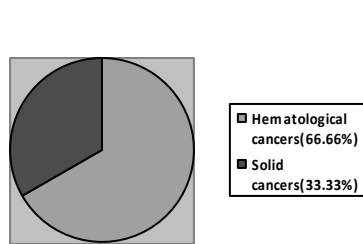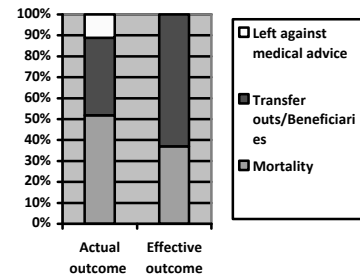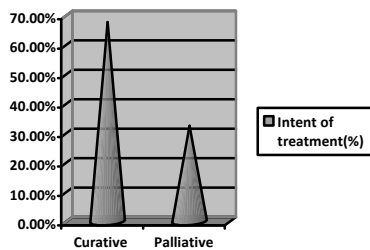
Figure 1

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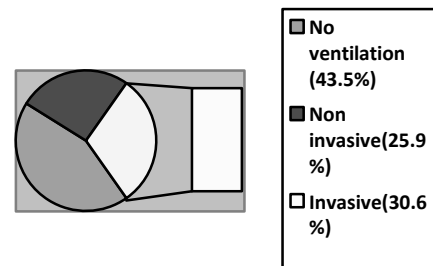

Figure 2

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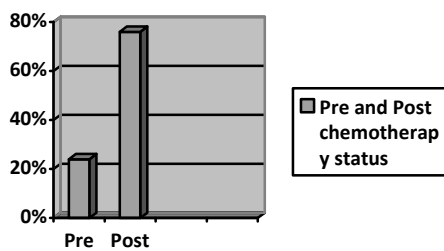
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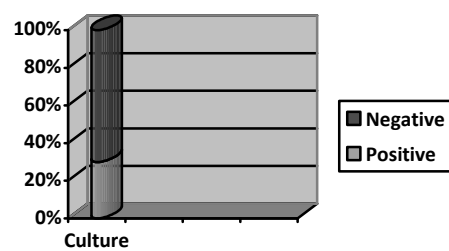
Figure 6

Table 1. Frequency of different cancers in ICU		
	Frequency	Percent
NON promyelocytic AML(Non M3)	23	21.3
ALL(acute lymphoblastic leukemia)	20	18.5
APML(acute promyelocytic leukemia- M3)	16	14.8
CA Breast	7	6.5
Lymphoma	7	6.5
CA Lung	6	5.6
Metastases of unknown primary	4	3.7
Germ Cell Tumour	3	2.8
CA Ovary	3	2.8
Acute leukemia nontypified	2	1.9
Mediastinal mass (undiagnosed)	2	1.9
CA Colon	2	1.9
CA Gall bladder	1	.9
PNET(primitive neuroectodermaltumour)	1	.9
HCC(hepatocellular carcinoma)	1	.9
CA stomach	1	.9
CA pancreas	1	.9
Multiple Myeloma	1	.9
ET (essential thrombocytosis)	1	.9
Mesothelioma	1	.9
CA Lower alveolus	1	.9
Hairy cell leukemia	1	.9
CA penis	1	.9
Glioma	1	.9
CA Prostate	1	.9
Total	108	100.0
AML- Acute myeloid leukemia , CA- Carcinoma		

Table 2. Reasons for ICU admission in cancer patients		
Reason for ICU	Frequency	Percent
Pneumonia	29	26.9
Neurological dysfunction	23	21.3
Airway compression	10	9.3
Septicemic shock	10	9.3
Lung Metastasis	7	6.5
Differentiation	6	5.6
Renal dysfunction	5	4.6
Cardiac Failure	4	3.7
Post surgical	3	2.8
Tumor lysis	3	2.8
DIC(disseminated intravascular coagulation)/Bleeding	2	1.9
Liver failure	2	1.9
Massive Pleural effusion	1	.9
Anasarca	1	.9
DKA (diabetic ketoacidosis)	1	.9
ARDS(acute respiratory distress syndrome)	1	.9
Total	108	100.0

DISCUSSION

Haematological patients were dominating the oncomedicalICU population. Malignancies with curative intent had more admissions in the ICU (n=73, 67.6%), but patients with palliative intent were not a minority (n=35, 32.4%).

Most patients who required the ICU were those who had received previous chemotherapy, this can be explained by the toxicity of the chemotherapy, neutropenia and immunocompromised status. Those patients who were admitted prior to chemotherapy had aggressive malignant course or advanced disease. But prechemotherapy or post chemotherapy status did not influence the outcome (p=0.079).

Very high mortality in cancer patients(upto 58%) in ICU is repeatedly reported in literatuere.[1,2,3]This is comparable with our result(51.85 % morality). Those evaluations which are not restricted to only medical oncology setting may report lower mortality. This is due to good prognosis of surgical patients (0-4% mortality) which are early stage cancers. Withfewer inclusions of haematological cancers and palliative patients, there can be lower reported mortalities. This is also attributable to theoncomedical emergencies with poor outcome, progressive and intractable nature of some malignancies, and resistant infections in patients with pre and post chemotherapy neutropenia.[1, 2, 3]Also operative patients are nonneutropenic and hence their prognosis does not differ from the general population of intensive care.[2] They were only a minimal part of medical ICU patient population in this study(Table 1).

Though the mortality rate in cancer patients in ICU has been reported near 50 %,as with general ICU population, the degree of multi-organ failure is systematically related to prognosis;mortality exceeds 70% if three or more organs areinvolved. The use of mechanical ventilationand/or inotropic support isother important prognostic factor. Their combination is associated with a worse prognosis, with mortality reaching 54% to 100%. It should be noted that patients ventilated because of airway compression have abetter outcome than those ventilated for lung disease.As in other studies the good outcome for patients requiring only ventilation, only inotrope, and both ventilation with inotrope were in declining trend .[2,3]

The effective ICU mortality was near one third of the evaluable ICU admissions. This was definitely satisfactory outcome considering the seriousness of patients.

The culture positivity counted 29.62% and major reported organisms were E.coli,Klebsiella, Staphylococcus and Acinetobacter.

Culture positivity was associated with prolonged hospitalisation (p=0.004) but culture positivity was not associated with increased deaths (p=0.211).

A fraction of critically ill cancer patients leave against medical advice. This may be due to lack of commitment of relatives, grave nature of disease, poor resources or psychological nonacceptance for further compliance.

The protocol of antibiotic use in neutropenic patients included piperacilin- tazobactum or cefoperazone- sulbactum in first line with addition of levofloxacin or amikacin for gram negative coverage. Vancomycin/ linezolid/ teichoplain were used for gram positive coverage. Imipenem/ meropenem were used in second line. Tigecyclin and colistin were used as reserved antibiotics for multiresistant organisms. As there is a lot of ongoing construction in hospital surroundings, the early institution of antifungals which is a proved strategy with improved outcome was an adapted practice. Ionotropic strategy was the use of dopamine when systolic blood pressure less than 90 mm Hg and noradrenalin when it is less than 70 mm Hg.

When compared with the previous evaluation of this institute reported in 2010 by PanchalHarsha et al, there is considerable increase in the admissions in medical ICU(132 versus 42). There is decrease in mortality than previous (52% versus 78%). While in the previous evaluation the emphasis was on comorbidities,presentation, various events specific to particular chemotherapy and disease, this evaluation classifies patients in curative/ palliative, explores the significance of association of various

reasons for ICU transfer, analyses the risk factors associated with mortality, reviews the culture flora of the ICU and denotes the antibiotic strategy used by the hospital in the study period.

This outcome in ICU may have been improved due to early transfer of critical patients to ICU along with advances in antibiotic and ventilator management.

Also when compared to worldwide outcome where the medical ICU mortality of cancer patients is upto 58%, the outcome at our ICU is equivalent or slightly better (mortality of 52%, effective mortality 37%).

Lacunae of the study:

1. Some patients did not get beds in medical ICU; they were kept in other ICU. We have not evaluated those patients. Also this study does not include the patients admitted in isolation ICU where the patients with parenterally transmitted infections are admitted because it is situated elsewhere.
2. There were no uniform criteria for ICU transfer.
3. As this study was a retrospective evaluation APACHE scores were not taken as a tool for analysis.

CONCLUSION

This evaluation of medical ICU in GCRI shows that there is improvement in patient care in Indian cancer patients. There is increased tendency of physicians to transfer patients to medical ICU when they need intensive care. Critically ill cancer patients do have poor prognosis than general medical ICU patients but there is trend towards decrease in the frequency of deaths and increase in the transfer outs as compared to previous reports.

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