RESEARCH ARTICLE

TREATMENT MODALITIES AND THROMBOCYTOPENIA AFFECT MORTALITY IN ELDERLY ICU PATIENTS- OBSERVATIONAL STUDY IN TERTIARY CARE HOSPITAL IN NORTHERN INDIA

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Manuscript Info	*Abstract*

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Ageing is a global phenomenon and number of patients admitted to Intensive Care Units (ICU) is increasing steadily. Number of studies assessing outcome in elderly South Asian patients in ICU is limited. Further research is necessary in this area so that the there is no bias in admitting the elderly in ICU especially in resource constrained units.
Objective: Examine age-related difference in outcomes of ICU treatment in the elderly. *Materials and Methods*: A retrospective observational study was conducted in 100 patients admitted in a medical ICU (MICU) of a secondary care hospital over one year study period from September 2015 to September 2016. A clinical database was collected which included age, sex, SOFA (Sequential Organ Failure Assessment) scores, patient outcome, average length of ICU stay, admitting diagnosis and the treatment modalities used in ICU including mechanical ventilation (invasive and non-invasive), inotropes, renal replacement therapy (RRT), and tracheostomy. We divided patients into two groups i.e. less than 65 years (Control group) and greater than 65 years (Geriatric age group). *Results*: The observed overall ICU mortality rate in the study population was 27%. The overall mortality between the control and geriatric age group was not statistically significant (P > 0.05). Mechanical ventilation (P = 0.003, odds ratio [OR] =0.473, 95% confidence interval [CI] =0.290-0.743) and use of inotropes (P = 0.000, OR =8.500, 95% CI = 2.848-25.370), Renal Replacement therapy (P = 0.049, OR =3.343, 95% CI = 0.955-11.707)and platelet count <150 (P = 0.000, OR =5.630, 95% CI =2.362-13.420)were found to be predictors of mortality in elderly population. On multivariate analysis, inotropic support was found to be an independent modality predicting ICU mortality in the geriatric age group (β coefficient = 1.221, P = 0.000). SOFA score 11.77 ± 2.93 was associated with higher mortality. Non-invasive ventilation (NIV) is associated with better outcome in elderly as compared to invasive ventilation (P=0.002, OR=0.154, 95% CI=0.042-0.567.*Conclusion*: Intensive Care Unit mortality rates increased in the geriatric population requiring mechanical ventilation, inotropes, RRT and platelet count <150 during ICU stay. Only inotropic support could be identified as independent risk factor formortality. Thrombocytopenia is a simple and readily available marker for mortality which is independent of and complementary to established severity of disease indices in the elderly.

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Introduction:-

Population ageing is a global phenomenon. [1] People aged over 65 years is the fastest growing segment of population worldwide [1]. It is predicted that by 2050, the elderly population of the world will exceed that of the young [2]. As the population demographics are changing, there is an increase in the number of geriatric patients being admitted to Intensive Care Units (ICUs). [2] The elderly patients comprise between 26% and 51% of ICU admissions. [3] This emphasizes the need for continued research on outcomes of intensive care for the elderly, especially in the medium income South-East Asian countries with a growing elderly population. Various studies have proposed for different predictors of mortality in geriatric ICU patients. [1],[2],[3] Multiple studies on the ICU outcomes of the geriatric population in the high income countries is available, but the studies on outcomes in ICUs of medium income countries like India is scarce. This is primarily due to overburdened healthcare with less resources. The aim of the study was to examine the age-related difference in mortality in medical ICU and ICU treatment modalities affecting mortality in elderly patients >65 years of age in a tertiaary care Indian ICU. We also assessed thrombocytopenia as a predictor of mortality in the elderly.

Materials and Methods:-

We first obtained approval from the hospital ethics committee, then a retrospective observational study was conducted in a medical ICU (MICU) of a tertiary care hospital, in Northern India. Case notes of a total of 100 consecutive patient admitted to medical ICU from September 2015 to September 2016were assessed. The criteria for admission is decided by the admitting intensivist based on the clinical condition and functional status of the patient. Primarily patients are admitted from Medicine, however patients are also admitted from other specialties if no beds are available in Surgical ICU. No patient is refused admission to the ICU based on age and no treatment option is restricted to a specific group of patients during the ICU stay.48patients with incomplete records were excluded. Data collected included age, sex, admitting diagnosis, SOFA (Sequential Organ Failure Assessment) scores at the time of ICU admission, average length of stay, treatment modalities and the patient outcome. The average length of stay (ALOS) was calculated from the time of admission in ICU to discharge from ICU or death. Data collected for treatment modalities used during the ICU stay included use of mechanical ventilation (invasive or non-invasive), inotropes, renal replacement therapy and tracheostomy. The patients were divided into two groups: <65 years as Control group (Group C) and >65 years as Geriatric age group (Group G). Statistical Data was expressed as mean ± standard deviation and percentages. Continuous variables were evaluated using Student's t-test and categorical variables using Chi-square test. Patient characteristics, odds ratio (OR) and confidence intervals (CI) were calculated by logistic regression analysis to identify independent risk factors and control confusion effects. Significant variables in univariate analysis were submitted to logistic regression. Significance probabilities (P values) of <0.05 were considered statistically significant. Statistical analysis was performed using the IBM SPSS statistics version 17.0.

Results:-

During the study period, a total of 148 patients were admitted in the ICU. 100 consecutive patient's records were assessed. The medical records of 48 patients were found to be incomplete, and these patients were excluded from the study. Of the 100 patients, 51 (51%) were in Group C, while 49 (49%) were in Group G. The average age in Group C was 30 ± 11.76 years while in Group G was 71 ± 9 years. Male to female ratio in Group C was 24(24%): 25 (25%) and in Group G was 26 (26%): 25 (25%). No statistical difference was observed in the demographic profile of two groups (P > 0.05) [Table 1 and 2]. The admitting diagnosis of patients is as shown in [Figure 1]. The maximum admissions were secondary to sepsis followed by poisoning. Our study patient was sicker as these were medical patients and evidenced by significantly higher SOFA score of 5.37 ± 2.85 in survivors and 11.77 ± 2.93 in non-survivors. The average duration of ICU stay in survivors was 12.14 ± 2.52 days and in non-survivors 5.709 ± 6.16 days.

Table 1:- Age versus mortality

	<65	≥65
Total patients, n (%)	51 (51)	49 (49)
Mortality, n (%)	17 (17)	27 (27)
Shifted to ward	34 (34)	22 (22)

Figure 1:- Admitting diagnosis to MICU

Diagnosis		Outcome		Total
		Shifted to ward	Died	
	AIDP	6	0	6%
	ARDS AKI/CKD	2	0	2%
	CAP T1RF	6	1	7%
	COPD T2RF	12	2	14%
	GTCS	2	2	4%
	stroke	1	11	12%
	cardiac causes	3	4	7%
	poisoning	12	7	19%
	surgical	1	1	2%
	trauma	1	1	2%
	Other	4	0	4%
	sepsis MODS	5	16	21%
Total		56	44	100
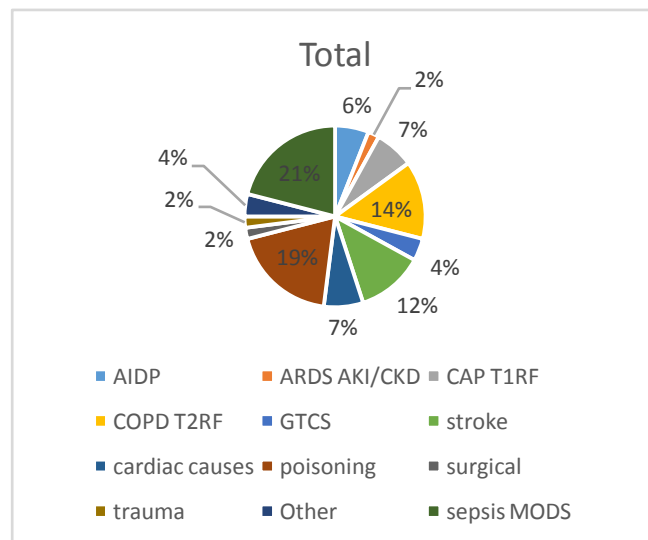
ARDS: Acute Respiratory Distress Syndrome, T1/T2 RF: Type 1 & 2 respiratory failure, CAP: Community Aquired Pneumonia,
GTCS: Generalised Tonic Clonic seizures, AKI: Acute Kidney Injury,AIDP: Acute Inflammatory Demyelinating Polyneuropathy,
CKD: Chronic kidney disease, COPD: Chronic Obstructive Pulmonary disease, MODS: Multiple Organ Dysfunction Syndrome

The overall observed ICU mortality was 44%. On statistical analysis, no association was found between mortality and sex ratio preference in both the age groups (P > 0.05). The ICU mortality rate in Group C was 17% (17 deaths), while in Group G, was 27% (27 patients) (P = 0.276). There was no statistical difference in the frequency of treatment modalities used in two groups in the form of mechanical ventilation, renal replacement therapy, inotropes and tracheostomy (P > 0.05).

Table 2:- Sex versus mortality

	Shifted to ward (%)	Died (%)	Total (%)	P value
Female	27	23	50	0.687
Male	29	21	50	
Total	56	44	100	

Overall 68 patients (68%) required mechanical ventilation. The mortality rate in patients requiring mechanical ventilation was 32%. 34 patients required ventilatory support in Group C (50%), of which 13 (38.23%) expired while 34 patients (50%) in Group G required ventilatory support, of which 20 (58.8%) expired. The mortality rate was significantly higher in geriatric patients requiring mechanical ventilation than the Group C patients (P = 0.003, OR = 0.473, 95% CI = 0.290-0.743.) [Table 3].

Table 3:- Predictors of mortality in geriatric age group

	Group C (%)	Group G (%)	P value	Odds ratio	95% confidence interval Upper	Lower
Invasive ventilation	13 (38.23)	20 (58.8)	0.003	0.473	0.290	0.743

Inotropes	7 (63.63)	15 (100)	0.000	8.500	2.848	25.370
Tracheostomy	0	0	0.259	0.397	0.076	2.070
Renal Replacement therapy	5 (62.5)	4 (80)	0.049	3.343	0.955	11.707

In total, 26 patients (26%) required inotropic support during ICU stay. The overall mortality rate for patients on inotropes was 80%. In Group C, 11 patients (11%) required inotropic support, of which 7 patients (63.63%) died, while 15 patients (15%) in Group G required inotropic support, of which 15 patients died (100%). There was a significant difference in mortality in geriatric and control groups requiring inotropes (P = 0.000, OR =8.500, 95% CI = 2.848-25.370).

In our study, 13 patients (13%) required renal replacement therapy (RRT) and the mortality rate for patients requiring renal replacement was 69.23%. A total of 8 patients (8%) in Group C required RRT out of which 5 (62.5%) expired while 5 patients (5%) in Group G underwent RRT during their ICU stay, of which 4 died (80%). Significant difference in mortality was observed in Groups G and C requiringRRT in ICU (P = 0.049, OR =3.343, 95% CI = 0.955-11.707).

Tracheostomy was done in 7 patients (7%) during the study period. The mortality rate for tracheostomized patients was 0%. In Group C, 6 patients (6%) required tracheostomy of which 0 (0%) died while 1 patient (1%) in Group G were tracheostomized during ICU stay, of which 0 died (0%). The mortality rate did not differ significantly in Group G and C patients requiring tracheostomy (P = 0.259, OR = 0.397, 95% CI = 0.076-2.070).

In total, 11 patients (11%) required only Non-invasive ventilation (NIV) during ICU stay. The overall mortality for patients was 1%. In Group C, 4 patients (4%) required NIV, of which 0 patients (0%) died, while 7 (7%) patients in Group G required NIV of which 1 (1%) died. NIV was associated with better outcome and lesser mortality in both groups (P=0.002, OR=0.154, 95% CI 0.042-0.567).

The SOFA score (11.77 ± 2.93) were significantly higher in non-survivors in the study (P < 0.05) as shown in [Table 4]. The SOFA score in survivors was 5.375±2.85.

Table 4:- SOFA scores as predictors of mortality

	Outcome	N (%)	Mean	Std. Deviation	Std. Error Mean
ALOS	survivor	56	12.143	25.29	3.38
	Non-survivor	44	5.709	6.16	0.92
SOFA	survivor	56	5.375	2.85	0.38
	Non-survivor	44	11.773	2.93	0.44

In Group G, Platelet count <150 (score of 1 on SOFA score) was present in 28 patients (57.14%) out of which 22 Patients (78.57%) died. Hence, platelet count <150 can be used as a simple predictor of mortality in the elderly (P = 0.000, OR =5.630, 95% CI = 2.362-13.420) (Table 5).

Table 5:- Platelet count as predictor of mortality in elderly.

Platelet Count	N (%)	p-value
Survivor	06(21.43)	0.000
Non-Survivor	22(78.57)	

On univariate analysis of the ICU treatment modalities, it was observed that need for mechanical ventilation (P = 0.003) and inotropes (P = 0.018) were predictors of mortality in geriatric age group.

On applying the regression model by means of multivariate analysis, it was observed that the inotropic support was the only variable that independently discriminated ICU mortality (P = 0.000).

Discussion:-
In our study we had 49 % patients >65 years similar to Indian study by Sodhi et al [4] which had52% patients >65 years. In the US study data,itvaried between 42% to 52%[5].We found overall ICU mortality of 27% in our study subjects, with no difference between the control group and the geriatric population (P >0.05). Different studies in the literature have studied the association of age with the outcome in geriatric patients. Rosenthal et al. in a

multihospital study of 38 ICUs found an age-related increase in mortality in 1,50,000 consecutive admissions [6]. However, many other studies could not establish a positive relationship between age and mortality. van den Noortgate et al. in their study in very elderly patients could not correlate age with greater in-hospital mortality [7]. Rockwood et al. in a two-center study on 1-year outcome observed that although ICU and 1-year mortality rates differed between >65 years and <65 years, but age was not a major contributor to the variance in outcome [8].deRooij et al., in a meta-analysis from 12 prospective and retrospective studies, also concluded that it is not age per se but factors such as severity of illness and premorbid functional status that are responsible for poor prognosis [9]. In a review by Boumendil et al., the authors commented that age itself explains only a small part of the increased hospital mortality, suggesting that specific information such as functional, cognitive, and nutritional status, as well as co-morbidities, should be collected to predict mortality in elderly ICU patients [10].Asa majority of studies conclude that age is not a major contributor towards mortality, treatment options should not vary with age and specific therapy should not be withheld for increasing age. However, It is not possible to define evidence-based recommendations for ICU admission of the elderly [10] In our study, we found no statistical difference in the treatment modalities offered to both the groups in the form of mechanical ventilation, inotropic support, renal replacement therapy or tracheostomy (P > 0.05) [Table 3].

We found the ICU mortality in geriatric patients to be 27%. Studies have reported the mortality rates in ICU patients varying from 3% to 64%, depending upon the type of subjects studied. [15] Our study population comprised primarily of medical cases and the overall mortality corresponds roughly to that expected as per the SOFA scores.

We observed that mechanical ventilation and inotropes were significant treatment factors for ICU mortality in geriatric patients. However, on multivariate analysis only inotropic support was found to be independently associated with increased mortality. Mortality rate for our geriatric patients on mechanical ventilation was 58.8%, which is similar to the previous studies in which overall mortality ranged between 41% and 78% [12],[13],[14],[15],[16]. In our study, we found that the odds of having survival in geriatric ICU patients on mechanical ventilation is 0.473.A Brazilian study in 199 elderly patients >65 years also found the need for mechanical ventilation as an independent determinant of mortality (P < 0.001, OR = 3.57, CI 95% 1.24-10.3) [1].van den Noortgate et al. found mechanical ventilation as a factor associated with mortality ($\chi2$; P = 0.00005) [7].

We also found that the odds ratio in geriatric patients requiring inotropic support is 8.500 (P = 0.000, β coefficient = 1.221). Inotropic support has been associated with mortality in literature. van den Noortgate et al. in a study on 104 patients >85 years found inotropes as an independent risk factor of mortality ($\chi2$; P = 0.00001, β-coefficient = 0.9698) [7]. Friedrich et al. also associated use of inotropes or vasopressors with long-term ICU mortality (OR = 7.1, 95% CI 2.6-19.3) [17].

In our study, 13 patients (13%) required renal replacement therapy (RRT) and the mortality rate for patients requiring renal replacement was 69.23%. A total of 8 patients (8%) in Group C required RRT out of which 5 (62.5%) expired while 5 patients (5%) in Group G underwent RRT during their ICU stay, of which 4 died (80%). Significant difference in mortality was observed in Groups G and C requiring RRT in ICU (P = 0.049, OR =3.343, 95% CI = 0.955-11.707). These results are similar to other studies (P = 0.543). Romao Junior in a series of 361 patients with acute renal failure (ARF) identified the need for dialysis as a poor prognostic factor in elderly patients with ARF [18].

We found no difference in outcomes of tracheostomised patients in two age groups in our study (P = 0.259). Numerous studies in the literature support our findings. Ho et al., in an audit of characteristics and outcomes in 168 adult ICU patients with tracheostomies concluded that tracheostomy appears to be a relatively safe technique in the ICU population and is not associated with adverse outcomes[21].Frutos-Vivar et al. in a vast study in 361 ICUs across 12 countries observed that adjusting by other variables, tracheostomy was independently related with survival in the ICU (OR = 2.22; 95% CI, 1.72-2.86) but in-hospital mortality was similar with or without tracheostomy (39% vs. 40%, P =0.65). [22]

The SOFA score (11.77 ± 2.93) were significantly higher in non-survivors in the study (P < 0.05) as shown in [Table 4]. The SOFA score in survivors was 5.375±2.85. This is similar to previous studies [19]

In our study, in Group G, Platelet count <150×10^9/μl (score of 1 on SOFA score) was present in 28 patients (57.14%) out of which 22 Patients (78.57%) died (Table 5). Hence, platelet count <150×10^9/μl can be used as a

simple predictor of mortality in the elderly (P = 0.000, OR =5.630, 95% CI = 2.362-13.420). This inference is similar to other studies. Thrombocytopenia is common in ICUs and is a simple and readily available marker for mortality, independent of and complementary to established severity of disease indices. [20]

Hence, in our study the ICU mortality rates were similar regardless of the age. However, mortality rates increased in the geriatric population requiring mechanical ventilation and inotropes during ICU stay. However, only inotropic support could be proposed as an independent risk factor for mortality in the geriatric population. Hence, the geriatric patients requiring mechanical ventilation and inotropic support in ICU should be prognosticated accordingly.

Limitations:-
A few limitations of our study need to be acknowledged. First, this is a retrospective, observational study, so both internal and external validity is relative and uncertain. Our analysis focused only on ICU mortality, and we did not examine mortality after discharge. We did not include information of baseline functional status and physiological parameters in our study as we wanted to especially study the impact of ICU treatment modalities and thrombocytopenia on geriatric mortality. We also did not assess the long-term mortality which could have modified our results. Finally, our study was limited to a small tertiary care hospital and this may limit the generalization of our findings to other hospital settings.

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