Original Article

A Study of Clinical Outcome of Young Critically ill Subjects Admitted in ICU & Health Related Quality of Life after Discharge

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ABSTRACT

Background : Health-related quality of life (HRQOL) in critically ill patients who survive treatment in an ICU is lower than that of the general population. Data on quality of life after intensive care discharge is limited in developing countries and we intended to explore this area further.

Aim and Objectives : Aim of the present research was to study the clinical outcome of young critically ill patients in the age group 20-40 years admitted in intensive care unit, to evaluate HRQOL of critically ill ICU survivors over the period of time (1st, 3rd and 6 months) and to assess influence of various clinical variables on HRQOL after discharge from the ICU.

Methodology : This prospective observational study was performed at a tertiary care hospital from May 2018 to October 2019 after taking approval from the Institutional Ethics Committee. APACHE II score was calculated on admission for 80 patients admitted to ICU within 24 hours. HRQOL was assessed using the Study 36-Item Short-Form Health Survey (SF-36), which was applied by telephone interview at the first, third and sixth months after hospital discharge.

Results : Among 80 patients, 12 patients died during the hospital stay, 6 patients died after discharge and 3 patients could not be contacted. Higher APACHE II score was significantly associated with increased mortality ($p<0.001$). HRQOL improved progressively after hospital discharge and was maximum at 6 months. Role emotional was the most affected domain. Physical and mental both components were affected. Physical component was mainly influenced by length of ICU ($p=0.0042$) and hospital stay ($p=0.0209$).

Conclusion : APACHE II scoring system is useful in predicting the in hospital mortality of critically ill patients. After discharge from the ICU patient's HRQOL was poor, which showed progressive improvement over time. ICU length of stay had the strongest impact on HRQOL.

Keywords : Critically ill, Quality of life, Intensive care unit, APACHE II score, Short Form-36

Introduction :

Critically ill patient is the one with severe respiratory, cardiovascular or neurological derangement, often in combination, reflected in abnormal physiological observations[1]. Intensive care has had phenomenal growth in the last few decades and the outcomes are constantly improving with the deployment of resources, drugs, consumables, and techniques in different intensive care units. Level of care varies among ICUs and within ICUs[2,3]. Survival / mortality rate of the unit makes a significant impact on the relatives of the patients, hospital authority, and the general mass in that locality[3,4]. Hence some scoring system should be in place to stratify severity status of the admitted patients and link it with the outcome. However, first general severity of illness score applicable to most critically ill patients was the Acute Physiology and Chronic Health Evaluation (APACHE)[5]. It was developed by William Knaus et al[6] at the George Washington University Medical Centre in 1981. The APACHE system demonstrated the ability to evaluate, in an accurate and reproducible form, the severity of disease in this population[7].

A growing body of evidence clearly demonstrates that intensive care survivors have severe physical, cognitive and mental health impairments such as neuromuscular dysfunction and weakness,

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respiratory impairment, posttraumatic stress disorder, anxiety and depression after discharge from ICU[8]. These adverse consequences of critical care have recently been described as the post-intensive care syndrome, defined as new or worsened deficiencies in physical, cognitive and mental health after discharge from ICU[9]. The evaluation of HRQOL can be performed by using the Medical Outcomes Study 36 - Item Short-Form Health Survey (SF-36)[10].

In a study conducted in a Scottish Teaching Hospital by **B H Cuthbertson et al[11],** ICU survivors presented lower scores of physical aspects of SF-36 three months after ICU discharge when compared to their score before admission to ICU. In the study conducted by **Hofhuis et al[12]** in Netherlands, A sharp multidimensional decline occurred during ICU admission, followed by recovery toward normal functioning that started immediately following discharge from the ICU.

The HRQOL of critically ill patients after ICU and hospital discharge has been addressed mostly in developed countries. In the few studies conducted in developing countries, HRQOL was reported as declined in survivors of critically ill patients. There are very few studies carried out in regard to outcome in young critically ill ICU admissions. Hence the present study was carried out to assess whether there is any correlation between APACHE II score and outcome of ICU admissions in Indian patients and various factors affecting the quality of life after ICU discharge.

Materials and Methods :

After obtaining Institutional Ethics Committee approval and written informed consent from all the patients or their relatives, this hospital-based prospective observational study was conducted in 80 young critically ill patients (age 20 to 40 years) admitted to medical ICU at tertiary care centre during a period from May 2018 to October 2019. ICU admissions were divided into cardiac, respiratory, gastrointestinal, neurological, intoxication, sepsis and others groups. All the patients were evaluated as per predesigned proforma.

Inclusion Criteria :

1. Young critically ill patients between the age group 20 to 40 years admitted to medical ICU

Exclusion Criteria :

1. Patients with the previous cognitive deficit, aphasia, neurological deficit.
2. Patients with tracheostomy
3. Patients with amputation of limbs.
4. Patients with Surgical Problems
5. Patients with Head Injury

Demographic data, time from symptom onset to ICU admission, severity of disease score (APACHE II score) on admission, cause of ICU admission, diagnosis, treatment (antibiotics, benzodiazepine / sedatives), vasopressors, duration of mechanical ventilation (invasive & non-invasive), renal replacement therapy (RRT), ICU length of stay and hospital length of stay, chronic co-morbid conditions were recorded. Patients were evaluated at discharge from the hospital. Two telephone contact numbers and address for future follow up were recorded. The evaluation of the QOL was performed by using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). The SF-36 has good acceptance, reliability, validity in ICU patients and has good adaptability to be applied by telephone call. The SF-36 comprises eight domains : physical functioning, role-physical, bodilypain, general health, vitality, social functioning, role-emotional, and mental health. The domains physical functioning, rolephysical, bodily pain and general health compound the physical component and the domains vitality, social functioning, role-emotional and mental health compound the mental component. The SF-36 score ranges from 0 to 100, and 0 is the worst and 100 is the best score for QOL. Patients' QOL was assessed by telephone calls at the first, third and sixth month after hospital discharge. The treating clinician did routine follow-up as per their clinical condition. Also, mortality, read missions, dropouts, over a period of six months was recorded.

Statistical Analysis :

Continuous variables were presented as Mean ± SD. Categorical variables were expressed in frequency

and percentages. Continuous variables were compared between non-survivors and survivors by performing an independent t-test for normalized data and the Mann-Whitney test was used for non-normalized data. Categorical variables were compared by performing the chi2-test. For small frequency, Fisher exact test was used wherever required. ANOVA test was performed for comparing the improvement in the quality of life at different follow-up periods for different components of QOL as well as for physical functioning score summary and mental health score summary. Pearson's correlation coefficient (r) was used to assess the magnitude and nature of the correlation between different study variables with physical component score (PCS) and the Mental Component Score (MCS). P-value < 0.05 was considered as statistical significance. Statistical software STATA version 14.0 was used fostatistical analysis.

Observations and Results :

Total 80 patients were enrolled in the study among them 35 (43.75%) were male and 45 (56.25%) were female patients. ***Table 1*** shows the demographic profile and clinical characteristics of the studied population and lost to follow-up patients after ICU discharge. In the ICU, 12 patients died, 68 patients received the discharge from the hospital. Out of 68 patients who received a discharge from the hospital, follow up was completed for 67 patients at first month, 63 patients at third month and 59 patients at the sixth month. Of the 9 patients lost to follow up, 6 died and 3 patients were uncontactable.

Table 2 shows that there was statistically significant association between APACHE II score and in-hospital mortality of patients (p=0.0001) suggesting that the APACHE II score was useful as a severity score in predicting the mortality outcome of patients as patients with higher APACHE II score had increased mortality. Out of total 28 patients with APACHE II score of $\geq$ 15, there were 9 ICU non-survivors and 19 ICU survivors whereas out of 52 patients with APACHE II score < 15, there were 3 ICU non-survivors and 49 ICU survivors. The calculated odds ratio for this data was 7.73 with 95% confidence interval of 1.65-42.76 and the difference was statistically significant with a p-value of 0.0016. ***Figure 1*** is a receiving operating characteristic curve for predicting best cut-off to differentiate non-survivors and survivors on the basis of APACHE-II Score. Area under the curve represents the accuracy of the test and in our study it was **0.8577** which suggests that APACHE II score was accurate enough to predict in-hospital mortality with a specificity of 73.85% and sensitivity of 75%. The risk of mortality was 7.73 times more in patients with APACHE II score of $\geq$ 15 as compared to those patients with APACHE II score <15.

The SF-36 score for HRQOL of intensive care survivors was obtained for 1st, 3rd and 6th month for 59 survivors. Statistical analysis showed that all dimensions of SF-36 changed significantly over time **(p<0.0001).** Consequently, PCS and MCS scores also changed significantly over time **(p=0.0001)** as shown in ***Table 3. Figure 2*** is a radar chart showing the evolution of the each SF-36 domain for all the patients 1, 3 and 6 months after hospital discharge. We can notice that the score increases over time. All domains of the SF-36 survey reflecting QOL were compromised after ICU discharge. Role emotional was the most compromised domain at the end of 6-month survey and Role Physical was the least compromised domain. The HRQOL at the end of 6 months after discharge was lower for all the domains of SF-36 when compared with the healthy young adults. MCS was lower in survivors as compared to PCS at the end of 6 month follow up suggesting mental health dimension of health-related quality of life was affected more as compared to physical health dimension.

Table 1 : **Demographic and Clinical Characteristics of the studied population (n=80)**

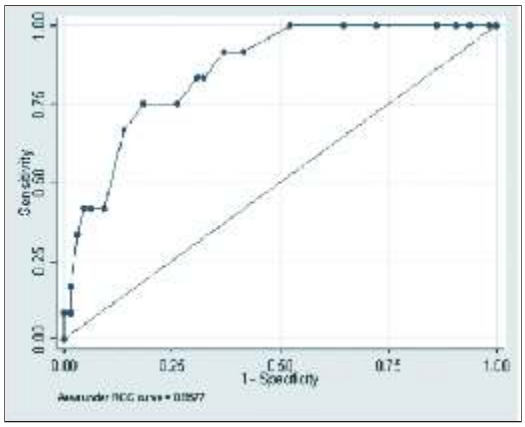
Parameters		Survivors (N=59)	Non-survivors (N=18)	Lost to follow up (n=9)
Mean Age (years)		29 ± 6.18	29 ± 6.16	28 ± 6.13
Gender	Male	24 (40.67%)	8 (44.44%)	4 (44.44%)
	Female	35 (59.32%)	10 (55.55%)	5 (55.55%)
Mean time from Symptoms to Admission (in hours)		90.38 ±102.78	73.22 ± 84.96	51 ± 46.23
Mean distance from Hospital (in km)		81.33± 81.53	55.35 ± 61.45	45 ± 65.69
Diagnosis	Sepsis	2 (3.39%)	2 (11.11%)	1 (11.11%)
	Cardiac	15 (25.42%)	4 (22.22%)	2 (22.22%)
	Respiratory	11 (18.64%)	0 (0%)	2 (22.22%)
	Neurological	5 (8.47%)	1 (5.56%)	1 (11.11%)
	Intoxication	16 (27.11%)	3 (16.67%)	0 (0%)
	Gastrointestinal	5 (8.47%)	3 (16.67%)	0 (0%)
	Others	5 (8.47%)	5 (27.78%)	3 (33.33%)
Mean APACHE II Score		10.32± 4.22	17.05 ± 5.17	15 ± 6.22
Invasive Mechanical Ventilation		14 (23.73%)	12 (66.67%)	3 (33.33%)
Non-invasive Mechanical Ventilation		5 (8.47%)	1 (5.56%)	1 (11.11%)
Treatment	Vasopressors	22 (37.29%)	14 (77.78%)	4 (44.44%)
	Sedation	12 (20.34%)	11 (61.11%)	3 (33.33%)
	RRT	4 (6.78%)	7 (38.89%)	2 (22.22%)
Mean ICU length of stay (days)		4.13 ± 1.96	4.11 ± 1.36	4.66 ±1.22
Mean Hospital Length of Stay (days)		9.66 ± 3.91	7 ±3.61	10.55 ± 3.43

RRT - Renal Replacement Therapy

Table 2 : **Correlation of APACHE II score with mortality outcome of patients**

APACHE II Score	Non-survivors (n=18)		Survivors (n=59)		Total (n=77)	p-value
	Frequency	Percentage	Frequency	Percentage		
0-5	1	16.66	5	83.33	6	
6-10	1	3.03	32	96.66	33	
11-15	3	17.64	14	82.35	17	**<0.0001***
16-20	8	53.33	7	46.66	15	
21-25	4	80	1	20	5	
26-30	1	100	0	0	1	
Mean APACHE II score	17.05 ± 5.17		10.32 ± 4.22			

Figure 1 : **Receiving operating curve for predicting best cut-off to differentiate non-survivors and survivors on the basis of APACHE-II Score**



The study found that length of ICU and hospital stay was significantly associated with physical health at 6 months after discharge. However, age, gender, APACHE II score on admission, duration of mechanical ventilation, sedation and renal replacement therapy were not associated with PCS and MCS at 6 month as shown in ***Table 4 and 5.***

Table 3 : **Change in Health-related quality of life (HRQOL) by using SF-36 and QOL after hospital discharge at 1, 3 and 6 months**

Component of SF-36	1 month (n=67)	3 month (n=63)	6 month (n=59)	p-value
PF	25.22 ± 25.25	51.54 ± 24.82	84.32 ± 14.30	<0.0001*
RP	18.01 ± 19.24	45.59 ± 22.27	76.81 ± 17.41	<0.0001*
RE	13.47 ± 19.63	41.32 ± 22.78	64.52 ± 13.80	<0.0001*
VT	23.16 ± 10.09	41.92 ± 10.68	67.03 ± 11.45	<0.0001*
MH	23.48 ± 10.66	41.26 ± 10.65	66.47 ± 12.17	<0.0001*
SF	26.91 ± 13.20	47.64 ± 10.63	69.72 ± 8.49	<0.0001*
BP	36.32 ± 13.91	52.81 ± 14.32	74.05 ± 11.40	<0.0001*
GH	19.54 ± 16.81	40.07 ± 14.8	66.86 ± 13.95	<0.0001*
PCS	26.39 ± 15.23	48.15 ± 15.68	75.47 ± 12.30	<0.0001*
MCS	22.39 ± 10.80	43.38 ± 10.25	67.19 ± 9.15	<0.0001*

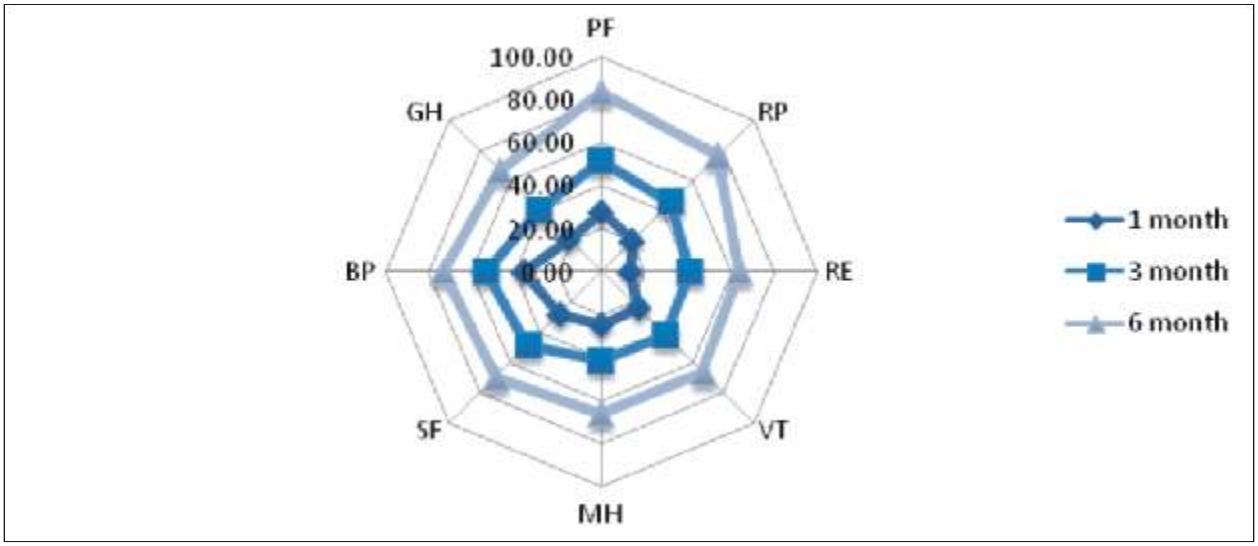
*Significant p-value, SF-36-Short Form 36 survey, PF : Physical Functioning, RP : Role-Physical, BP : Bodily Pain, GH : General Health, VT: Vitality, SF : Social Functioning, RE : Role-Emotional, PCS - Physical component score, MCS - Mental component score MH : Mental Health. HRQOL : Health-related quality of life

Table 4 : **Correlation of different study parameters with physical and mental health component of quality of life**

Variable	PCS at 3 month		PCS 6 month		MCS at 3 month		MCS at 6 month	
	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value
Age (years)	0.0208	0.8779	0.0476	0.7252	-0.0660	0.6256	-0.0190	0.8885
ICU stay	-0.3086	**0.0195***	-0.3737	**0.0042***	-0.2620	**0.0490***	-0.1902	0.1565
Hospital length of stay	-0.2530	0.0575	-0.3054	**0.0209***	-0.1817	0.1762	-0.1202	0.3732
APACHE II score	-0.1813	0.1771	-0.2140	0.1100	-0.2690	**0.0426***	-0.2811	0.0342
Duration of MV	-0.1714	0.4458	-0.2328	0.2972	-0.2559	0.2504	-0.1997	0.3730

*Significant p-value, PCS - Physical Component Score, MCS - Mental Component Score, MV - Mechanical Ventilation

Figure 2 : **Radar chart showing improvement in all 8 domains of SF- 36 at 1, 3 and 6 months after hospital discharge**



SF-36 : Study 36-Item Short-Form Health Survey. PF : Physical Functioning, RP : Role-physical, BP : Bodily Pain, GH : General Health, VT : Vitality, SF : Social Functioning, RE : Role-emotional, MH : Mental Health. QOL : Quality of Life

Table 5 : **Comparison of improvement in physical & mental health component at 3rd and 6th month**

Variable		PCS at 3 month	PCS 6 month	MCS at 3 month	MCS at 6 month
Gender	Male	49.32±13.66	51.5±18.13	76.46±11.62	66.45±8.41
	Female	47.36±17.07	47.26±15.07	74.08±12.87	67.69±9.70
	P-value	0.6480	0.4112	0.6204	0.6195
Sedation	Yes	50.25±16.22	44.62±7.04	76.81±11.27	66.27±9.89
	No	47.6±15.68	43.05±10.99	75.11±12.65	70.64±4.25
	P-value	0.6076	0.6407	0.6753	0.1432
RRT	Yes	55.81±19.94	49.87±7.13	85.56±7.06	71.93±3.07
	No	47.58±15.61	42.89±10.33	74.71±12.31	66.83±9.36
	P-value	0.3159	0.1917	0.0891	0.2866

PCS - Physical Component Score, MCS - Mental Component Score, RRT - Renal Replacement Therapy

Discussion :

The particular realities of life habits, health care system and rehabilitation settings for each country may interfere in the recovery of post critically ill patient[13]. While in developed countries QOL in post-critical patients has been verified after six months to two years in general, in developing countries there are very few studies in this area13 and the existent studies show results from specific population.

The mean age of subjects in our study was 29.86 ± 6.15 years with female preponderance (male to female ratio of 0.77). The mean age reported in previous studies[6,12,14-17] were more than mean age observed in present study, as our study mainly focused on the young population. We found that there was insignificant association observed between duration of mechanical ventilation and mortality outcome of patients (p=0.2018).These findings of our study are comparable with the results

of study carried out by **Sharon McKinley et al[14].** Similar findings were reported in the studies carried out by **Jürgen Graf et al[18]** & Nathan Ferrand et al[19].

Majority of the patient among survivors belonged to cardiovascular and intoxication groups with 15 (25.42%) patients in each group. There was no significant association between the type of diagnosis and mortality outcome. Length of hospital stay influenced the mortality outcome of patients in our study which was also reported by **Sharon et al[14], Graf et al[18], Ferrand et al[19] and Vedio et al[21]**. Among the survivors, the sedation was required for 37.29%, vasopressors were required for 20.34%, renal replacement therapy was required for 6.78%, and antibiotics were required for 94.92% of patients. Patients who required vasopressors, sedation and renal replacement therapy during their ICU stay were significantly associated with increased in-hospital mortality. This was in accordance with the results in the previous studies[12,19].

The mean APACHE II score among survivors was 10.32 ± 4.22 and among non-survivors was 17.05 ± 5.17 with the difference being statistically significant suggesting that the APACHE II score was useful as a severity score in predicting the mortality outcome of patients as patients with higher APACHE II score had increased mortality. Results of present study showed a meaningful association between APACHE-II score and the risk of mortality. In each successive APACHE-II score interval the mortality rates were higher than that of the preceding interval. Similar findings are reported in prior studies14-16,22. Chronological age is well-documented risk factor for death from acute illness that is independent of the severity of diseases; age of critically ill patients may have an impact on the severity score.

Several studies have assessed the post-ICU HRQOL. However, these studies are heterogeneous because of the difference in the type of population admitted in ICU, the method used to evaluation of HRQOL and the duration of follow-up. The majority of these studies found an initial post-ICU decrease in the HRQOL followed by a slow improvement during the follow-up, sometimes reaching the ICU preadmission HRQOL status. Our study showed that all dimensions of SF-36 changed significantly over time **(p-value < 0.0001).** Consequently PCS and MCS scores also changed significantly over time **(p-value=0.0001).** All domains of the SF-36 survey reflecting QOL were compromised after ICU discharge. Role emotional was the most compromised domain at the end of the 6-month survey and role physical was the least compromised. When compared to HRQOL in healthy young populations in the study conducted by **Wilma et al[23]** by using SF-36 survey, the HRQOL at the end of 6 month follow-up, the values were lower for almost all the 8 domains of SF-36 survey.

We found that ICU stay (r=-0.3737, p=0.0042) and hospital length of stay (r=-0.3054, p=0.0209) were significantly associated with physical health at 6 month after discharge. However age, APACHE II score on admission, duration of mechanical ventilation, sedation, RRT and sex of patients were not associated with PCS at 6 month. Similarly, mental health at 6 month was also not influenced by age, APACHE II score on admission, duration of mechanical ventilation, sedation, RRT and sex of the patient. This was in accordance with the studies carried out by **Hofhuis et al[12] and Sharon McKinley et a[14],** where physical health was affected by ICU and hospital stay suggesting that these were universally associated with HR QOL. Age was also associated in most of the studies with physical as well as mental health component of quality of life after discharge. However, in current study we didn't find any significant association between age and HRQOL.

Conclusion :

1. Inconclusion we found that there was statistically significant association between the risk of mortality in patients with higher APACHE II scores.
2. Survivors of critical illness even in the younger age groups present a multidimensional deterioration of quality of life, which improves over time for both physical and mental components. However, recovery was not consistent in all dimensions of quality of life. Role emotional was the most compromised domain at the end of 6 month follow-up.

3. Health-related quality of life was influenced by length of ICU and hospital stay.

Limitations :

1. It was a single centre study with smaller sample size, younger age of population with exclusion of surgical patients and patients of cerebrovascular episodes with severe neurological deficit.
2. These factors may have influenced our findings but importantly, despite the limitations, we found significant deficits in health-related quality of life. Present study is one of few on the prospective measurement of potentially modifiable patient factors that affect health-related quality of life in ICU survivors; thus, our findings are an important contribution to the small amount of knowledge on this topic.

Implications

1. Comprehensive care can be provided for those patients who have severity scores with higher mortality rates. Furthermore, therapeutic measures can be adopted and evaluated to compare the level of care with international standards and minimize the gaps and bring them closer to standard values.
2. This study shows that the recovery of health-related quality of life already starts at ICU discharge so that rehabilitation programs should start early. As role limitations due to emotional and physical problems remained impaired at the 6-month follow-up, specific interventions directed toward these dimensions of health-related quality of life may help to improve quality of life following ICU discharge.

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