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PSYCHOLOGICAL REPERCUSSION IN MECHANICALLY VENTILATED AND NON-VENTILATED PATIENTS DURING CRITICAL CARE HOSPITALIZATION

A Prospective Observational Assessment and Evaluation Of Delirium By Richmond Agitation-Sedation Scale

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Abstract: Mechanical ventilation associated with delirium is the most commonly reported repercussion in intensive care unit patients, characterized by hypoxia, inflammatory storm and sometimes due to sedatives. The most common types of delirium in these cohort patients are hypoactive and mixed-type of delirium which develops in 2-24 hours from admission. Delirium is known to develop due to an imbalance in the synthesis, release, and inactivation of some neurotransmitters, specifically by acetylcholine deficiency and dopamine activation. Delirium usually presents as a group of symptoms with an acute onset and a fluctuating course which have been categorized into cognitive and behavioral groups. This is a prospective observational cohort study conducted at Gleneagles Aware Global Hospitals, L.B Nagar, Hyderabad for a study period of six months. 200 patients admitted with the hospitalization history of more than 24 hours in critical care units were enrolled as study population. Patient data collection form, contains the socio-demographic details of the patients and Observational study Informed Consent form was prepared for patients understanding for agreeing to participate in the study. In this study, out of the 200 study population 133 patients were not ventilated during the course of therapy in the ICU based on current disease state (66.5%) in which 25 developed mild, 22 developed moderate, 14 developed severe type of delirium and 72 were assessed to be non-delirious. Out of 67 ventilated patients based on current therapy in the ICU (33.5%), 8 developed mild, 13 developed moderate, 41 developed severe type of delirium and 5 were assessed to be non-delirious and from the P-value <0.0001, there is significant correlation between mechanical ventilation due to current disease status and development of delirium in ICU. Mechanically ventilated patients were assessed (92.5%) to be at greater risk of developing delirium compared to that are not ventilated. Ventilation is clinically significant (P-value <0.0001) when correlated to delirium, indicating ICU patients are at risk of developing delirium which is temporary within the ICU during the course of hospitalization (resolves with relevant patient orientated management).

Index Terms - Delirium, ICUS, mechanical ventilation, prospective, observational, evidence-based study, CAM-ICU, RASS, intensive care unit, critical care, terminal care, dexmedetomidine, antipsychotics, haloperidol

I. INTRODUCTION

The intensive care unit (ICU) syndrome is a range of psychological reactions leading to organic brain dysfunction, including fear, anxiety, depression, hallucinations, fluctuating levels of consciousness and delirium. ICU syndrome could be a temporary disorder in which the patient experiences a cluster of significant psychological symptoms, which can be within the sort of reversible mental illness, delirium or acute brain failure [1]. Delirium is the most common repercussion in critically ill patients that is associated with clinical outcomes such as increased mechanical ventilation days, duration of hospitalization, irreversible cognitive impairment, post-discharge monitoring episodes/criteria, and mortality. However, potential pharmacologic agents such as antipsychotics, dexmedetomidine and non-pharmacologic therapies are known to reduce delirium and improve its associated outcomes in the critically ill patients. The relationship between mechanical ventilation and delirium has been demonstrated to be directly proportional in the critically ill patients; that is the onset is hypothesized due to an imbalance in neurotransmitters and their altered metabolism. A better exploration is required in the aspects of mechanism & factors that affect the hypoxic conditions (mechanical ventilation) and delirium, which can be implemented in the development of new methods for preventing and control of aggravating outcomes in the critically ill patients [4].

The RASS (Richmond Agitation Sedation Scale) contains 2 levels, each denoting a state of response that is voice (score -1 to -3) and touch (score -4 & -5). The scores are allotted based on the condition of the patient that is +4 combative, +3 very agitated, +2 agitated, +1 restless, zero alert and calm, -1 drowsy, -2 light sedation, -3 moderate sedation, -4 deep sedation, and -5 unarousable (unconscious). The

scale can be rated within 1-2 minutes from observation. The score zero indicates the patient is normal, any score greater than or equal to 3 indicates to proceed to the CAM-ICU scale.

The Richmond Agitation–Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behaviour toward staff
+2	Agitated	Frequent non purposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

1. Observe patient. Is patient alert and calm (score 0)?
- Does patient have behavior that is consistent with restlessness or agitation (score +1 to +4 using the criteria listed at the Richmond Agitation–Sedation Scale table, under Description)?
2. If patient is not alert, in a loud speaking voice state patient's name and direct patient to open eyes and look at speaker. Repeat once if necessary. Can prompt patient to continue looking at speaker.
- Patient has eye opening and eye contact, which is sustained for more than 10 seconds (score-1).
- Patient has eye opening and eye contact, but this is not sustained for 10 seconds (score -2).
- Patient has any movement in response to voice, excluding eye contact (score -3).
3. If patient does not respond to voice, physically stimulate patient by shaking shoulder and then rubbing sternum if there is no response to shaking shoulder.
- Patient has any movement to physical stimulation (score -4).

Table 1: RASS worksheet for delirium assessment

The most widely used scale for assessing delirium in critically ill patients is CAM-ICU which can be used at beside in nonverbal mechanically ventilated patients44. Four main features that are important for assessing delirium in CAM-ICU are:

1. Feature-1: Acute Onset or Fluctuating Course
2. Feature-2: Inattention
3. Feature-3: Altered level of Consciousness
4. Feature-4: Disorganized Thinking**.**

The most widely used scale for assessing delirium in critically ill patients is Confusion Assessment Method for Intensive Care Unit (CAM-ICU) which can be used at beside in nonverbal mechanically ventilated patients44. Four main features that are important for assessing delirium in CAM-ICU are: Acute Onset or Fluctuating Course, Inattention, altered level of Consciousness, Disorganized Thinking. Few studies indicate different sensitivities for the CAM-ICU. This difference in sensitivities can be illustrated by a wide range of heterogeneity seen in the patients included in the study but mainly by a different level of training and experience among the assessors involved in the reviews. Thus, it is difficult to demonstrate with what efficacy these instruments work without adequate preparation, but it is sensible to state that a considerable proportion of critically ill patients with delirium remain undiagnosed if these instruments are applied without proper training to the health care providers. In recent times, two systematic reviews evaluated the accuracy of CAM-ICU

[11,12] and concluded that it is an accurate instrument for the diagnosis of delirium in critically ill patients. However, in the only study which was conducted in a non-research setting, most of the delirious patients were not detected by CAM-ICU [11,13].

CAM-ICU Worksheet

Feature 1: Acute Onset or Fluctuating Course	Score	Check here if Present
Is the patient different than his/her baseline mental status? OR Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e., RASS/SAS), GCS, or previous delirium assessment?	Either question Yes →	☐
Feature 2: Inattention		
Letters Attention Test (See training manual for alternate Pictures) Directions: Say to the patient, *"I am going to read you a series of 10 letters. Whenever you hear the letter 'A,' indicate by squeezing my hand."* Read letters from the following letter list in a normal tone 3 seconds apart. S A V E A H A A R T or C A S A B L A N C A or A B A D B A D A A Y **Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A."**	Number of Errors >2 →	☐
Feature 3: Altered Level of Consciousness		
Present if the Actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	☐
Feature 4:Disorganized Thinking		
Yes/No Questions (See training manual for alternate set of questions) 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does one pound weigh more than two pounds? 4. Can you use a hammer to pound a nail? **Errors are counted when the patient incorrectly answers a question.** Command Say to patient: "Hold up this many fingers" (Hold 2 fingers in front of patient) "Now do the same thing with the other hand" (Do not repeat number of fingers) *If the patient is unable to move both arms, for 2nd part of command ask patient to "Add one more finger" **An error is counted if patient is unable to complete the entire command.**	Combined number of errors >1→	☐

Overall CAM-ICU Feature 1 plus 2 and either 3 or 4 present = CAM-ICU positive	Criteria Met →	☐ CAM-ICU Positive (Delirium Present)
	Criteria Not Met →	☐ CAM-ICU Negative (No Delirium)

Table 2: CAM-ICU worksheet for delirium assessment

Epidemiology:

The medical practitioner ought to take into account delirium, or acute central nervous system pathology, as the brain's type of "organ pathology." Delirium is very common in ICU patients because of factors like comorbidity, critical ill health, and iatrogenesis. This complication of hospital stay is very risky in older persons and has associated with prolonged hospital stays, institutionalization, and death. Neurological pathology compromises the patient's ability to be off from mechanical ventilation or attain full recovery and independence [5]. It postulated that aspects of the intensive care unit, such as sleep deprivation and sensory overload or monotony, are causes of the syndrome [1]. In summary, an intensive care unit psychopathy doesn't develop in all patients. Instead, several patients are in danger of hypoactive, hyperactive, or mixed hypoactive and hyperactive delirium [3].

Etiology:

1. Uncontrollable pain in the ICU experienced by the patients.
2. Critical illness – The severity of illness, pathophysiology of disease or traumatic incident, the amount of stress a patient experiences during an illness/disease can cause a wide variety of psychological symptoms.
3. Infection-related fever and toxins in the body.
4. Metabolic disturbances – electrolyte imbalances – specially altered serum sodium levels, elevated metabolic enzymes and hypoxia.
5. Heart failure (inadequate cardiac output).
6. Drug reaction or side effects – Various new medications typically administered to the patient's in the hospital or ICU.
7. Dehydration.
8. Post-operative outcomes.

Pathophysiology:

In a study, it was found that the delirium in the ICU patients who are mechanically ventilated is somehow related to altered levels of tryptophan [16]. However, it is also possible that production of other metabolites of tryptophan – kynurenine, leads to a pathway that results in neurotoxins predisposing to delirium [17]. In patients who are more prone to delirium, i.e., elderly and those with pre-existing neurological diseases, it was found that quicker central nervous system response to inflammatory mediators will be present [18]. On the contrary, declining levels of tryptophan (Figure 1) which is an amino acid that crosses Blood Brain Barrier and a precursor to neurotransmitters – serotonin and melatonin, are associated with delirium in postoperative patients older than 50 years [6]. In a study, it was found that the delirium in the ICU patients who are mechanically ventilated is somehow related to altered levels of tryptophan [7]. However, it is also possible that production of other metabolites of tryptophan – kynurenine, leads to a pathway that results in neurotoxins predisposing to delirium [8] In patients who are more prone to delirium, i.e., elderly and those with pre-existing neurological diseases, it was found that quicker central nervous system response to inflammatory mediators will be present [9].

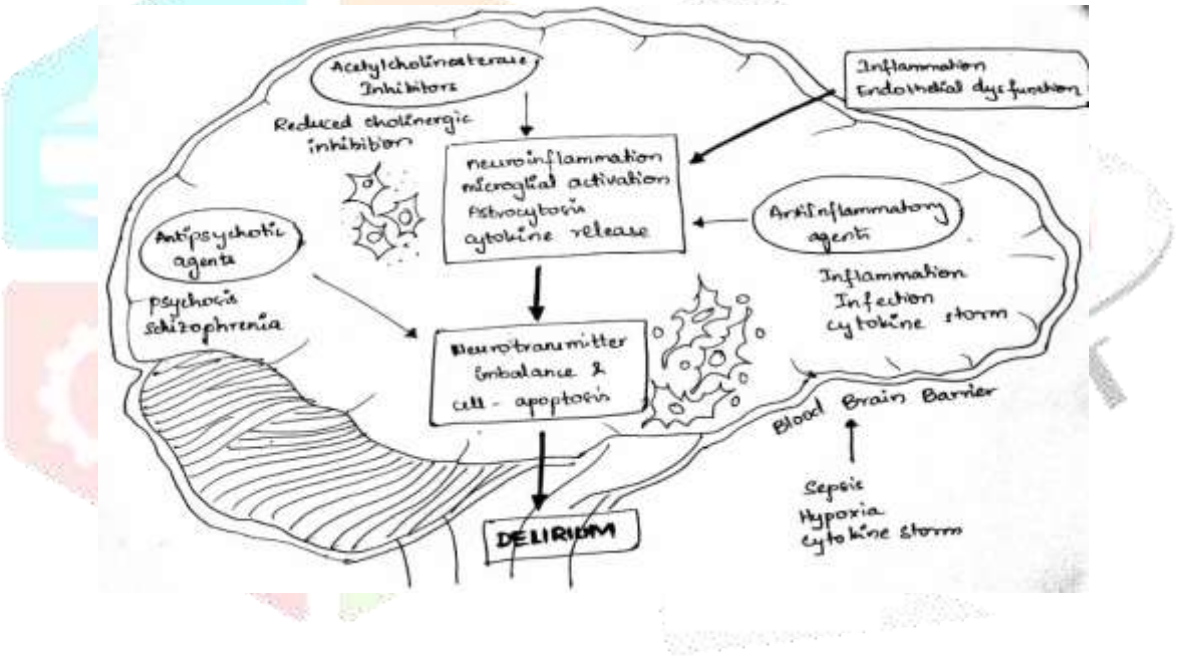

Figure 1: Brief diagrammatic representation of Mechanical ventilation and delirium pathophysiology

Clinical manifestations:

Delirium usually presents as a group of symptoms with an acute onset and a fluctuating course. These symptoms have been categorized into cognitive and behavioral groups. Cognitive symptoms include disorientation, inability to assist attention, diminished visuospatial ability, altered level of consciousness and impaired short-time memory. Behavioral symptoms include disturbed sleep-wake cycle, hallucinations, irritability, and delusions [10].

Pharmacotherapy:

Pharmacological therapy in the treatment of delirium usually involves the administration of haloperidol. However, the efficacy to treat delirium in the ICU by using haloperidol must be studied more through placebo-controlled trials. As an alternative for the therapy of delirium, second-generation antipsychotics came into view and had a better safety profile. Dexmedetomidine, a highly selective alpha-2 adrenergic agent, may be used as an adjunctive for delirious patients in the ICU. Sedatives have the potential to manage the delirium [19]. In an observational cohort study, it was found out that lorazepam is an independent risk factor for the development of delirium whereas other sedatives had no direct relationship with delirium [21]. In a randomized, double-blind study, chlorpromazine, haloperidol or lorazepam are used in the treatment of 30 hospitalized AIDS patients with delirium. In contrast, treatment with haloperidol or chlorpromazine resulted in remarkable improvement in the symptoms of delirium and low incidence [i]of its side effects, whereas treatment with lorazepam had no growth from delirium, instead developed treatment-related adverse effects [20].

Non-pharmacological Management:

Non-pharmacological approaches, such as physical and occupational therapy, decrease the duration of hospital and ICU stay and also provide better management of delirium and hence should be encouraged. The ultimate goal is to correct any imbalances, restore patient's health, and bring them back to normal as quickly as possible. To prevent ICU syndrome, several critical care units are: Providing periods for sleep, Using more liberal visiting policies, Preventing the patient from unnecessary excitement, Orienting the patient to date, time and place, Asking the patient if there are any concerns, Communicating with the family to obtain information regarding cultural and religious beliefs, Coordinating ICU lights with the normal day-night cycle, Monitoring patient's fluid and nutrition status, Reorientation methods, Avoiding physical restraints correction of sensory deficits, Behavior modification, Usage of ear plugs in prevention of agitation induced by instrumental beeping and sounds, Psychiatric consultation (if required).

II. OBJECTIVE

To assess, evaluate and compare the delirium epidemics in the mechanically ventilated patients and non-ventilated patients in a tertiary care hospital, specifically in the critically ill patients. To evaluate and provide management approaches to overcome this repercussions in the ICU settings and to achieve better therapeutic outcomes.

III. METHODOLOGY

This is a prospective observational cohort study conducted at Gleneagles Aware Global Hospitals, L.B Nagar, Hyderabad. for a study period of six months. 200 patients admitted with the hospitalization in the Intensive Critical Care Unit, Medical Intensive Care Unit, Cardiac Intensive Care Unit, Respiratory Intensive Care Unit were enrolled as study population. Subjects with age limit greater than or equal to 18 years with history of hospitalization into critical care for at least 24 hours were included in the study. Pregnant and lactating women, pediatric patients and patients with history of psychological illness & dysfunctions were excluded from the study. Patient data collection form, contains the socio-demographic details of the patients and Observational study Informed Consent form was prepared for patients understanding for agreeing to participate in the study. The delirium assessment was done using RASS worksheet and CAM-ICU Scale in both mechanically ventilated and non-ventilated patients. Patient relevant data for the study was obtained from patient case records, ICU charts, medication charts, directly from patient/ attenders.

IV. RESULTS AND DISCUSSION

Among 200 patients admitted into the ICU, 67 patients were found to be on ventilation (33.50%), whereas 133 patients were found to be non-ventilated (66.50%) (Table 3, Figure 2).

Ventilation	No. of subjects	% of subjects
NO	133	66.50
YES	67	33.50
TOTAL	200	100.00

Table 3: Distribution of patients based on Ventilation

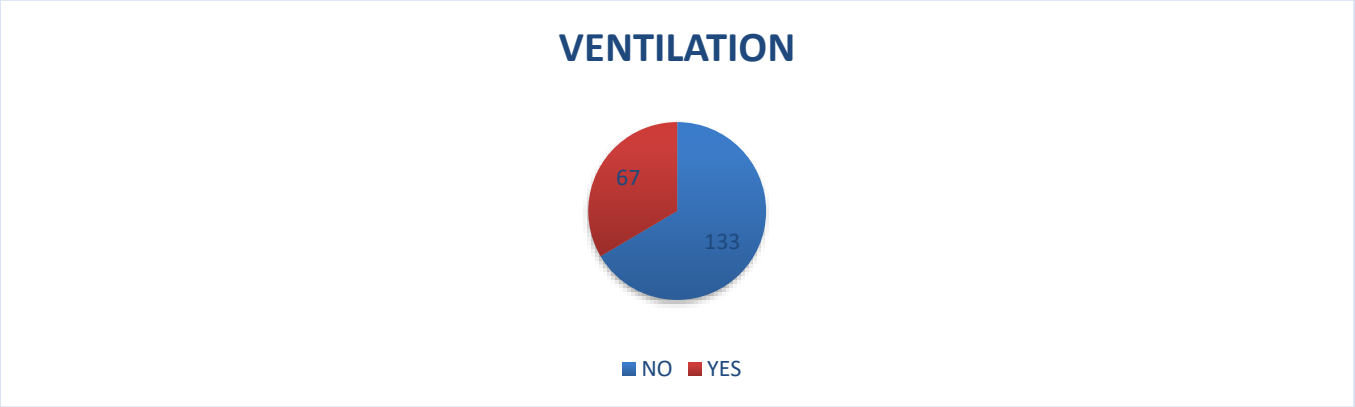

Figure 2: Distribution of patients based on Ventilation

Among 200 patients admitted into the ICU, 19 patients were found to be in between -5 to -4 scale readings (9.50%),whereas 26 patients were found to be in between -3 to -2 scale readings (13.00%), 96 patients were found to be in between -1 to 0 scale readings (48.00%), 48 patients were found to be in between 1 to 2 scale readings (24%), 11 patients were found between 3 to 4 scale readings (5.50%), whereas 0 patients were found between 5 – 6 scale readings (0.00%) (Table 4, Figure 3).

RASS	No. of subjects	% of subjects
-5 to -4	19	9.50
-3 to -2	26	13.00
-1 to 0	96	48.00
1 to 2	48	24.00
3 to 4	11	5.50
Total	200	100.00

Table 4: Distribution of patients according to RASS scoring

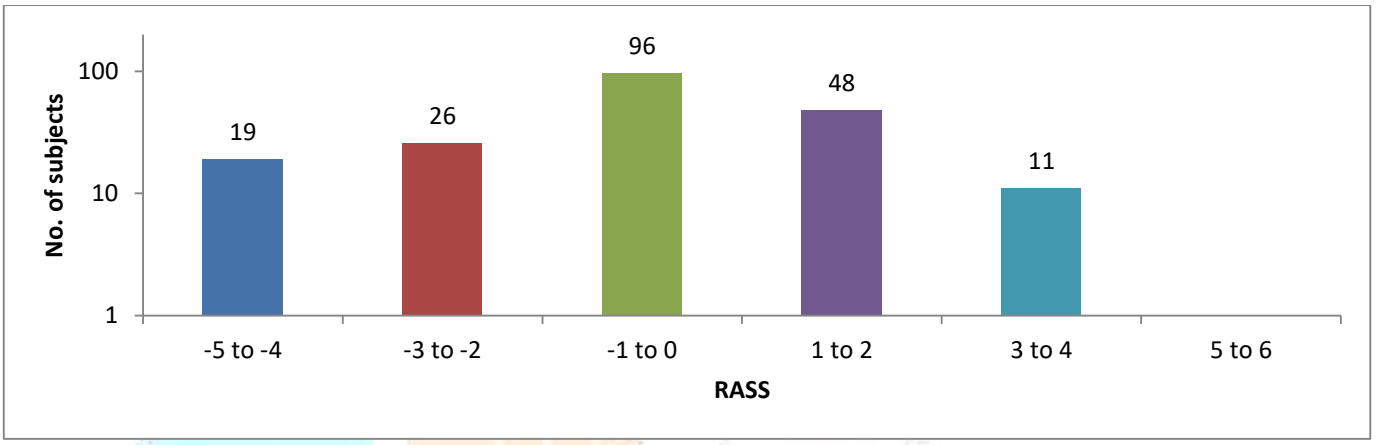

Figure 3: Distribution of patients according to RASS scoring

Among the 200 study population 133 patients were not ventilated during the course of therapy in the ICU based on current disease state (66.5%) in which 25 developed mild, 22 developed moderate, 14 developed severe type of delirium and 72 were assessed to be non-delirious. Out of 67 ventilated patients based on current therapy in the ICU (33.5%), 8 developed mild, 13 developed moderate, 41 developed severe type of delirium and 5 were assessed to be non-delirious. Therefore from the above P-value <0.0001, there is significant correlation between mechanical ventilation due to current disease status and development of delirium in ICU. Mechanically ventilated patients were assessed (92.5%) to be at greater risk of developing delirium compared to that are not ventilated. Ventilation is clinically significant (P-value <0.0001) when correlated to delirium (Table 5, Figure 4).

		Delirious				TOTAL	P-value
		MILD	MODERATE	SEVERE	NO		
Ventilation	NO	25	22	14	72	133	< 0.0001
	YES	8	13	41	5	67	
TOTAL		33	35	55	77	200	

Table 5: Correlation of ICU syndrome with ventilation

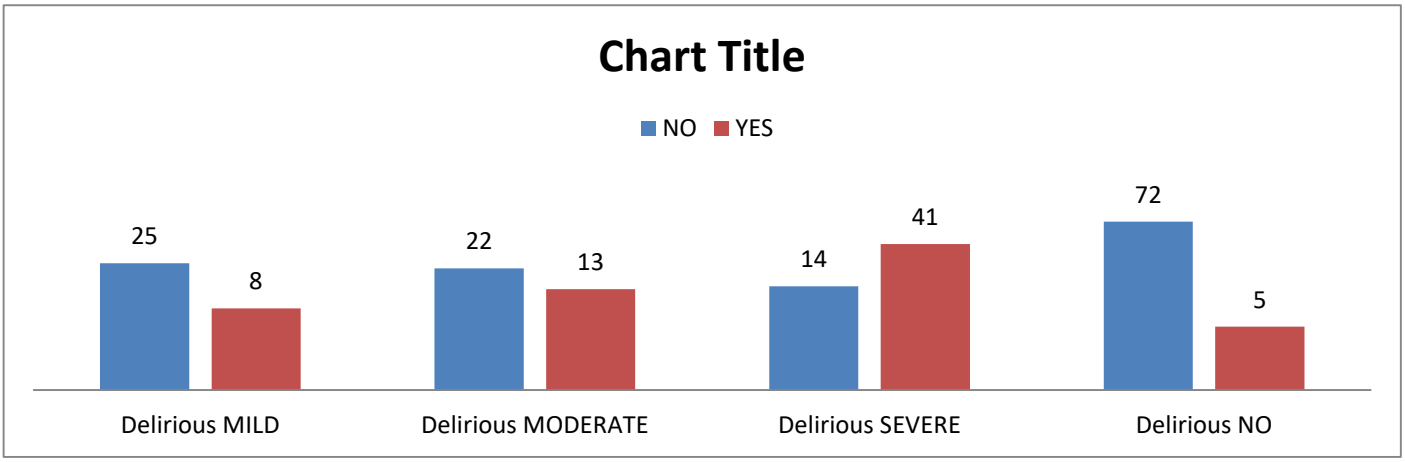

Figure 4: Correlation of ICU syndrome with ventilation

V. CONCLUSION

In this prospective observational cohort study, to assess the prevalence and incidence of delirium in a cohort of medical intensive care unit patients, respiratory intensive care unit patients and High dependency unit patients and its duration in the hospital. The study was carried out in a single center tertiary care hospital in 200 critically ill patients for a period of six months duration. The baseline data was collected from verbal questionnaire and medical chart review. Delirium was assessed and evaluated daily in the wards using the RASS worksheet. Therefore from the above P-value <0.0001, there is significant correlation between mechanical ventilation due to current disease status and development of delirium in ICU. Mechanically ventilated patients were assessed (92.5%) to be at greater risk of developing delirium compared to that as non-ventilated. Ventilation is clinically significant (P-value <0.0001) when correlated to delirium.

VI. CONFLICT OF INTEREST

The authors declare conflicts of interest to none.

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