

A Study among Trauma Patients - Younger Patients with Ventilator Associated Pneumonia Have Poor Outcome Compared to Older Patients, Government General Hospital, Nizamabad

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ABSTRACT

BACKGROUND

Considerable morbidity is associated with ventilator-related pneumonia. Although gender association with outcomes in trauma patients has been debated for years, some authors have shown a difference recently. We wanted to compare results in younger men and women, with those of older men and women in critically ill patients with pneumonia (VAP) combined with ventilator.

METHODS

We reviewed our trauma database between May 2018 and January 2020 for patients with ventilator-associated pneumonia admitted to our Intensive Trauma Care unit. Data obtained included age, accident cause and severity (ISS), vital signs at the time of admission, test results as well as outcome factors including hospital duration of stay, ICU stay and survival. In order to account for the hormonal status, patients were also divided into younger (< 50) and older (about 50). Linear regression and binary logistic regression models were developed to compare younger men with older men and younger women with older women, and investigate the correlation between gender and hospital length of stay (LOS), ICU stay (ICUS) and survival.

RESULTS

42 trauma patients admitted to our trauma intensive care unit during the study period had VAP. The average age with mean ISS of 196 ± 7.8 was 56.9 ± 18.7 years. There were 26 (61.90%) men, 16 (38.10%) women and 38 (90.48%) men who had blunt trauma. The median ICU stay was 15.6 ± 10.6 days and the median overall period of stay in hospital (LOS) was 23.5 ± 13.5 days. Younger men with VAP had longer 26.6 ± 16.6 days in the hospital relative to older men 14.4 ± 5.6 days ($p = 0.061$) and 20.7 ± 14.3 days in the intensive care unit compared to older men 10.9 ± 6.2 days ($p = 0.079$), there was no substantial change of extent of injuries (ISS was 22.8 ± 6.9 vs. 18.90 ± 1.6 , $p = 0.131$).

CONCLUSIONS

In trauma patients with VAP, there was a longer hospital stay for younger people, and a trend for longer ICU stay. Using a broader collection, further research is necessary to evaluate the factors behind the disparity in results.

KEYWORDS

Trauma, Ventilator-Associated Pneumonia, Younger Patients, Hospital Length of Stay

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DOI: 10.18410/jebmh/2020/313

How to Cite This Article:

Ramulu L, Sujay Kumar P, Thirupathi Rao J, et al. A study among trauma patients - younger patients with ventilator associated pneumonia have poor outcome compared to older patients, government general hospital, Nizamabad. J. Evid. Based Med. Healthc. 2020; 7(30),1484-1489. DOI: 10.18410/jebmh/2020/313

*Submission 11-05-2020,
Peer Review 02-06-2020,
Acceptance 14-06-2020,
Published 27-07-2020.*

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BACKGROUND

Trauma and injury result in a systemic reaction of the body marked by an acute non-specific immune response that may be associated with compromised immunity and decreased infection resistance.^{1,2} This can result in multiple organ damage from the initial cascade of inflammation, exacerbated by subsequent sepsis for which the body has become vulnerable.³ Despite major improvements in ventilator-dependent patient care methods and the widespread use of successful procedures to clean respiratory equipment, ventilator-associated pneumonia (VAP) continues to complicate the trajectory of 8 to 28 per cent of mechanical ventilation (MV) patients^{4,5} Pneumonia levels are considerably higher among patients hospitalized in intensive care units (ICUs) compared to those in hospital wards, and the risk of pneumonia for the incubated patient receiving MV is increased 3- to 10-fold^{5,6} VAP remains the most common nosocomial infection in trauma patients needing extended mechanical ventilation⁷ Unlike infections of more frequently involved organs (e.g., urinary tract and skin), for which mortality is small, ranging from 1 to 4 percent, the mortality rate for VAP, described as pneumonia that occurs more than 48 hours after end-tracheal intubation and initiation of MV, ranges from 24 to 50 percent and can reach 76 percent in some particular settings or when lung infection is caused by **h**. Since multiple studies have shown that ventilator-associated pneumonias in different patient populations are a significant cause of morbidity and mortality.⁸⁻¹⁰ It is associated with extended hospital and intensive care unit periods of stay, mechanical ventilation days and nearly 13 percent attributable mortality¹¹ Sex hormones have been shown to be correlated with earlier outcomes; after burn injury: oestrogen is considered to have an inhibitory role in the inflammatory response¹² and an antecedent ovariectomy has been shown to enhance survival¹³ while researchers have not decided on the gender-related disparity in trauma patient outcomes^{14,15} We hypothesized that injured VAP males and females had different outcomes depending on their age. We sought to compare the outcomes of younger (<50) men and women with older (>50) men and women among critically ill patients with ventilator-associated pneumonia (VAP) in order to use this association for clinical purposes.

METHODS

Patient Selection and Identification of Variables

Approval of the institutional committee was taken before the study was started, and written consent was obtained from all participants prior to their inclusion in the study. Knowledge confidentiality was held on time and the fundamental rules of ethics were strictly observed in clinical research. The trauma database was used to perform a retrospective study of trauma patients admitted to the treatment unit of our emergency department, Government

General Hospital, Nizamabad between January 2017 and January 2020 with ventilator-associated pneumonia. The patients came to the hospital as activations of the trauma system and they needed admission to the trauma ICU by duty judgment of the trauma surgeon.

Criteria for Inclusion and Exclusion

All adult trauma patients admitted to trauma ICU during the research time were eligible for inclusion; minors (under the age of 18) were excluded from the research. Data collected included demographics (age, gender, and race), injury mechanism (blunt, penetrating), injury severity score (ISS), presence of ventilator-associated pneumonia (VAP), admission vital signs and laboratory data including International Standardization Ratio (INR), haematocrit, platelet counts, creatinine, and blood transfusion data (red blood cells, fresh frozen plasma, and platelets). Health endpoints included disposal (home, rehabilitation center, hospice, and skilled nursing facility), center length of stay (total number of days in-patient), ICU stay (total number of days in intensive care) and death.

Sample Size

Total patients admitted 998, 956 patients with pneumonia associated with a ventilator, remaining patients with pneumonia associated with a ventilator (N=42), a total of 42 patients admitted to the ICU trauma ward were recruited during the study period.

Statistical Analysis

Descriptive statistics were used to describe populations and clinical features (mean and standard deviation for continuous variables; frequency and percentage for categorical variables). Patients were divided into younger (< 50 years old) and older (approximately 50 years old). The cut-off age was selected to compensate for changes in women's hormonal status, and was also used for men.

Analyses compared younger to older men, and younger to older women, changing the severity score (ISS) for injury. All analyses were performed to compare outcomes (length of stay, ICU days, recovery, and tracheostomy) in patients with ventilator-associated pneumonia (VAP), using the gender and age predictor variables (<50, 50+). T-tests were used to examine ISS as a function of age and sex. The detection of potential age by gender gaps or patterns was of particular interest.

Pearson and point biserial correlations were used to determine predictive factors for these tests. Multiple regression and binary models of logistic regression were used to analyse primary outcomes when accounting for the ISS impacts. Regressions were fit for ISS monitoring and included age (<50, 50+), gender, and age by gender interaction were used as predictor variables using the enter method and a contrast indicator. Follow-up regressions were then conducted independently stratified by age and gender to investigate in greater detail potential differences in age

and gender. All analyses were two-tailed, and $p \leq 0.05$ was considered significant. Data were entered into Epi info system version 7.2.3.1, exported to statistical software SPSS 20.0, origin pro 8.5 and statistical software Origin Pro 7.6 used for analysis. During a diarrheal episode, bi-variate and multivariable analyses were made to determine variables correlated with feeding practices. Throughout the diarrheal case, odds ratio with 95 percent CI was used to assess a statistically relevant correlation between independent variables and feeding activity.

RESULTS

During the research period, forty-two trauma patients admitted to our trauma intensive care unit had related pneumonia in Ventilator. The average age with mean ISS of 19.6 ± 7.8 was 56.9 ± 18.7 years. There were 26 (61.90%) males, 16 (38.10%) were female and 38 (90.48) had blunt trauma. Average ICU stay was 15.6 ± 10.60 days and average total hospital stay (LOS) was 23.5 ± 13.50 days (Table 1).

Demographics	Data
Mean age (Years)	56.9 ± 18.7
Gender, n (%)	
Male	26 (61.90)
Female	16 (38.10)
Injury, n (%)	
Blunt	38 (90.48)
Penetrating	04 (9.52)
Clinical	
ED Systolic BP	140 ± 28
ED Heart rate	96 ± 20
ED Respiratory rate	20 ± 18
Platelet count at admission	220 ± 56
Platelet count at 24 h	178 ± 96
INR at admission	1.2 ± 0.1
INR at 24 h	1.2 ± 0.2
Haematocrit at admission	36.9 ± 5.9
Haematocrit at 24 h	33 ± 7.2
Creatinine at admission	1.4 ± 1.8
Lactic acid on admission	2.9 ± 1.6
Lactic acid at 24 h	1.8 ± 1.3
Packed red blood cells received first 24 h	2.0 ± 0.9
Packed red blood cells transfused (total)	2.4 ± 0.9
ISS (Injury Severity Score)	19.6 ± 7.8
Tracheostomy, n (%)	31 (73.81)
Disposition, n (%)	
Home	4 (9.50)
Rehab. hospital	12 (28.50)
Skilled nursing facility (SNF)	15 (35.71)
Hospice	5 (11.90)
Hospital length of stay (days)	23.5 ± 13.50
ICU length of stay	15.6 ± 10.60
Dead, n (%)	6 (14.29)

Table 1. Demographics, Injuries and Clinical Features of All Patients with VAP, N= 42

Younger men patients with VAP have longer hospital LOS 26.6 ± 16.6 days relative to older men 14.4 ± 5.6 days ($p=0.061$) and longer intensive care unit 20.7 ± 14.3 days compared to older men 10.9 ± 6.2 days ($p= 0.079$), no major change in extent of injuries was found (ISS was 22.8 ± 6.9 vs. 18.90 ± 1.6 , $p= 0.131$). Younger patients have equal duration of stay in hospital, stay in ICU and ISS relative to older women. They had a higher haematocrit value at 24 h (41.8 ± 7.2 vs. 32.8 ± 5.6 , $p= 0.029$) (Table 2).

Separately analysed by sex and age, ICU days trended to longer stays for younger males than older males, $p=$

0.079 ; ICU days were comparable for females of all sexes, $p= 0.782$. Younger men than the elderly mean age, INR at admission, Lactic acid on admission there was no significant difference (<0.001). There was no substantial gap (< 0.001) between younger women and older women of mean age, ED Systolic BP, Lactic acid on entry, Packed red blood cells transfused (total). Adjusted for ISS, younger men with VAP had longer LOS ($p= 0.07$), ICU stays trended to longer stays for younger males but did not achieve statistical significance ($p= 0.05$). There had been no disparity between younger and older people in LOS and ICUS.

Injury types (head, chest, and abdomen) were distributed similarly amongst younger and older men for head injuries, $p= 0.99$, and chest injuries, $p= 0.99$, but younger males were more likely to have abdomen injuries than older men, $p= 0.042$. Younger and older females had similar injury rates for head, $p= 0.548$, chest, $p= 0.999$, and abdomen, $p= 0.42$.

Post-hoc power analyses showed that two-tailed regression analyses of three predictor variables, alpha 0.05, obtained power of 0.81 (survival), 0.28 (tracheostomy), 0.16 (hospital length of stay) and 0.49 (hospital length of stay) for cumulative models with sex association level.

DISCUSSION

We find that hospitalized chronically ill younger men with ventilator-associated pneumonia had slightly longer periods of stay in hospital relative to older men, even after correction for seriousness of injury. Intensive care unit stay trended towards sense among younger men, this was not important in women. This discovery will have consequences for trauma patients with ventilator-associated pneumonia and can help guide the services available in the future. Significant trauma provokes a strong inflammatory reaction. Gender variations in the inflammatory response have been seen in the literature; while some scholars attributed the shift in X chromosome expression to the cell acid-base balance¹⁶ others attributed it to the specific effects of oestrogen and testosterone on the immune response that induced improvements in the innate immune cell responses following injury.¹⁷ This inflammatory reaction has recently been related to the outcomes of patients with seriously ill trauma.^{18, 19}

Testosterone has been seen to play a role in multiple organ systems, but it is also understood to decrease in older people.²⁰ while gender disparities in patient outcomes have been identified in patients suffering from ruptured aortic aneurysms, traumatic brain injury and Achilles tendon injury. Major trials of trauma patients have not demonstrated any difference of gender-assigned outcomes. Duraid et al.,²¹ used the trauma database in a review of 1,259 trauma patients confined to the intensive care unit of the trauma center for two years for 6 months, with ventilator-associated pneumonia. In trauma patients with VAP, there was a longer hospital stay for younger people, and a trend for longer ICU stay.

Variable	Male			Female		
	Younger Men (n= 9)	Older Men (n= 17)	* p	Younger Women (n= 6)	Older Women (n= 10)	* p
Mean age (Years)	35.9 ± 8.9	63.6 ± 10.12	<0.001*	32.6 ± 10.8	68.6 ± 9.8	<0.001*
Injury, n (%)						
Blunt	5 (55.56)	10 (58.82)		6 (100.00)	9 (90.00)	
Penetrating	4 (44.44)	7 (41.18)	0.99*	0 (0.00)	01 (10.00)	0.99
Clinical						
ED Systolic BP	141 ± 18	136 ± 24	0.481	116 ± 14	154 ± 21	<0.001*
ED Heart rate	79 ± 9	89 ± 13	0.031	110 ± 16	103 ± 19	0.445
ED Respiratory rate	18 ± 4	16 ± 3	0.211	22 ± 7	16 ± 2.8	0.092
Platelet count at admission	219 ± 92.6	201.6 ± 89.2	0.651	196.6 ± 42.3	206.6 ± 52.8	0.684
Platelet count at 24 h	164.2 ± 42.9	173.2 ± 58.6	0.66	182.3 ± 32.3	142 ± 48.9	0.068
INR at admission	0.9 ± 0.1	1.2 ± 0.2	<0.001*	1.1 ± 0.06	1.13 ± 0.25	0.724
INR at 24 h	1.3 ± 0.2	1.1 ± 0.1	0.018	1.1 ± 0.04	1.10 ± 0.03	0.99
Haematocrit at admission	31.8 ± 6.1	29.6 ± 0.2	0.311	40.6 ± 6.9	36.2 ± 4.8	0.207
Haematocrit at 24 h	28.6 ± 4.8	26.7 ± 3.5	0.314	41.8 ± 7.2	32.8 ± 5.6	0.029
Creatinine at admission	1.0 ± 0.01	1.0 ± 0.02	0.99	0.5 ± 0.01	1.8 ± 0.1	<0.001*
Lactic acid on admission	1.0 ± 0.3	2.7 ± 0.5	0.069	1.8 ± 0.1	1.8 ± 0.1	0.99
Lactic acid at 24 h	2.1 ± 0.2	1.9 ± 0.3	0.055	-	1.1 ± 0.1	<0.001
Packed red blood cells received first 24 h	3.2 ± 0.5	2.5 ± 1.2	0.048	0.00 ± 0.00	0.5 ± 0.6	0.029
Packed red blood cells transfused (total)	3.8 ± 1.8	2.6 ± 1.4	0.105	0.00 ± 0.00	0.5 ± 0.3	<0.001*
ISS (Injury Severity Score)	22.8 ± 6.9	18.9 ± 1.6	0.131	20.8 ± 2.42	15.6 ± 4.8	0.012
Tracheostomy n (%)	1 (11.11)	4 (23.53)	0.63	1 (14.29)	3 (30.00)	0.60
Disposition, n (%)						
Home	3 (33.33)	2 (11.76)		0 (0.00)	0 (0.00)	
Rehab. hospital	4 (44.44)	3 (27.27)		4 (66.66)	7 (70.00)	
Skilled nursing facility (SNF)	1 (11.11)	6 (54.54)		1 (16.66)	2 (20.00)	
Hospice	0 (0.00)	2 (18.18)	0.224	0 (0.00)	0 (0.00)	0.126
Hospital length of stay (days)	26.6 ± 16.6	14.4 ± 5.6	0.061	32.6 ± 18.6	21.9 ± 3.9	0.22
ICU length of stay	20.7 ± 14.3	10.9 ± 6.2	0.079	12.8 ± 7.8	13.9 ± 6.9	0.782
Dead, n (%)	1 (11.11)	4 (23.53)	0.62	1 (14.29)	1 (10.00)	0.99

Table 2. Demographic, Injury, and Clinical Characteristics, of Male and Female Trauma Patients with VAP

* P-value is result of t-test and chi-squared or Fisher's exact tests for continuous and categorical variables, respectively

In a survey of 22,332 trauma patients admitted to trauma centers in Pennsylvania over two years, Gannon et al.¹⁶ found that female gender had little effect on mortality when stratified for ISS and age, and Magnotti et al.,¹⁷ found that gender was not correlated with mortality in a longitudinal review of trauma patients over ten years. Both studies did not specifically look at VAP patients and did not study differing age groups.

Rello et al.,²² and others found that male gender was independently associated with the development of VAP in a multiple logistic regression analysis, and Sharpe et al.,²³ found that females developed less VAP but experienced increased mortality. Many scholars reported significant gender differences in pneumonia incidence,^{24, 25} while testosterone is known to have anti-inflammatory properties and to decrease with age²⁶ in this sample, seriously injured men younger than 50 years of age with ventilator-associated pneumonia had considerably longer hospital stay than older men irrespective of extent of injury and had a tendency towards longer ICU stay. On the other hand, women younger than 50 years of age, along with those older than 50 years of age, had no slightly higher ISS, obtained comparable amounts of packed red blood cells, had similar levels of lactic acid, had no different duration of stay in hospital or ICU. We didn't have enough patients in the category of less than 50 to demonstrate a disparity in outcomes between the two. To the best of our understanding, this is the first research that describes outcome discrepancies between different age groups

Although younger men with ventilator-associated pneumonia had no greater degree of injury or a substantial differential in injury cause relative to older men, they had more abdominal injuries. This could have contributed to the noted length of stay in these patients and the intensive care

unit. There was no difference between younger and older women in the forms of injuries reported.

While hospitals have recorded extended cycles of reduced ventilator-associated pneumonia levels and even VAP-free times in the past²⁷⁻²⁹ recognizing a patient demographic at risk for worse outcomes (younger men) may help guide the treatment and services provided to this community in the future and thereby enhance their outcome. Larger longitudinal trials will help determine the impact of these patients' identity and hormone status on outcomes.

Our clinical trial makes the point that when healing from a VAP, oestrogen may be a preventive factor. Present oestrogen laboratory research highlights beneficial effects on cytokine production, neutrophil chemotaxis, heat shock protein expression, and post-shock and sepsis regeneration of organ function^{30,31} In our longitudinal research, the main conclusion is that, at the time of trauma, age and sex correlate with hormone level (oestrogen level) in patient. A retrospective research evaluating the amount of testosterone at the time of entry will help determine the relationship between the duration of stay and the amount of hormones. In fact, we do not take into account the differing levels of oestrogen at various menstrual periods, or the amounts of oestrogen correlated with an obesity / fat market. Our research supports the hypothesis that oestrogen can minimize the inflammatory cascade in VAP and thereby reduce the average duration of stay. Although men with VAP have trended toward a longer ICU length of stay, our underpowered research cannot confirm this result. We propose additional work that focuses on the duration of stay of ICU in male VAP patients as a sufficiently driven analysis can achieve significance.

We will also review our analysis in light of its limitations. Second, the research is retrospective, conducted at a single

location, reducing our results' generalizability. Second, the available data were limited to two and a half years in the trauma database and this resulted in a small sample size. Having a greater population would have allowed us to accurately assess the outcomes of women with ventilator-associated pneumonias of different age groups and thereby equate them equally with men's outcomes. Third, other factors unknown to us might have contributed to the difference in outcome of VAP among younger and older men. Fourth, to comply with findings, we did not have levels of hormones for these cases. Fifth: the haematocrit was substantially higher among younger and older women although the severity of the injury and the transfusion was not higher. This will have implications for the treatment of these patients, as the ability to hold oxygen can vary and this will impact the handling and weaning of the ventilator.

CONCLUSIONS

Younger men with ventilator-associated pneumonia had longer stay in hospital and trended to stay longer in the intensive care unit despite having a severity of injury that was not significantly different. No significant differences in outcomes among younger and older women were identified. We need more research to examine these results.

Acknowledgement

Authors would like to thank the department, faculty, and the study participants.

Ethical Approval

The study was approved by the Institutional Ethics Committee of Government General Hospital, Nizamabad, Telangana, India.

Financial or Other Competing Interests: None.

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