Protein-Energy Malnutrition Increases Mortality in Patients Hospitalized With Bacterial Pneumonia: A Retrospective Nationwide Database Analysis

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Abstract

Background

Malnutrition is a less commonly recognized risk factor for various infections. It encompasses both undernutrition or protein-energy malnutrition (PEM) and overnutrition, including obesity. This study aimed to evaluate whether PEM impacts bacterial pneumonia (BP) and, if so, to quantify the degree of impact on inpatient outcomes.

Methods

This was a retrospective cohort study involving adult hospitalizations for BP using the nationwide inpatient database. Outcomes included comparing inpatient mortality, total hospital charges, length of hospital stay, as well as complications from bacterial pneumonia.

Results

The in-hospital mortality for adults with BP was 2.62%. Patients with PEM had a higher adjusted odds ratio (aOR) of inpatient mortality (adjusted odds ratio (aOR): 2.31, 95% confidence interval (CI): 2.14 - 2.48, p<0.001) as compared to non-PEM patients. PEM was also associated with higher odds of sepsis (aOR: 2.24, 95% CI: 2.04 - 2.46, p<0.001), septic shock (aOR: 3.29, 95% CI: 2.82 - 3.85, p<0.001), requiring mechanical ventilation (aOR: 2.51, 95% CI: 2.31 - 2.71, p<0.001), requiring vasopressors (aOR: 2.90, 95% CI: 2.20 - 3.83, p<0.001), acute respiratory distress syndrome (ARDS) (aOR: 1.63, 95% CI: 1.33 - 2.00, p<0.001), acute kidney failure (AKI) (aOR: 1.24, 95% CI: 1.18 - 1.29, p<0.001), deep vein thrombosis (DVT) (aOR: 1.80, 95% CI: 1.62 - 2.00, p<0.001), and pulmonary embolism (PE) (aOR: 1.25, 95% CI: 1.08 - 1.45, p=0.003).

Conclusion

The study concluded that PEM was an independent mortality predictor for those with BP, with an increased risk of systemic complications, as well as increased healthcare utilization costs.

Categories: Internal Medicine, Infectious Disease, Pulmonology

Keywords: protein energy malnutrition (pem), respiratory bacteria, morbidity and mortality, community acquired pneumonia

Introduction

Community-acquired pneumonia (CAP) is defined as an acute infection of the lung parenchyma acquired outside of the hospital. In the United States, pneumonia accounts for over 1.2 million emergency room visits annually [1]. Risk factors for pneumonia include older age, diabetes mellitus, chronic lung diseases (e.g., asthma, chronic obstructive pulmonary disease, bronchiectasis), heart failure, smoking, and alcohol use. CAP may have bacterial or viral causes [2].

Malnutrition is a less commonly recognized risk factor for various infections. It encompasses both undernutrition or protein-energy malnutrition (PEM) and overnutrition, including obesity. Malnutrition has been reported to increase the risk of infection and impacts the hospital outcomes of various disease conditions [2-9]. The World Health Organization (WHO) estimates that 462 million adults have PEM [10]. Diagnostic criteria have been set forth by the Academy of Nutrition and Dietetics (Academy) and the American Society for Parenteral and Enteral Nutrition (ASPEN), which defines PEM as two or more of the following: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, a localized or generalized fluid accumulation that may mask weight loss, and diminished functional status as measured by handgrip strength [11]. PEM in the adult population has been shown to increase health care utilization, with longer hospital stays and poor functional outcomes [12].

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There is a paucity of large population-based studies on the effect of PEM on bacterial pneumonia. Hence, this study aimed to evaluate whether PEM impacts bacterial pneumonia (BP) and, if so, to quantify the degree of impact on inpatient outcomes.

**Materials And Methods**

**Design and data source**

This was a retrospective cohort study involving adult hospitalizations principally for bacterial pneumonia (BP) in the US in 2016 and 2017. Data were obtained from the Nationwide Inpatient Sample (NIS) database. The NIS is a database of hospital inpatient stays derived from billing data submitted by hospitals to statewide data organizations across the US, covering more than 97% of the U.S. population [13]. It approximates a 20% stratified sample of discharges from U.S. community hospitals, excluding rehabilitation and long-term acute-care hospitals. This dataset is weighted to obtain national estimates [14]. The database was coded using the International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System (ICD-10-CM/PCS). The NIS has primary and secondary diagnostic codes corresponding to the principal reason for admission and all other discharge diagnoses, respectively.

**Study population**

We queried the NIS 2016 and 2017 databases for patients 18 years and above who had a principal discharge diagnosis of BP. From the literature review, prior studies utilized ICD-10 codes for BP, including J13, J14, and J15 [15]. This cohort was divided based on the presence of a secondary discharge diagnosis of PEM.

**Outcome measures**

Inpatient mortality between non-PEM and PEM with BP groups was assessed as the primary outcome. Secondary outcomes assessed included odds of sepsis, septic shock, acute hypoxic respiratory failure (ARF), acute respiratory distress syndrome (ARDS), non-ST segment elevation myocardial infarction (NSTEMI), acute kidney failure (AKI), deep vein thrombosis (DVT), pulmonary embolism (PE), cerebrovascular accident (CVA), need for mechanical ventilation, vasopressors, as well as mean length of hospital stay (LOS) and mean total hospital charges (THC).

**Statistical analysis**

We analyzed the data using Stata® Version 16 software (StataCorp, Texas). The proportions of comorbid diseases and baseline characteristics were compared using chi-squared tests. Multivariate regression analysis was done to adjust for possible confounders while calculating the primary and secondary outcomes. These were obtained from prior related studies reviewed and included variables from the validated pneumonia severity index [16]. A univariate screen was done to further confirm these factors affected outcomes with variables having a p-value less than 0.2 included in the multivariate analysis [17-20]. The threshold for statistical significance was 0.05.

**Ethical considerations**

The NIS database lacks patient identifiers and contains only retrospective data. Hence, this study was exempt from Institutional Review Board approval.

**Results**

**Patient characteristics**

Table 1 contains patient and hospital characteristics of hospitalizations involving adults with BP. A total of 1,256,109 hospitalizations were studied. Compared to non-PEM patients, those with PEM had an older mean age (71.8 vs 68.4 years, p<0.001) with a lower proportion of women (51.0 vs 53.3%, p<0.001). Patients with PEM had higher proportions of CKD (18.8 vs 16.9%, p<0.001), chronic obstructive pulmonary disease (COPD) (37.5 vs 31.5%, p<0.001), and anemia (46.8 vs 27.1%, p<0.001). However, they had lower proportions of hypertension (56.1 vs 42.6%, p<0.001), diabetes (24.0 vs 31.6%, p<0.001), and dyslipidemia (51.6 vs 37.4%, p<0.001).

| Variable          | PEM %     | Without PEM % | p-value |
|-------------------|-----------|---------------|---------|
| N= 1,236,109      | n= 86,585 (7.0) | n= 1,149,524 (93.0) |         |
| Patient characteristics |           |               |         |
| Age, mean years   | 71.8      | 68.4          | <0.001  |
| Women             | 51.0      | 53.3          | <0.001  |
| Racial distribution |          |               | <0.001  |
| Category          | 2020 (%) | 2021 (%) |
|------------------|----------|----------|
| White            | 71.0     | 71.8     |
| Black            | 12.2     | 11.8     |
| Hispanic         | 7.2      | 7.9      |
| Others           | 9.6      | 8.5      |
| Insurance type   |          | <0.001   |
| Medicaid         | 75.7     | 69.2     |
| Medicare         | 10.4     | 10.9     |
| Private          | 12.3     | 16.9     |
| Uninsured        | 1.6      | 3.0      |
| Charlson Comorbidity Index score |          | <0.001   |
| 0                | 10.3     | 17.3     |
| 1                | 22.0     | 25.7     |
| 2                | 19.6     | 19.5     |
| ≥3               | 48.1     | 37.5     |
| Median annual income in patient’s zip code, US$ |          | 0.013   |
| 1-43,999         | 33.4     | 33.1     |
| 44,000-55,999    | 26.6     | 28.0     |
| 56,000-73,999    | 22.7     | 22.1     |
| ≥74,000          | 17.2     | 16.8     |
| Co-morbidities   |          | <0.001   |
| Hypertension     | 36.1     | 42.6     |
| Diabetes         | 24.0     | 31.6     |
| Smoking history  | 43.2     | 42.0     |
| CHF              | 25.9     | 25.0     |
| CKD              | 18.8     | 16.9     |
| Dyslipidemia     | 31.6     | 37.4     |
| Chronic IHD      | 24.4     | 25.4     |
| Prior CVA        | 3.7      | 2.6      |
| COPD             | 37.5     | 31.5     |
| Oxygen dependent | 10.6     | 8.6      |
| History of malignancy | 24.8     | 12.0     |
| Anemia           | 46.8     | 27.1     |
| Hospital characteristics |      | <0.001   |
| Hospital region  |          |         |
| Northeast        | 15.5     | 17.9     |
| Midwest          | 25.1     | 24.3     |
| South            | 40.1     | 41.9     |
| West             | 19.3     | 15.9     |
Outcomes in patients with PEM

The in-hospital mortality for adults with BP was 2.62%. Patients with PEM had a higher adjusted odds ratio (aOR) of inpatient mortality (aOR: 2.31, 95% confidence interval (CI): 2.14 - 2.48, p<0.001) as compared to non-PEM patients. PEM was also associated with higher odds of sepsis (aOR: 2.24, 95% CI: 2.04 - 2.46, p<0.001), septic shock (aOR: 3.29, 95% CI: 2.82 - 3.85, p<0.001), requiring mechanical ventilation (aOR: 2.51, 95% CI: 2.31 - 2.71, p<0.001), requiring vasopressors (aOR: 2.90, 95% CI: 2.20 - 3.85, p<0.001), ARDS (aOR: 1.65, 95% CI: 1.33 - 2.00, p<0.001), AKI (aOR: 1.24, 95% CI: 1.18 - 1.29, p<0.001), DVT (aOR: 1.80, 95% CI: 1.62 - 2.00, p<0.001), and PE (aOR: 1.25, 95% CI: 1.08 - 1.45, p=0.003). Patients with PEM also had a significantly longer LOS, as well as higher THC, as compared to non-PEM patients (Table 2).

### TABLE 2: Clinical outcomes in patients with bacterial pneumonia and PEM

*; statistically significant, #; Adjusted mean difference, aOR: Adjusted odds ratio, CI: Confidence interval, ARDS: Acute respiratory distress syndrome, NSTEMI: Non-ST segment elevation myocardial infarction, PEM: Protein-energy malnutrition
Discussion

Risk factors for PEM in adults include age, frailty in institutionalized persons, excessive polypharmacy, general health decline, including physical function, Parkinson disease, constipation, poor or moderate self-reported health status, cognitive decline, which dementia, eating dependencies, poor appetite, basal oral dysphagia, signs of impaired efficacy of swallowing, and institutionalization [21]. Synergism exists between malnutrition and infection, wherein malnutrition increases the risk of infection, and infection can lead to malnutrition. This leads to the formation of a vicious cycle. Our study reveals an increased incidence of chronic medical conditions such as chronic kidney disease, chronic obstructive pulmonary disease, and anemia in patients with PEM.

Our study demonstrated PEM as an independent mortality predictor for those with bacterial pneumonia. The estimated mortality in patients with PEM that are admitted with bacterial pneumonia is over two times higher when compared to those without PEM. Patients with PEM are at a higher risk of complications from bacterial pneumonia, including sepsis, septic shock, acute respiratory distress syndrome, acute kidney injury, deep vein thrombosis, and pulmonary embolism.

Various factors could explain the findings of this study. Malnutrition is the most common cause of secondary immunodeficiency, affecting up to 50% of at-risk populations [22]. Malnutrition affects both cell-mediated and humoral immunity. It leads to a reduction in the number of antigen-presenting-cells, such as B-lymphocytes, Kupffer cells, macrophages, and dendritic cells. The complement system is also affected, limiting the phagocytic function. Severe protein-energy malnutrition in neonates and infants was associated with atrophy of bone marrow and the thymus, resulting in low B and T lymphocytes. Also, there is reduced activation of T-lymphocytes. Changes in the microanatomy of barrier epithelium also led to an increased risk of infection [23].

Our study was based on the NIS administrative database, where the diagnosis was based on ICD-10 codes and not microbiologic confirmation, which may affect the data [24-26]. The number of patients with protein-energy malnutrition may be underrepresented owing to under coding in an acute setting. A patient may have multiple admissions reflected in the NIS. NIS studies cannot determine causation, only potential association. These are important limitations of this study.

Conclusions

PEM is an independent mortality predictor for those with bacterial pneumonia, with an increased risk of systemic complications as well. There is a need for a multidisciplinary approach against malnutrition, which can mitigate the risk, leading to lower mortality, morbidity, and health care expenditure.

Additional Information

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue.
Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.
Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors declare that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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