ORIGINAL ARTICLE

# Effect of Raised Cardiac Troponin Levels on Inpatient Mortality in Patients with Community Acquired Pneumonia

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## Abstract

**Objective:** To ascertain the frequency of raised cardiac troponin level and its association with in-hospital mortality among patients presenting with severe community-acquired pneumonia (CAP) at a public-sector tertiary care hospital in Karachi.

**Methodology:** This prospective, observational study was performed at Jinnah Postgraduate Medical Center, Karachi throughout September 2020 till March 2021 with the approval of the hospital ethics committee. 146 patients who met the diagnostic measures were included. Serum cardiac troponin levels≥0.034 ng/mL were labeled as elevated. A detailed history of patients was taken upon their hospital admission to note down their demographic and clinical features.

**Results:** A total of 146 patients were studied with the majority of age range 46-70 years (n=91, 62.3%). 95 (65.1%) had elevated troponin levels. Age was significantly different among patients with and without elevated troponin levels (p=0.038). 87 (59.6%) patients did not survive and 57 (65.5%) of them had elevated troponin levels. The risk of mortality was greater among patients having elevated troponin levels but it was not statistically significant (OR=1.05, 95% CI: 0.53 – 2.10).

**Conclusion:** The study did not find evidence of a greater likelihood of mortality for patients having elevated troponin levels.

**Keywords:** *Troponin levels, community-acquired pneumonia, in-hospital mortality, cardiac risk, patients' outcomes.*

## INTRODUCTION

Community-acquired pneumonia (CAP) is an acute disease triggered by a lung parenchyma infection acquired outside the hospital premises. Globally it is considered a prominent source of morbidity and mortality particularly in immunocompromised and immunocompetent patients [1]. Worldwide estimates suggest that CAP incidence ranges from 1.5-14 cases per thousand person-years which may be varied by population features, geography and season [2]. A Karachi-based study that was related to seasonal variation in CAP incidence stated that on average 77 cases in a month were reported in the hospital of Karachi [3].

CAP is one of the important bases of hospital admissions and death which imposes a significant healthcare cost and burden. The disease features greatly range from mild cases that may be treated as out-patient to severe cases that require management in ICU settings. Appropriate care with early diagnosis and timely management is highly essential for successful patient outcomes [4].

Recently many researchers showed in their work that cardiac issues are frequent in CAP cases which are linked to severe disease and may also predict disease course [5]. Worldwide the two leading causes of morbidity and mortality, pneumonia and cardiac complication have been seen to coexist in some patients [6]. A reported frequency of coexistence of pneumonia with myocardial infarction (MI) ranges from 2.3-7% [7, 8]. Modern work has proposed that raised troponin levels are frequently observed in severe diseases, even among patients admitted for non-cardiac illness. Furthermore, higher troponin levels have been related to adverse clinical outcomes in such cases [9, 10].

To the best of our information, previous investigations have not examined mortality in patients with severe pneumonia having positive cardiac troponin levels rather evaluated it in severely disease patients. Therefore we aimed to ascertain the frequency of raised cardiac troponin levels and its association with in-hospital mortality among patients presenting with severe community-acquired pneumonia at a public-sector tertiary care hospital in Karachi with an intention to discover the local perspective as there is a scarcity of this data locally. Data from this study will help design interventions with the goal of identifying the severity through regular screening of suspected patients with cardiac troponin levels. Furthermore, data from our study would help health care providers to develop better treatment strategies, hospital administrators to develop more efficient discharge policies, hospital infection control strategies and policymakers to devise plans to counter these factors on a holistic level.

## METHODOLOGY

This prospective, observational investigation was performed at Chest Medicine Department, Jinnah Postgraduate Medical Center (JPMC), Karachi

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throughout September 2020 till March 2021 with the approval of the hospital ethics committee. The prerequisite sample size came out to be 146 patients by taking prevalence of elevated cardiac troponin level 40.9% [11], the margin of error = 8% and a confidence level of 95%. This sample size was calculated using the WHO software. Informed written consent was taken from patients or their attendants before enrolling them into the study. Patients presenting with severe community-acquired pneumonia of either gender of age 20-70 years were involved in the study. Patients with tuberculosis, unstable angina, ST-elevation MI and non-ST-elevation MI, history of hypokalemia, hyperkalemia, hypocalcemia, hypercalcemia, pulmonary embolism, hypo or hyperthyroidism, congestive cardiac failure, asthma, chronic liver disease, COPD and stroke were excluded from this study. Non-probability consecutive sampling technique was used to recruit study participants.

Patients having CURB-65 score (confusion, blood urea >19 mg/dl, respiratory rate> 30/min, blood pressure < 90/60 mm Hg, age> 65 years) ≥3 [12] and developing new pulmonary infiltrate (opacity with or without air bronchogram) on chest radiograph along with the presence of one or more of the following for more than 3 days persistent productive cough for more 3 days; fever (body temperature ≥ 37.8°C) for more 3 days, heart rate >100 beats per minute at presentation or white blood cell count ≥9,000 cells/mm3 were considered as a case of severe community-acquired pneumonia. Serum cardiac troponin levels ≥0.034 ng/mL were labeled as elevated. Patients were labeled as diabetic and hypertensive based on their past medical records or evidence of taking medications against these conditions. Patients who were smoking at least 1 cigarette a day for the last two years were considered smokers.

A detailed history of patients was taken upon their hospital admission to note down their demographic and clinical features. All patients were started with empirical antibiotic therapy as per hospital protocol. Patients' laboratory investigation was done after their admission. Patients were followed during admission and in-hospital mortality due to any cause was recorded. Data were recorded in a pre-designed proforma.

Data were entered into SPSS version 21 for data analysis. Qualitative variables were shown as frequency and percentage. Continuous variables were presented as mean ± standard deviation after evaluating the normality assumption with the Shapiro-wilk test. Chi-square/ Fisher exact test was applied to compare participants' characteristics among two groups of patients. Binary logistic regression was applied to determine the association of study variables with in-hospital mortality and the univariate odds ratio was computed. Effects of variables with p<0.25 and variables of clinical significance were adjusted in the final regression model to compute adjusted odds ratios with a 95% confidence interval. A two-tailed p-value of ≤0.05 was defined as statistically significant throughout the study.

## RESULTS

Data of 146 patients were recorded with a mean duration of 21.72±8.24 hours for severe CAP. The mean age of study participants was 49.14±8.49 years with the majority of age range 46-70 years (n=91, 62.3%). Most of the study participants were males (n=84, 57.5%), employed (n=107, 73.3%), belonging to urban areas (n=137, 93.8%) and had no history of smoking (n=86, 58.9%). 110 (75.3%), 22 (15.1%), 2 (1.4%), 9 (6.2%) and 3 (2.1%) patients were belonging to lower, lower-middle, middle, upper-middle and upper socioeconomic status respectively. Nearly half of the patients were diabetic (n=75, 51.4%) and around one-third were hypertensive (n=47, 32.2%). Almost all of the patients required ICU admission (n=141, 96.6%).

Out of 146 enrolled study subjects, 95 (65.1%) had elevated troponin levels. Table **1** represents the association of participants' characteristics with troponin levels. Age was significantly different among patients with and without elevated troponin levels (p=0.038). Gender (p=0.411), smoking status (p=0.988), coexistence of diabetes (p=0.267) and hypertension (n=0.598) and duration of severe CAP (p=0.089) were not identified as significantly related to troponin levels.

**Table 1:** Comparison of patients' characteristics among patients with and without elevated troponin levels.

| Variables | Groups | Elevated troponin levels | | p-value |
|---|---|---|---|---|
| | | Yes n(%) | No n(%) | |
| Age | 20-45 years | 30(54.5) | 25(45.5) | 0.038 |
| | 46-70 years | 65(71.4) | 26(28.6) | |
| Gender | Male | 57(67.9) | 27(32.1) | 0.411 |
| | Female | 38(61.3) | 24(38.7) | |
| Residence | Urban | 92(67.2) | 45(32.8) | 0.066 |
| | Rural | 3(33.3) | 6(66.7) | |
| Smoking status | Yes | 39(65) | 21(35) | 0.988 |
| | No | 56(65.1) | 30(34.9) | |
| Diabetes | Yes | 52(69.3) | 23(30.7) | 0.267 |
| | No | 43(60.6) | 28(39.4) | |
| Hypertension | Yes | 32(68.1) | 15(31.9) | 0.598 |
| | No | 63(63.6) | 36(36.4) | |
| Duration of severe CAP | ≤7 days | 55(71.4) | 22(28.6) | 0.089 |
| | >7days | 40(58) | 29(42) | |
| ICU admission | Yes | 92(65.2) | 49(34.8) | 1 |
| | No | 3(60) | 2(40) | |

**CAP:** Community-acquired pneumonia, ICU: Intensive care unit

More than half of the patients did not survive during their stay in hospital (n=87, 59.6%) and among them, 57 (65.5%) had elevated troponin levels but the difference in the proportion of mortalities among patients with and without elevated troponin was not significantly different (p=0.890). Table **2** shows a univariate and multivariable association of participants' characteristics with mortality. In univariate analysis, the mortality risk was higher among patients having elevated troponin levels but

**Table 2:** Univariate and multivariable analysis for association of patients' features with in-hospital mortality.

| Variables | Groups | OR (95% CI) | p-value | aOR (95% CI) | p-value |
|---|---|---|---|---|---|
| Age | 20-45 years | 0.56 (0.28 - 1.11) | 0.098 | 0.55 (0.26 -1.15) | 0.110 |
| | 46-70 years | Ref | | Ref | |
| Gender | Male | 0.88 (0.45 - 1.73) | 0.719 | 0.90 (0.45 - 1.81) | 0.767 |
| | Female | Ref | | Ref | |
| Residence | Urban | 0.72 (0.17 - 3.01) | 0.656 | 0.59 (0.13 -2.77) | 0.507 |
| | Rural | Ref | | Ref | |
| Smoking status | Yes | 0.72 (0.37 - 1.42) | 0.346 | 0.74 (0.36 - 1.51) | 0.409 |
| | No | Ref | | Ref | |
| Diabetes | Yes | 0.58 (0.3 - 1.14) | 0.115 | 0.52 (0.26 - 1.05) | 0.067 |
| | No | Ref | | Ref | |
| Hypertension | Yes | 1.30 (0.64 - 2.66) | 0.472 | 1.38 (0.62 - 3.07) | 0.435 |
| | No | Ref | | Ref | |
| Duration of severe CAP | ≤7 days | 1.01 (0.52 - 1.96) | 0.990 | 1.06 (0.53 - 2.14) | 0.866 |
| | >7days | Ref | | Ref | |
| Elevated troponin levels | Yes | 1.05 (0.53 - 2.10) | 0.890 | 1.02 (0.49 - 2.16) | 0.952 |
| | No | Ref | | Ref | |

**CAP:** Community-acquired pneumonia, CI: confidence interval, ICU: Intensive care unit, Ref: Reference category, aOR= adjusted odd ratio, OR=odd ratio,

statistically, it was not significant (OR=1.05, 95% CI: 0.53 – 2.10). The association of elevated troponin levels and mortality was remain non-significant even after adjusting for other covariates such as age, gender, residence, smoking status, diabetes, hypertension and duration of severe CAP.

## DISCUSSION

CAP is a common cause for hospitalization and regardless of antibiotic usage, patients have a substantial risk of dying. Pneumonia and cardiac illness are foremost bases of morbidity and mortality universally, and these illnesses repeatedly co-occur in identical patients [13]. The earlier study stated that raised serum troponin concentration might be an indicator for risk stratification in pneumonia [14]. The frequency of elevated troponin was 65.1% in our study. There is a variation in the reported frequency of raised troponin values in literature. Frencken *et al.* [15], Efros *et al.* [16] and Putot *et al.* [17], demonstrated a prevalence of 85%, 39.1% and 42% respectively. Lee and coworkers conducted a similar study and reported that 58% of patients had detectable troponin levels [11]. The variation in frequency can be due to differences in population, their underlying conditions and health settings.

In our study, we found a statistically substantial difference in age groups among patients having and not having raised troponin values with a higher frequency of older age group among patients with elevated troponin values than patients who did not have raised troponin values. This finding was consistent with other similar studies [11, 16]. Efros *et al.* also reported that patients found to have higher troponin levels had considerably greater rates of underlying diseases such as hypertension, ischemic heart diseases renal diseases, diabetes and other cardiac illnesses (arrhythmias, cardiomyopathy, and heart failure) [16]. Putot *et al.* conducted a similar study to assess whether troponin I is a predictor of cardiac events and death in acute pneumonia patients. He divided the patients into two groups; troponin ≤ 100 ng/L and >100 ng/L and analyzed that patients' age, gender, cardiac triggers like smoking, hypertension, dyslipidemia and diabetes were not considerably unlike among these two groups [18]. In the current studies, two groups of patients also did not differ in terms of underlying diseases.

It is a well-known fact that cigarette smoking is a prominent avoidable basis for cardiovascular-related morbidity and mortality [18]. It has been proposed in numerous investigations that even after doing adjusted analysis for other coronary diseases, current smokers and to some level past smokers are vulnerable to experiencing heart failure [19, 20]. A larger community-based study conducted in the United States reported that cumulatively exposure to cigarettes, evaluated by overall pack-years, was linked with higher natriuretic peptide amount and high sensitivity troponin among ever smokers and established that cigarette smoking was connected with indicators of myocardial wall stress and baseline injury and also with a continual quantifiable rise in these indicators after a follow-up of 15 years [21]. The current study, cross-sectional in nature with limited sample size, did not find an association of smoking with raised troponin levels. Acosta *et al.* conducted a study to determine risk factors of myocardial injury and measurable troponin levels in cases of hypertensive crisis. The authors analyzed that smoking was not associated with troponin levels. However, just like our study, the sample size in their study was also not very large [22].

The current study also studied the impact of raised troponin levels on mortality. Although the literature documents that cardiac troponin is a particular indicator for myocardial injury. However, higher troponin quantity

has been conveyed in various conditions of hospitalized patients other than cardiac illness such as trauma, pulmonary disease, cocaine use, stroke, sepsis, pericarditis and myocarditis [11]. Evaluation of troponin levels has been used as a predictive indicator for all-cause death among suspects of an upset cardiac event [23, 24].

Several pieces of evidence propose a link between the extent of the rise in troponin and death [24, 25]. Usually, it is a prevalent perception among clinicians that patients with higher troponin levels are at higher death risk. In the present study, the risk of mortality was higher among patients with raised troponin levels but statistically, it was not significant. In contrast to our findings, another study conducted in Korea enrolling 152 critically ill pneumonia patients who had no acute coronary syndrome reported that the frequency of mortality was considerably higher for patients with increased troponin levels than patients having normal ranges (38.6% versus 21.9%). This direct link between troponin and death remained statistically significant when controlling was done for other covariates [11]. A multicenter study was conducted in the US to assess the association of increased troponin levels and mortality risk in the elderly population and it was concluded that troponin levels higher than the normal range were associated with 15% higher absolute mortality risk regardless of age [26].

The present study suffers from some serious limitations. Firstly, the sample size of our study was not very large which could impact results. Secondly, hospital length of stay was not recorded as a continuous variable. The presenting features and laboratory investigations such as complete blood count parameters, urea, creatinine, albumin C-reactive protein, *etc.* were not assessed. Further microbiology organisms could also be detected to further compare their distribution among study groups. Echocardiographic findings could also be compared to further understand the relationship. We recommend multi-center studies with a larger sample size to further confirm the association of troponin levels and mortality in our local settings.

## CONCLUSION

The study did not find evidence of a greater likelihood of mortality for patients having elevated troponin levels. However, we recommend cases with increased troponin levels should be evaluated for cardiac risk and modifications should be made in the management plan to lower mortality risk. Since the association was not significant, thereby we suggest replicating this study with larger sample size and addressing other limitations to confirm the association of troponin levels and mortality in our local settings.

## ETHICS APPROVAL

The ethical approval for the study was issued by the Ethical Committee of Jinnah Postgraduate and Medical Center and after acquiring the letter, the study was conducted. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki declaration.

## CONSENT FOR PUBLICATION

Written informed consent was taken from all of the patients who participated in this study

## AVAILABILITY OF DATA

Data sets generated or analyzed during the current study are not made public due to confidentiality. However, data may be shared at a reasonable request to the corresponding author.

## FUNDING

None

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

## AUTHOR'S CONTRIBUTION

Dr. Parshad conceptualized the study. Dr. Parshad and Nausheen Saifullah developed the study protocol. Saima Akhter and Nausheen Saifullah supervised the data collection and entry. Saima Akhter performed data analysis, interpreted and wrote the results. Saima Akhter and Dr. Parshad prepared an initial draft of the manuscript. Nausheen Saifullah and Noureen Durrani critically revised it.

All authors read and approved the manuscript.

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