

Association and outcomes of bacterial infections with acute coronary syndrome; a cross-sectional study from a tertiary care hospital in Pakistan

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Abstract

Objective: To identify the association between acute infection and acute coronary syndrome, and to evaluate the outcomes in such cases.

Method: The cross-sectional, retrospective, analytical study was conducted at the Aga Khan University Hospital, Karachi, from July to December 2020, and comprised data from January to December 2019 of acute coronary syndrome patients aged >18 years. Data related to demographics, comorbidities, smoking status and history of dyslipidaemia. Binary logistic regression was used to explore the association of infections with acute coronary syndrome. Data was analysed using SPSS 26.

Results: Of the 1202 patients with acute coronary syndrome, 189(15.7%) had infection before the coronary event. The mean age of the patients was 68.5±12.4 years, and 97(51.3%) of them were females. Community-acquired pneumonia was found in 105(55.6%) patients, followed by urinary tract infection 64(33.9%) and cellulitis 8(4.2%). For pneumonia, the odds of having non-ST elevated myocardial infarction was 1.1 (95% confidence interval: 0.4-3.0). With urinary tract infections, unstable angina was associated with an odd ratio of 4.2 (95% confidence interval: 1-17.4), and ST elevated myocardial infarction was associated with odd ratio of 3.7 (95% confidence interval: 0.4-31).

Conclusion: Bacterial infections were found to be associated with acute coronary syndrome. Bacterial infections with pneumonia and urinary tract infections showed a higher risk of myocardial ischaemia.

Key Words: Acute coronary syndrome, Bacterial infections, NSTEMI, Pneumonia, STEMI, Urinary tract infections. (JPMA 73: 547; 2023) DOI: 10.47391/JPMA.6576

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Introduction

Acute infection is a broad term that covers infections caused by either bacteria or viruses. It has a significant impact on populations as most of the people acquire some form of infection in their lifetime.¹ Infections were once considered deadly till a few decades ago when treatment for microorganisms was discovered.² Acute coronary syndrome (ACS) is a complex term which includes angina, myocardial ischaemia and myocardial infarction. It had major impact on the health of many individuals and is the world's biggest cause of morbidity and mortality.³ It occurs due to diverse physiological phenomena which include increased myocardial oxygen demands, altered inflammatory activity, disturbed haemodynamic homeostasis and a favourable pro-thrombotic condition.⁴

Acute bacterial infection via a different process triggers myocardial ischaemia. It enhances systemic inflammatory

response, increases cell lineage that promotes thrombosis and induces vasoconstriction. All these events help trigger myocardial infarction.⁴ In 1897, Sir William Osler established the first-ever potential association between acute infection and atherosclerosis. Influenza as a potential trigger for acute cardiac events (ACE) was identified in the early 20th century. But it took many years to identify any relationship between infections and cardiovascular disease (CVD).⁵ In patients with pneumococcal pneumonia, there is a 6-8% increased risk of myocardial infarction.⁶ Several acute infections, including pneumonia⁷, urinary tract infection (UTI)⁸, influenza and viral infections,^{9,10} have reportedly been associated with myocardial infarction.

The current study was planned to identify the association between bacterial infections and ACE in a South Asian setting.

Materials and Methods

The cross-sectional, retrospective, analytical study was conducted at the Aga Khan University Hospital, Karachi, from July to December 2020, and comprised data of ACS patients of either gender aged >18 years who had a bacterial infection three months prior to ACS and who

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admitted between January and December 2019. Exemption was obtained from the institutional ethics review committee (ERC).

ACS is a broad category covering ST-elevated myocardial infarction (STEMI), Non-ST elevated myocardial infarction (NSTEMI) and unstable angina (UA).¹¹ STEMI is defined as a patient having chest pain with elevated cardiac enzymes, and electrocardiographic (ECG) changes showing ST segment elevation.¹² NSTEMI is defined as a patient with chest pain and increased cardiac enzymes without ECG changes, while UA is described as chest pain without elevation in cardiac enzymes and ECG changes.¹³ Data of all patients who had ACS and infection concomitantly was excluded.

The sample size was estimated assuming the prevalence of exposed with outcome 24% and odds ratio (OR) of acquiring ACS after respiratory infections around 6%¹⁴, with a 95% confidence interval (CI) and 90% power of the study. However, to enhance the strength of the study, data of all the cases that met the inclusion criteria was included.

Data collected from patient files related to demographics, comorbidities, smoking status and history of dyslipidaemia. Bacterial infection was labelled on the presence of any of the three criteria: clinical features favouring infection and improvement in symptoms with antibiotics; identified radiological evidence of infection; and cultures growing micro-organisms.¹⁵

Troponin levels, ECG changes and their disease management details were noted. Mortality and length of hospital stay (LOS) were the targetted outcomes.

Data was analysed using SPSS 26. Quantitative variables were expressed as mean and standard deviation (SD), and categorical variables as frequencies and percentages. Binary logistic regression was used to analyse the association of infections with ACS. OR and 95%CI were calculated as appropriate.

Results

Of the 1202 patients with acute coronary syndrome, 189(15.7%) had infection before the coronary event. The mean age of the patients was 68.5 ± 12.4 years, and 97(51.3%) of them were females. Hypertension 154(81.5%) and diabetes 128(67.7%) were the major comorbidities, 7(3.7%) patients were active smokers, dyslipidaemia was found in 6(3.2%), and 86(45.5%) patients had a prior history of

Table-1: Demographic and clinical characteristics of patients (n = 189).

		n	%
Age years	Mean $\pm$ S.D.	68.5 $\pm$ 12.4	
Gender	Male	92	48.7
	Female	97	51.3
Comorbid	Diabetes	128	67.7
	Hypertension	154	81.5
	Prior Coronary Heart Disease	86	45.5
	Stroke	29	15.3
	Obstructive Airway Disease	24	12.7
	Atrial Fibrillation	11	5.8
	Chronic Kidney Disease	53	28
	Thyroid Disorder	9	4.8
	Others*	54	28.5
Smoking	Yes	7	3.7
	No	175	92.6
	Ex-smoker	7	3.7
Dyslipidaemia	Yes	6	3.2
	No	183	96.8

*Other comorbidities included chronic liver disease, dementia, epilepsy, osteoarthritis, bipolar disorder, malignancy, autoimmune disorders. SD: Standard deviation.

heart disease (Table 1).

The history of community-acquired pneumonia (CAP) was found in 105(55.6%) patients, followed by UTI 64(33.9%) and cellulitis 8(4.2%) (Figure). The median duration between infection and ACS was 21 (interquartile range [IQR]: 48 days).

With pneumonia, the odds of NSTEMI were 1.1 (95% CI: 0.4-3.0), while those with UA were 0.3 (95% CI: 0.09-1.5), and those with STEMI were 0.4 (95% CI: 0.07-2.0).

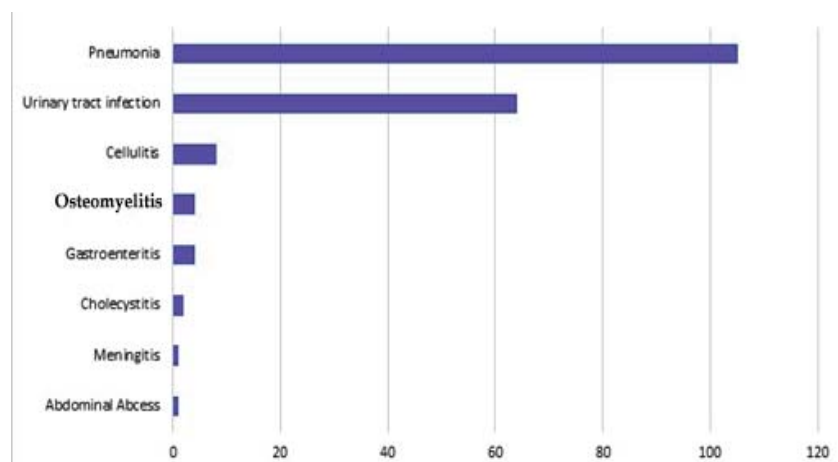


Figure: Infections prior to acute coronary syndrome (ACS)

Table-2: Diagnosis and management of acute coronary syndrome (ACS) and outcomes (n = 189)

		Mean $\pm$ S.D
Troponin I	Initial	3.5 $\pm$ 8.2
	After 6 hours	12.7 $\pm$ 83.3
ECG Changes		n (%)
	ST Elevation	8 (4.2)
	Q-wave	1 (0.5)
	LBBB	1 (0.5)
	Atrial Fibrillation	1 (0.5)
	Nonspecific ST-T Changes	5 (2.6)
ACS Diagnosis	No changes	173 (91.5)
	Unstable Angina	9 (4.8)
	NSTEMI	172 (91%)
	STEMI	8 (4.2)
Management	Medical Management	134 (70.9)
	Percutaneous Intervention	31 (16.4)
	Coronary Artery Bypass Grafting	24 (12.7)
Outcomes	Length of hospital stay (in days)	6.5 $\pm$ 5.0
	Mortality	19 (10.1)

SD: Standard deviation, ECG: Electrocardiography, LBBB: Left bundle branch block, ACS: Acute coronary syndrome, NSTEMI: Non-ST elevated myocardial infarction, STEMI: ST elevated myocardial infarction.

In UTI patients, UA had an OR of 4.2(95% CI: 1-17.4), STEMI 3.7(95% CI: 0.4-31), and NSTEMI 0.7(95% CI: 0.2-1.9).

The two main symptoms of ACS were chest pain 135(71.4%) and dyspnoea 75(39.7%). NSTEMI was the definitive diagnosis in 172(91%) patients, and 134(70.9%) patients were treated with medications. Mean LOS was 6.5 $\pm$ 5.0 days and mortality was 19(10.1%) (Table 2).

Discussion

CAP and UTI were the most prevalent infections prior to ACS. Among comorbid illnesses, diabetes and hypertension were common in the patients, but other risk factors for ACS, like smoking and dyslipidaemia, were not common. Prior coronary heart disease was present in almost half of the patients. Among infectious syndrome, recent CAP was strongly associated with NSTEMI, while UTIs predisposed to UA and STEMI.

Bacterial infections can cause ACS by accelerating the process of atherosclerosis. The development of atherosclerotic plaque can be directly affected by bacterial pathogens via various processes.¹⁶ A recent study on coronavirus disease-2019 (COVID-19) patients showed a prevalence of myocardial injury around 25%.¹⁷ Menendez et al. reported that CAP patients may have cardiac events for as long as a year.¹⁸ Occurrence of

bacterial pneumonia prior to a myocardial injury was reported around 7% in another study.⁶ The current study found that 15.7% of patients with coronary disease had prior bacterial infections. It shows that infections pose a significant risk of ACE. Besides, 45.5% of patients had a history of ischaemic heart disease, which shows that they already had an atherosclerotic burden and the infection precipitated another cardiac event.

CAP can account for approximately 14% of cardiac complications.¹⁹ Pneumonia caused by streptococcus pneumonia was the major culprit preceding ACS.²⁰ The incidence ratio for ACS after pneumonia has been reported to be around 5.98 (95%CI: 2.47-14.4).¹⁴ A review article reported 3-6-fold increased risk of ACS following pneumonia.²¹ The current study also identified 105(7.8%) CAP patients who developed ACS. Similarly, it observed a 1.1 times higher risk of developing NSTEMI after pneumonia. In previous studies, the OR was higher than what the current study found. There could be two possible explanations for these differences. First of all, we assessed UA, NSTEMI and STEMI separately. Second, the severity of infection could be different as it was not evaluated in the current study.

UTIs are one of the most common infections requiring hospitalisation.²² Putot et al. reported 17% of their patients having acute cardiac syndrome with UTI.⁸ Similar to other infections, genitourinary infections also play a crucial role in activating an inflammatory cascade with the surge of interleukins, resulting in accelerating plaque formation and plaque instability, resulting in coronary disease.²³ Interestingly, in the current cohort, 33.9% patients with UTI had myocardial injury, and there was a 3-4-fold increased risk of unstable angina and STEMI with UTI. Other than pneumonia, all other infections have the potential to cause coronary disease.²¹ According to the current study, not only pneumonia and UTIs contributed to ACS, but other infections did as well. These infections mainly included severe cellulitis, osteomyelitis, abdominal sepsis and meningitis. It could have been caused by the chronic inflammatory response that occurs with these infections, causing coronary vessel occlusion.

Time span between an acute infection and ACS is also highly variable. Patients with acute infections have a greater chance of suffering ACE 90 days after admission to hospital.²⁴ Myocardial infarction is more common following pneumonia during the first week post-infection.²⁵ Besides, in patients with sepsis, the risk of acquiring myocardial infarction persists not only for months, but also for several years before reaching baseline.²⁶ The current study also found a median duration of 21 days between infection and ACS. The

possible explanation could be that in the initial phase of recovery there is more inflammation compared to the later part of the recovery.

ACS carries a poor prognosis despite the availability of appropriate medications and interventions.²⁷ Putot et al. had reported an in-hospital mortality of 8-13%²⁸, while Fanta et al. reported 20.4% in-hospital mortality with ACS.²⁹ The current study reported an in-hospital mortality of 10.1% in patients with post-infection myocardial infarction. The cause of mortality in the current patients were heart failure, shock, multi-organ failure, and nosocomial infections. Mean duration of hospital stay after AXS was estimated to be around 9 days (range: 1-25 days).³⁰ In our study the average LOS was 6.5 days after ACS.

The current study has various limitations. Firstly, it was a single-centre study with a small sample size. Secondly, the patients had major co-morbidities which would have impacted their outcomes. Thirdly, the study did not analyse the role of smoking and dyslipidaemia on precipitating ACEs because of the small sample size.

Despite the limitations, the current study, to our knowledge, is the first of its kind in the South Asian region. Future studies are recommended to better understand the phenomena, and to see whether anything can be done to prevent coronary artery disease in post-infection period.

Conclusion

Bacterial infections were found to be associated with ACS. Bacterial infections with pneumonia and UTIs showed a higher risk of myocardial ischaemia. The risk of ACS persisted for weeks after recovering from infection.

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Conflict of Interest: None.

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