

## ORIGINAL ARTICLE

## EARLY USE OF ASPIRIN AFTER SYMPTOMS IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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**Objectives:** To determine the frequency of pre-hospital aspirin use in patients presenting with ST-segment elevation myocardial infarction and to assess the demographic and clinical characteristics of the patients taken pre-hospital aspirin.

**Methodology:** It was a prospective study conducted at tertiary care hospital for the duration of six months. About 657 patients aged between 18-80 years, of either gender and diagnosed with ST-elevation myocardial infarction were included in the study. Use of pre-hospital aspirin after symptoms was assessed in all patients, then followed and outcomes such as discharge status and length of hospital in days were evaluated.

**Results:** Overall mean age was 54.60±12.06 years and most of them were males (79.1%). About 254 patients (38.7%) received aspirin before transfer to hospital and 403 patients (61.3%) received aspirin after arrival in hospital. Frequency of pre-hospital use of aspirin was significantly associated with gender (p=0.001), educational status (p=0.006), and monthly income (p=0.003). The mean rank of length of hospital stay was similar significantly lower in STEMI patients who received pre-hospital aspirin as compared to those who did not receive pre-hospital aspirin (p=0.001). Moreover, the death rate was lower in patients with pre-hospital aspirin administration as compared to those who did not receive pre-hospital aspirin (1.2% vs 2%). However, the difference between pre-hospital aspirin use and discharge status was not statistically significant (p=0.434).

**Conclusion:** Frequency of pre-hospital aspirin use was lower in patients with STEMI. Gender, educational status, and socio-economic status were the significant factors for pre-hospital aspirin use.

**Keywords:** Aspirin, chest pain, length of stay, mortality, myocardial infarction, pre-hospital therapies, ST-elevation myocardial infarction

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## INTRODUCTION

ST-elevation myocardial infarction (STEMI) is a clinical syndrome characterized by abnormalities in the electrocardiogram (ECG), myocardial infarction, and chest pain.<sup>1, 2</sup> STEMI is caused by a thrombotic blockage of a coronary artery along with a ruptured atherosclerotic plaque.<sup>1</sup> When compared to patients with persistent occlusion, about 10% to 20% of acute STEMI patients have spontaneous coronary recanalization prior to angioplasty, and their prognosis is much better in terms of infarction size, heart failure incidence, and early and late survival.<sup>3, 4</sup>

Pre-hospital treatments such as aspirin, oxygen, morphine, and nitroglycerin have largely remained

unchanged in most developed countries during the last 25 years.<sup>1, 5</sup> Other drugs, such as beta-blockers and clopidogrel have also been utilized as a pre-hospital pharmaceutical intervention, but only under strict settings.<sup>5</sup>

Aspirin intervention is one of the most effective and immediate medication of patients with STEMI.<sup>6</sup> The standard guidelines recommend that aspirin 300 mg be given orally as soon as possible by emergency medical personnel.<sup>7</sup> As a result, pre-hospital aspirin use has been found to improve the outcome of STEMI and is considered safe.<sup>6, 8</sup> Patients who got aspirin during the first four hours after start of symptoms had a reduced death rate than those who received aspirin after five to eight hours.<sup>9</sup> Even after adjustment for potential confounders like gender, age, history of heart disease

and medication, early use of aspirin remained independently correlated with smaller infarct size and non-Q wave.<sup>10, 11</sup> Furthermore, early use of aspirin significantly decreased non-fatal stroke and re-infarction, and was not correlated with any higher risk of bleeding or cerebral hemorrhage needing transfusion.<sup>9</sup> Based on these findings, societies of cardiology have assigned class I level of evidence to A to immediate aspirin use.<sup>7, 12</sup>

Aspirin inhibits platelet activation as well as aggregation to some extent.<sup>13</sup> Hence, a higher platelet response to aspirin is likely to increase the likelihood of early spontaneous coronary reperfusion in a subset of patients with acute STEMI, and a home-based aspirin therapy for these patients can be implemented. Hence, the aim of this study was to determine the frequency of pre-hospital aspirin use in patients presenting with STEMI and to assess the demographic and clinical characteristics of those patients who taken pre-hospital aspirin.

## METHODOLOGY

It was a prospective study conducted at the Department of Adult Cardiology, National Institute of Cardiovascular Disease (NICVD), Karachi for the duration of six months from May 2021 to October 2021. Sample size of 657 patients was estimated using Open Epi online sample size calculator, by taking statistics of self-administered aspirin as 19% of the suspected myocardial infarction,<sup>14</sup> 95% confidence level, and 3% margin of error. The study included all consecutive patients diagnosed with ST-elevation myocardial infarction (STEMI) between the ages of 18 and 80, regardless of gender. STEMI was diagnosed in patients who had any two of the following symptoms: typical chest pain lasting more than 20 minutes (retrosternal pain radiating to the left arm or shoulder, aggravated by exertion or emotional stress, relieved by rest or nitroglycerin) or new ST elevation in at least two contiguous leads >2mm in men or >1mm in women in leads V2 to V3 and/or of >1mm in other contiguous chest or limb leads. The study excluded individuals with stable CAD, cardiogenic shock, patients currently on DAPT or with a history of MI, and those with a history of bleeding problems.

This study was conducted after approval of the ethical review committee of NICVD, Karachi, Pakistan. Verbal informed consent regarding participation and publication without disclosing identity of the patient was taken.

Patients were first assessed for confirmation of STEMI at the time of presentation at hospital. After that pre-hospital aspirin self-administration after symptoms by the patient, administration by ambulance staff or other

healthcare professional or NICVD chest pain were recorded in all patients. Timing of onset of chest pain to aspirin administration and onset of chest pain to emergency room presentation were obtained by the attendant or ambulance staff or referral chart. All patients were followed and outcomes such as discharge status (survived/expired) and length of hospital in days were evaluated. Data regarding demographic and clinical characteristics of the patients was also noted on pre-designed questionnaire.

Statistical package for social sciences (SPSS) version 25 was used for the analysis of data. Descriptive statistics such as mean  $\pm$  SD, median (IQR) for numeric variables or frequency and percentages for categorical variables were computed. Frequency of pre-hospital aspirin use was compared with age groups, gender, educational status, monthly income, comorbidities, Killip class, family history of coronary artery disease, family history of ischemic heart disease and mortality using Fisher-exact or chi-square test. Length of hospital stay was compared using Mann-Whitney U test between patients who received and who did not receive pre-hospital aspirin. A p-value of  $\leq 0.05$  was taken as criteria for statistical significance.

## RESULTS

Table 1 displays the baseline characteristics of included patients. The overall mean age was  $54.60 \pm 12.06$  years and most of them were males (79.1%). About 41.6% of the patients were illiterate and 61.8% had monthly income  $\leq 30,000$  PKR. Of 657 patients, 21.8% were smokers, 45.5% were hypertensive, 47.3% were diabetic and only 0.8% of the patients had chronic kidney disease. Almost 12% of the patients had family history of coronary artery disease and 6.4% had family history of ischemic heart disease. Majority of the patients had Killip class I to III on admission.

Out of 657 patients, 65.9% patients were transported to hospital by self, 12% by public and 22.1% by ambulance. About 254 patients (38.7%) received aspirin before transfer to our hospital and 403 patients (61.3%) received aspirin after arrival in our hospital. Only 5 patients out of 160 who got pre-hospital aspirin self-administered the medication. Furthermore, aspirin was given to 145 patients by other healthcare professionals, 9 patients by ambulance staff, and 95 patients received aspirin in the NICVD chest pain unit. Of 254 patients with pre-hospital aspirin administration, 251 were treated with clopidogrel and 250 were treated with heparin in hospital, respectively. Median time from onset of chest pain to aspirin use

was 3 hours (IQR=2 to 4 hours). Median time from onset of chest pain to presentation in emergency room was 4 hours (IQR=2.3 to 6 hours).

**Table 1: Baseline characteristics of patients with STEMI (n=657)**

Variables	Statistics
Age in years	54.60±12.06
<b>Gender</b>	
Male	520 (79.1)
Female	137 (20.9)
<b>Educational status</b>	
Illiterate	273 (41.6)
Primary	198 (30.1)
Matric	104 (15.8)
Graduate	82 (12.5)
<b>Monthly income</b>	
≤ 30k PKR	406 (61.8)
30-50k PKR	170 (25.9)
50-100k PKR	43 (6.5)
>100k PKR	38 (5.8)
<b>Smoking</b>	
Yes	143 (21.8)
No	514 (78.2)
<b>Hypertension</b>	
Yes	299 (45.5)
No	358 (54.5)
<b>Diabetes mellitus</b>	
Yes	311 (47.3)
No	346 (52.7)
<b>Chronic kidney disease</b>	
Yes	5 (0.8)
No	652 (99.2)
<b>Family history of coronary artery disease</b>	
Yes	79 (12)
No	578 (88)
<b>Family history of ischemic heart disease</b>	
Yes	42 (6.4)
No	615 (93.6)
<b>Killip class</b>	
I	547 (83.3)
II	63 (9.6)
III	31 (4.7)
IV	16 (2.4)

Data presented as mean ± SD or n (%)

The proportion of males in pre-hospital aspirin group were significantly higher than females (85.8% vs. 14.2%) with p-value=0.001. Most of the pre-hospital aspirin users were educated (primary to graduate level) and 37% were illiterate. Statistically significant difference in proportion of educational level was observed between pre-hospital aspirin users and non-users (p=0.006). Most of the pre-aspirin users had monthly income less or equal to 30,000 PKR. There was statistically significant association between pre-hospital aspirin use and monthly income (p=0.003). Patients with negative family history of coronary artery disease were more in pre-hospital aspirin group than patients with positive history of coronary artery disease (86.2% vs 13.8%). (Table 2)

Moreover, the death rate was lower in patients with pre-hospital aspirin administration as compared to those who did not receive pre-hospital aspirin (1.2% (3) vs. 2% (8)). However, the difference between pre-hospital aspirin use and discharge status was not statistically significant (p=0.434).

**Table 2: Comparison of demographic and clinical characteristics between pre-hospital aspirin users and non-users**

	Pre-hospital aspirin		P-value
	Yes	No	
<b>Age in years</b>	54.15±13.08	54.89±11.38	0.441
<b>Gender</b>			
Male	218 (85.8)	302 (74.9)	0.001
Female	36 (14.2)	101 (25.1)	
<b>Educational status</b>			
Illiterate	94 (37)	179 (44.4)	0.05
Primary	77 (30.3)	121 (15.6)	
Matric	41 (16.1)	63 (15.6)	
Graduate	42 (16.5)	40 (9.9)	
<b>Monthly income</b>			
≤30,000 PKR	138 (54.3)	268 (66.5)	0.001
30,000-50,000 PKR	74 (29.1)	96 (23.8)	
50,000-100,000 PKR	22 (8.7)	21 (5.2)	
>100,000 PKR	20 (7.9)	18 (4.5)	
<b>Family history of coronary artery disease</b>			
Yes	35 (13.8)	44 (10.9)	0.272
No	219 (86.2)	359 (89.1)	
<b>Hypertension</b>			
Yes	118 (46.5)	181 (44.9)	0.699
No	136 (53.5)	222 (55.1)	
<b>Diabetes mellitus</b>			
Yes	132 (52)	179 (44.4)	0.06
No	122 (48)	224 (55.6)	
<b>Smoking</b>			
Yes	53 (20.9)	90 (22.3)	0.657
No	201 (79.1)	31 (77.7)	
<b>Family history of ischemic heart disease</b>			
Yes	20 (7.9)	22 (5.5)	0.218
No	234 (92.1)	381 (94.5)	
<b>Chronic kidney disease</b>			
Yes	4 (1.6)	1 (0.2)	0.057
No	250 (98.4)	402 (99.8)	
<b>Killip class</b>			
I	206 (81.1)	341 (84.6)	0.584
II	27 (10.6)	36 (8.9)	
III	15 (5.9)	16 (4)	
IV	6 (2.4)	10 (2.5)	

**DISCUSSION**

The pre-hospital use of aspirin is inexpensive, widely applicable and simple therapy in patients with confirmed or suspected acute myocardial infarction.<sup>15</sup> In the present study, we measured the frequency of pre-hospital aspirin use in patients with STEMI, and also assessed its association with demographic and clinical factors.

The benefits of aspirin have been shown, with a trend toward greater benefit with earlier therapy.<sup>9</sup> As a result

of this advantage, it is the most important therapeutic in the pre-hospital situation.<sup>5</sup> Patients with suspected acute myocardial infarction treated with pre-hospital aspirin range from 19 percent to 78 percent in prior studies from various countries.<sup>14-20</sup> In the current study, pre-hospital aspirin usage was found to be 38.7 percent. The low level of adherence to standard guidelines of aspirin can be attributed to a number of factors. According to a previous research by Hooker et al., the most frequent reason of paramedics not to administering aspirin was that the chest pain was not thought to be of a cardiac nature (33%). Moreover, another common reason for not providing aspirin was that emergency medical service personnel were unable to do so (15%).<sup>16</sup>

Self-administration of aspirin was also one of the reason that emergency healthcare providers did not administered aspirin.<sup>16</sup> In the study by Strandmark et al. found that 38% of patients were already taking aspirin on a regular basis before to the occurrence of myocardial infarction. This might have impacted the decision of emergency medical staff, even while recommendations did not urge withholding the loading dosage of aspirin from these patients.<sup>5</sup> In the present study, only 5 patients self-administered aspirin before arriving at the hospital, whereas in 145 patients aspirin was administered by other healthcare professionals, in 95 patients aspirin was administered at NICVD chest pain unit and 9 patients received aspirin by ambulance staff. It's possible that the lower proportion of self-administered aspirin in the current study is attributable to a lack of public knowledge. The lower proportion of pre-hospital aspirin administered by ambulance workers, on the other hand, could be attributable to a lack of good ambulance service in the city with trained healthcare experts. These findings clearly demonstrate the need for increased public awareness, as well as the importance of on-call ambulance services with on-call healthcare professionals for early intervention in order to enhance STEMI patient outcomes.

In the current study, a positive family history of coronary artery disease was high in pre-hospital aspirin use. Similarly, a previous study shown history of myocardial infarction was a significant predictor of aspirin use.<sup>5</sup> Furthermore, in our study gender ( $p=0.001$ ), educational status ( $p=0.006$ ) and monthly income ( $p=0.003$ ) were associated with the pre-hospital aspirin use. However, in the study by Zijlstra et al. found pre-hospital use of aspirin did not differ significantly between males and females ( $p=0.24$ ).<sup>15</sup> While, Barbash et al. revealed proportion of females was significantly higher in late aspirin administration group versus early aspirin administration ( $p=0.001$ ).<sup>21</sup> Hence, these demographic factors should be

considered for the successful and early intervention of aspirin in suspected STEMI cases.

In our study, length of hospital stay was significantly lower in patients with pre-hospital administration of aspirin as compared to patients received aspirin in hospital setting. In the study by Spencer et al., also found that use of aspirin significantly shorter the length of hospital stay.<sup>22</sup> Furthermore, we also found lesser deaths among patients who received pre-hospital aspirin, but there was no statistical significance observed between pre-hospital aspirin administration and mortality. In the study by Zijlstra et al. also found insignificant difference death rate between the in-hospital and pre-hospital use of aspirin.<sup>15</sup> Barbash et al. has observed significantly lesser in-hospital complications and mortality in patients who received early aspirin versus patients who received late aspirin.<sup>21</sup> Becker et al. also found that mortality rate (OR=0.24, 95% CI=0.22 to 0.26,  $p=0.0001$ ) and recurrent MI (OR=0.90, 95% CI=0.78 to 1.00) was lower in patients who received early aspirin than late aspirin.<sup>23</sup> These findings suggest the early and pre-hospital use of aspirin in order to give immediate benefit to the patients with acute myocardial infarction.

Our study had a few limitations, including the fact that it was a single institute study with a limited sample size. Another drawback was that because it was an observational study, we were unable to assign patients randomly to pre-hospital or in-hospital aspirin use groups. Another disadvantage is that the percentage of patients who were already taking aspirin on a regular basis prior to admission to the hospital is unknown. However, this study has provided local data on aspirin use in myocardial infarction patients. Hence, aspirin used at the right time and in the right dose can minimize early cardiovascular events and improve survival.

## CONCLUSION

Patients with STEMI had a reduced rate of pre-hospital aspirin usage. Pre-hospital aspirin usage was associated with gender, educational status, and socioeconomic position. Furthermore, pre-hospital use of aspirin improves the outcomes of STEMI patients. Aspirin should be given to suspected myocardial infarction patients as soon as possible.

## AUTHORS' CONTRIBUTION

VM and RA: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AA, MK, AAS, RK, AH, NUK, JAS, and TS: Data acquisition,

interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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## REFERENCES

- McGinley C, Mordi IR, Kell P, Currie P, Hutcheon S, Koch S, et al. Prehospital Administration of Unfractionated Heparin in ST-Segment Elevation Myocardial Infarction Is Associated With Improved Long-Term Survival. *J Cardiovasc Pharmacol.* 2020;76(2):159-63.
- Akbar H, Foth C, Kahloon RA, Mountfort S. Acute ST Elevation Myocardial Infarction. [Updated 2021 Aug 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
- Allahwala UK, Weaver JC, Bhindi R. Spontaneous coronary collateral recruitment in patients with recurrent ST elevation myocardial infarction (STEMI). *Heart Vessels.* 2020;35(3):291-6.
- Li Z, Zhang F, Gao F, HE Q, LI Y, Xie P. Correlation between procalcitonin and spontaneous recanalization of infarct related artery in patients with ST-segment elevation myocardial infarction. *Chinese Crit Care Med.* 2016;1108-12.
- Puymirat E, Lamhaut L, Bonnet N, Aissaoui N, Henry P, Cayla G, et al. Correlates of pre-hospital morphine use in ST-elevation myocardial infarction patients and its association with in-hospital outcomes and long-term mortality: the FAST-MI (French Registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction) programme. *Eur Heart J.* 2016;37(13):1063-71.
- Bugiardini R, Pavasović S, Yoon J, van der Schaar M, Kedev S, Vavlukis M, et al. Aspirin for primary prevention of ST segment elevation myocardial infarction in persons with diabetes and multiple risk factors. *EClinicalMedicine.* 2020;27:100548.
- Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. *J Am Coll Cardiol.* 2016;67(10):1235-50.
- Enhos A, Karacop E. Impact of antecedent aspirin use on infarct size, bleeding and composite endpoint in patients with de novo acute myocardial infarction. *Ther Clin Risk Manag.* 2021;17:441.
- Somuncu MU, Demir AR, Karakurt ST, Karakurt H, Karabag T. Long term cardiovascular outcome based on aspirin and clopidogrel responsiveness status in young ST-elevated myocardial infarction patients. *Arq Bras Cardiol.* 2018;112:138-46.
- Mazlan-Kepli W, Sie TS, Ren CS, Hakimi MH, Fui LJ, et al. Abdul MA. Prior antiplatelet use and cardiovascular outcomes in patients presenting with acute coronary syndrome. *Int J Med Toxicol Leg Med.* 2019;22(3and4):104-9.
- Basra SS, Wang TY, Simon DN, Chiswell K, Virani SS, Alam M, et al. Ticagrelor use in acute myocardial infarction: insights from the National Cardiovascular Data Registry. *JAHA.* 2018;7(12):e008125.
- Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39(2):119-77.
- Danchin N, Puymirat E, Cayla G, Cottin Y, Coste P, Gilard M, et al. One-Year Survival After ST-Segment-Elevation Myocardial Infarction in Relation With Prehospital Administration of Dual Antiplatelet Therapy. *Circ Cardiovasc Interv.* 2018;11(9):e007241.
- Woollard M, Smith A, Elwood P. Pre-hospital aspirin for suspected myocardial infarction and acute coronary syndromes: a headache for paramedics? *Emerg Med J.* 2001;18(6):478-81.
- Zhang X, Qi L, Liu Y. Aspirin in combination with clopidogrel in the treatment of acute myocardial infarction patients undergoing percutaneous coronary intervention. *Pak J Med Sci.* 2019;35(2):348.
- Hooker EA, Benoit T, Price TG. Reasons prehospital personnel do not administer aspirin to all patients complaining of chest pain. *Prehosp Disaster Med.* 2006;21(2):101-3.
- Meisel ZF, Armstrong K, Mechem CC, Shofer FS, Peacock N, Facenda K, et al. Influence of sex on the out-of-hospital management of chest pain. *Acad Emerg Med.* 2010;17(1):80-7.
- Rittenberger JC, Beck PW, Paris PM. Errors of omission in the treatment of prehospital chest pain patients. *Prehosp Emerg Care.* 2005;9(1):2-7.
- McVane KE, Macht M, Colwell CB, Pons PT. Treatment of suspected cardiac ischemia with aspirin by paramedics in an urban emergency medical services system. *Prehosp Emerg Care.* 2005;9(3):282-4.
- Bång A, Herlitz J, Grip L, Caidahl K, Karlsson T, Kihlgren S, et al. The relative influence of age, previous history and therapeutic strategies prior to hospital admission among ambulance transported patients with ST-elevation myocardial infarction. *Int J Cardiol.* 2009;136(2):213-4.
- Barbash I, Freimark D, Gottlieb S, Hod H, Hasin Y, Battler A, et al. Outcome of myocardial infarction in patients treated with aspirin is enhanced by pre-hospital administration. *Cardiology.* 2002;98(3):141-7.
- Spencer FA, Lessard D, Gore JM, Yarzebski J, Goldberg RJ. Declining Length of Hospital Stay for Acute Myocardial Infarction and Postdischarge Outcomes: A Community-Wide Perspective. *Archives of Internal Medicine.* 2004;164(7):733-40.
- Becker RC, Burns M, Gore JM, Lambrew C, French W, Rogers WJ. Early and pre-discharge aspirin administration among patients with acute myocardial infarction: current clinical practice and trends in the United States. *J Thromb Thrombolysis.* 2000;9(3):207-15.

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