Original Article
DOI: https://doi.org/10.70749/ijbr.v3i4.1239

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Gender Differences in Presentation and Outcomes of Acute Coronary Syndrome: A Multicenter Study

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ARTICLE INFO

Keywords: Acute Coronary Syndrome, Gender Differences, Myocardial Infarction, In-Hospital Outcomes, Pakistan.

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Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History
Received: 29-12-2024 Revised: 06-04-2025
Accepted: 20-04-2025 Published: 30-04-2025

ABSTRACT

Introduction: Gender disparities in acute coronary syndrome (ACS) have been increasingly recognized, with women often experiencing atypical symptoms, delayed care, and poorer outcomes. However, limited local data are available on this subject in Pakistan. **Objective**: To evaluate gender-based differences in clinical presentation, management, and in-hospital outcomes among patients with ACS in a tertiary care setting. **Materials and Method**: A prospective observational study was conducted at Hayatabad Medical Complex Peshawar, Pakistan from June, 2024 to November, 2024. A total of 300 ACS patients (180 males and 120 females) were enrolled. Data on demographics, clinical features, treatment modalities, and outcomes were recorded and analyzed using SPSS v26. **Results**: Female patients were older, had more comorbidities, and presented more frequently with atypical symptoms. They experienced longer delays in hospital presentation, lower rates of reperfusion therapy, and higher rates of complications and in-hospital mortality compared to males. **Conclusion**: Significant gender disparities exist in ACS presentation and outcomes, warranting gender-sensitive diagnostic and treatment strategies.

INTRODUCTION

Acute coronary syndrome (ACS) still poses a great threat to human life and health in that it has a high prevalence rate as a cause of morbidity and mortality across the globe despite current concentrated efforts on early identification and management, as well as enhanced healthcare procedures. Nevertheless, gender differences are still apparent in the presentation, management, and prognosis of ACS. For several reasons, ACS is a gendered disease in terms of its onset, presentation, treatment, and prognosis for women and men (1). This disparity in cardio care has received much attention over the last decade, especially in light of expanding information from various populations stressing the importance of sex and gender as predictors for cardio health. This study from Malaysia shows that women with ACS were less likely to have typical symptoms, and they had worse outcomes during hospitalization than men, even after controlling for clinical factors.

More recent registries, including the CORALYS registry, reinforce the distinct trends and outcomes observed between men and women following an ACS event. This indicates that women have a higher susceptibility to developing heart failure after ACS, independent of the patient's baseline characteristics or the treatments received (2). Stated differently, these variations in post-ACS complications signify inherent biological, social, and healthcare disparities that also apply to women. Concerning the choice of treatment, the patient's gender has an influence on it: females had lower rates of invasive management and higher 30-day mortality, which might point to under-treatment as one of the reasons for worse outcomes among women (3). For instance, a meta-analysis conducted in the last five years also showed that women present to the hospital later and receive care that does not meet the guidelines recommendations for ACS than men (4).

These findings are also in tune with the global trends. In other words, across North America, Europe, and Asia, the pattern of sex-based sex disparity holds as the result of a widespread, systemic problem (5). One reason for these discordances is atypical ACS symptoms presenting

in women, such as nausea, fatigue, and epigastric discomfort, may result in misdiagnosis or delayed diagnosis (6). Even with timely diagnosis, elderly women are less often referred for invasive procedures, such as coronary angiography or percutaneous coronary intervention (PCI), in particular (6). A study from Switzerland also found that the inequities persisted in a universal healthcare setting, stressing these inequities are ingrained at their deepest (7).

Therefore, the aforesaid disadvantages are not exclusive to older patients. Research also shows that young women fare even worse when they have myocardial infarctions compared to young men, attributed to psychosocial factors, delay in seeking medical attention, and gender differences in treatment (5). Similarly, data from the MONICA registries of France contributes to the strength of evidence that, while ACS management undergoes a progressive evolution, the 12-month lethality is still higher than in males, meaning that there has not been an efficient equal distribution of improvements in management (9). Such disparities are worrying as awareness of cardiovascular disease risks among women is rising, including diabetes, hypertension, and obesity, thus may worsen an outcome if not controlled well (10). This principle is that another factor that prevents the earliest delivery of the best care is that women with STEMI are often not admitted to the hospital early. Specifically, a multicenter study conducted among women in New York City found that they took one day longer than men to seek medical attention after experiencing the symptoms, which was a critical factor influencing the outcomes (11). They include sociocultural aspects, caregiving responsibilities, lack of knowledge regarding the disease, and underestimation of their disease risk (11). Like any other aspect of the health care systems across the globe, women who are within the health care system are also at a disadvantage as there are differences in the effectiveness and bleeding risks between male and female patients on antiplatelet therapy (12). Nonetheless, there is very scarce guidance addressing the sex-specific management of patients on multiple antiplatelet regimens, which restricts the individualization of therapy options (12).

Additionally, gaps in secondary prevention practices also persist along the sex-separatist lines. Specifically, the rate of prescription of statins, beta-blockers, or attendance to cardiac rehabilitation is lower among women even when there is improved evidence of the efficacy post-ACS (13). Such low rates of use contribute to worse clinical outcomes and a higher likelihood of further adverse events. Gender disparities are also revealed within pharmacological therapies as distinct prescription preferences emerge from various healthcare facilities (14). A population-based study showed that clinicians behave in a way that channels prescription according to a patient's sex despite the fact that this may be justified in some circumstances but leaves women underserved (14). Finally, analyzing the outcomes of patients with ACS who had CABG, it was identified that the female sex was an independent predictor of higher postoperative mortality and complication rates, although procedural success was comparable with male patients (15).

These data altogether show that gender inequity in ACS is systematically observed irrespective of age, specialties, and treatment options. There is a significant need to distinguish the roles of sex and gender in the presentation of ACS and its outcomes. To close all these gaps, institutional change is needed alongside individual medical staff's understanding of issues of fairness in treatment. Therefore, as awareness rises, future clinical practice guidelines must incorporate sex-specific evidence in an effort to create clearer cardiovascular care for all. Therefore, this study helps to extend these differences in the Pakistani population to the global database on ACS and indicate how to minimize gender disparities and enhance patient outcomes.

Objective

To compare clinical presentation and management of acute coronary syndrome between male and female patients and short-term prognosis in a Multicenter hospital-based study in Pakistan.

MATERIALS AND METHODS

Design: Prospective observational study.

Study setting: The study was conducted at Hayatabad Medical Complex Peshawar, Pakistan.

Duration: The study was carried out over a six-month period, from June, 2024 to November, 2024.

Inclusion Criteria

The study was carried out in the Cardiology Department of Hayatabad Medical Complex Peshawar, Pakistan, a teaching hospital patient of 18 years and above diagnosed clinically with Acute Coronary Syndrome inclusive of ST elevation Myocardial Infarction (STEMI), Non-ST elevation Myocardial Infarction (NSTEMI), and unstable angina were included. The patient selection was not made based on gender deliberately in order to avoid excluding any gender, and all the patients were provided with advanced cardiac care facilities.

Exclusion Criteria

Patients with missing medical records or who were discharged from the hospital against medical advice, Medicare patients with other severe concurrent diseases, such as advanced cancer, or patients who have undergone percutaneous coronary intervention within the last six months.

Methods

Consequently, all eligible patients who were diagnosed with acute coronary syndrome (ACS) during the period

of 6 months beginning June, 2024 to November, 2024 at the Hayatabad Medical Complex Peshawar, Pakistan after taking informed consent. Participants' details were obtained by using a pretested structured data collection form containing demographic characteristics, clinical presentation, coexisting medical conditions, laboratory investigations, ECG abnormalities, therapy, and complications encountered during hospitalization. ACS was confirmed by clinical signs and symptoms, changes in the ECG, and increased levels of cardiac biomarkers in accordance with the principles of ESC/AHA. The treatments of patients followed institutional guidelines, including medical therapies, thrombolysis, or percutaneous coronary intervention where necessary. Additional primary criteria for classifying the patients included gender-specific variables concerning atypicality, time of admission to hospital, and therapeutic response. These included length of stay, adverse outcomes, heart failure, and arrhythmias, among other related complications and in-hospital mortality. All statistical data were analyzed using the Statistical Package of Social Science (SPSS) version 26. Numeric data were expressed as means ± standard deviations when the data for a variable were usually distributed. Otherwise, it was expressed as frequencies and proportions. For data analysis, chi-square and t-tests were applied for gender differences, and all the differences having $p<0.05$ were considered significant.

RESULTS

There were 300 patients with ACS, among them 180(60%) males and 120(40%) females. The men were significantly younger than the women, and their mean age was 56.2 ± 10.4 years, while the women was 59.8 ± 11.1 years ($p = 0.02$). Diabetic and hypertensive patients were mostly females ($p < 0.05$) while smoking history and dyslipidemia were more among males ($p < 0.01$). Female patients also complained more of non-gastric related symptoms like nausea, fatigue, epigastric discomfort, and others than male patients, and chest pain remained the most common single symptom in the male patients (p-value < 0.001).

Table 1

Baseline Characteristics of Patients with ACS by Gender

Variable	Male (n=180)	Female (n=120)	p-value
Mean Age (years)	56.2 ± 10.4	59.8 ± 11.1	0.02
Hypertension (%)	54.4	70.8	0.01
Diabetes Mellitus (%)	39.4	55.8	0.004
Smoking (%)	64.4	4.2	<0.001
Dyslipidemia (%)	58.9	42.5	0.008

With regard to type of ACS, ST-elevation myocardial infarction (STEMI) was observed in 65% of male and 52% of female patients, whereas non-ST elevation myocardial infarction (NSTEMI) was more common in females (38%) than males (25%) ($p = 0.03$). Women experienced significantly longer delays in seeking medical attention after symptom onset, with an average of 5.1 hours compared to 3.6 hours in men ($p = 0.01$). Reperfusion therapy (either thrombolysis or PCI) was performed more often in males (72.2%) compared to females (58.3%) ($p = 0.02$).

Table 2

Clinical Presentation and Management by Gender

Parameter	Male (n=180)	Female (n=120)	p-value
STEMI (%)	65.0	52.0	0.03
NSTEMI (%)	25.0	38.0	0.03
Atypical Symptoms (%)	18.3	46.7	<0.001
Time to Hospital (hours, mean)	3.6 ± 1.9	5.1 ± 2.4	0.01
Received Reperfusion Therapy (%)	72.2	58.3	0.02

In-hospital complications, including heart failure and arrhythmias, were significantly more frequent in female patients. Heart failure occurred in 20.8% of women compared to 10.6% of men ($p = 0.01$), and arrhythmias were observed in 18.3% of females versus 9.4% of males ($p = 0.02$). In-hospital mortality was also higher among female patients (7.5%) than males (3.3%) ($p = 0.04$). The average length of hospital stay was longer in females (5.6 days) than in males (4.2 days) ($p = 0.02$).

Table 3

In-Hospital Outcomes by Gender

Outcome	Male (n=180)	Female (n=120)	p-value
Heart Failure (%)	10.6	20.8	0.01
Arrhythmias (%)	9.4	18.3	0.02
In-hospital Mortality (%)	3.3	7.5	0.04
Hospital Stay (days)	4.2 ± 1.5	5.6 ± 1.9	0.02

These findings indicate notable gender differences in presentation, treatment, and outcomes of ACS, with women experiencing delays in care, higher complication rates, and poorer short-term outcomes compared to men.

DISCUSSION

The present work brings out several prototypes regarding the gender disparity in aspects of ACS, including anti-ischemic presentation, management, and hospital results for a tertiary healthcare organization in Pakistan. Such findings are not unique to this study, as there is a rising trend in the global literature linking sex and gender to cardiovascular disease results. Among the patients in the study, 40% were women, who had different clinical characteristics compared with male patients, for which it becomes crucial to use a gender perspective in ACS diagnosis and management (1). One of the studies that has also been observed in other studies, including an investigation, is the advanced age of female patients with ACS. This means that in the study, women were presented nearly four years later than men. This trend has been noticed in different registries, such as the Malaysian NCVD-ACS registry, where authors pointed

to older age in women partly because atherosclerosis tends to be initiated later in women than in men due to estrogen's protective effect on the cardiovascular system before the onset of menopause.

However, as the women advance in their age, they also develop other diseases like hypertension and diabetes, which were found to be present in many women in the group. This comorbidity burden may explain the worse outcome seen for women, as noted from the CORALYS registry on the higher incidence of heart failure post-ACS in females. Among all the gaps identified in this study, the most significant was in the manifestation of symptoms by the two sexes. Female patients also complained much less frequently of chest pain and more often of fatigue, nausea, epigastric discomfort, etc. This is consistent with evidence from across the world where women tend to develop more vague complaints that can be easily explained away or overlooked, thus delaying diagnosis (3). These cases contribute to the significant time required to seek and receive medical help. This study found that women arrived at the hospital much later after developing symptoms, similar to what Lunova et al.'s meta-analysis concluded, and a large study conducted in New York City also reported pre-hospital delay in women with STEMI (4).

Finally, the delay, combined with a less aggressive management approach, is still shortening a woman's lifespan and prevents her from getting the reperfusion in time. In the present work, reperfusion therapy has been used as an option in female patients less frequently than in male patients. Zhou et al. and Cader et al. have also done a few more studies identifying that there is underuse of invasive interventions such as coronary angiography and PCI in women even though their risk factor profile is comparable to or more than men. These may be due to the underestimation of women's cardiovascular risk by physicians, biased/willingness of patients, pharmaceutical inertia, and clinical underestimations. As per the ACS subtypes, female patients in this study were found to be more affected by NSTEMI, while STEMI affected mostly male patients. This trend is consistent with de Rosa et al. who reported a similar dichotomy in gender differences, particularly among elderly patients undergoing PCI (6). NSTEMI is less dramatic than STEMI, and this may contribute to the development of further delays in diagnosis, particularly in women.

However, women underwent invasive treatment less frequently, yet they developed in-hospital complications such as heart failure, arrhythmias, and so on. These findings are also similar to those of a national study conducted in Switzerland, which stated that dissected gender bias in service led to worse predictive results for female patients in an advanced economy setting. Being in their youthful age, young women are also not an exception to these disparities. However, there are some signs that they may actually be worse off than older women in certain regards. Lv et al., in their study, also revealed that women who were victims of myocardial infarction were more likely to have a high level of depression, psychosocial stress, and complications after discharge compared to male individuals of young age. These are worrying prospects, particularly for LMICs, where there is poor knowledge of cardiovascular living among the young female population and limited availability of psychosocial support services.

The time trend analysis has further indicated that there is a gender disparity with ACS despite advancements in its management over the last couple of years. Gauthier et al., in the MONICA registries in France, found that women had higher mortality at 12 months after ACS at every time point studied, indicating that such system improvements are not felt equally by both sexes, and this can be seen in the index and one year follow up (9). As stressed by Negrea et al., such cases remain an important diagnostic issue, particularly in non-ST segment elevation ACS (10). The findings also established that one of the major inefficiencies is the low prescription and use of guideline-directed medical therapy in women. These findings on lower reperfusion are supported by studies where women are less likely to receive antiplatelet therapy, beta-blockers, statins, or engage in cardiac rehabilitation programs (11). Hyun et al. showed that these gaps in secondary prevention have a poor effect on the survival of female patients after ACS (12).

However, pharmacodynamics and pharmacokinetics are also different in male and female persons, which is described in the work of Occhipinti et al. and Sotorra-Figuerola et al., who mentioned sex differences in drug efficacy and prescription (13). Lastly, it is still important to note that surgical outcomes are also influenced by gender. In a streak with this study where only a few of the patients admitted had CABG during their hospital stay, women who develop CABG post-ACS are observed to have higher mortality and more complications compared to men. These differences remain significant even after controlling for age, pathology, and technical factors, which may point to inherent frailty or inadequate 'readiness' for female patients undergoing major surgery (15).

Finally, this study confirms a relatively large literature on sex-related disparities in ACS, continuing from risk factors and manifestation to diagnosis, management, and prognosis. These conclusions call for specific training programs for doctors and patients, which aim at raising awareness of non-typical symptoms in women and achieving early and gender-sensitive treatment. There is a need for sex-specific management guidelines, and future trials should include enough women to provide a sizable rate of meta-analysis. The cardiovascular disparities bring disparity in the related outcomes, and it is only through assuming the responsibility that the

improvement of masculinities and femininities can be improved in relation to cardiovascular health.

CONCLUSION

These findings reveal a male preponderance in the patients presenting with acute coronary syndrome with variations in their management and in-hospital outcomes in Pakistani tertiary care hospitals/systems. Most of the female patients were older in age, were more likely to present with hypertension and diabetes or other comorbid conditions, and presented with symptoms that were more atypical and led to delays in admission to the hospital. The female patients undergoing reperfusion therapy got it less often and had more in-hospital complications like heart failure and arrhythmias and higher thirty-day mortality rates along with longer hospital stays. These findings corroborate data from other countries and suggest that ACS must receive enhanced recognition and earlier diagnosis in women, as well as provide equal access to accurate treatment based on the available evidence sources. Making this possible requires targeted educational interventions to health care professionals as well as public relations to counter these disparities. Further clinical practice recommendations and studies should include sex-based analyses to enhance the positive outcomes for male and female patients suffering from acute coronary syndrome.

REFERENCES

1. Lee, C.Y., Liu, K.T., Lu, H.T., Mohd Ali, R., Fong, A.Y.Y. and Wan Ahmad, W.A., 2021. Sex and gender differences in presentation, treatment and outcomes in acute coronary syndrome, a 10 year study from a multi-ethnic Asian population: The Malaysian National Cardiovascular Disease Database—Acute Coronary Syndrome (NCVD-ACS) registry. PLoS One, 16(2), p.e0246474. https://doi.org/10.1371/journal.pone.0246474
2. Elia, E., Bruno, F., Crimi, G., Wańha, W., Leonardi, S., Mauro, M., Roubin, S.R., Fabris, E., Giannino, G., Mancone, M. and Severino, P., 2024. Gender differences in the development of heart failure after acute coronary syndrome: Insight from the CORALYS registry. International Journal of Cardiology, 397, p.131622. https://doi.org/10.1016/j.ijcard.2023.131622
3. Zhou, S., Zhang, Y., Dong, X., Zhang, X., Ma, J., Li, N., Shi, H., Yin, Z., Xue, Y., Hu, Y. and He, Y., 2023. Sex disparities in management and outcomes among patients with acute coronary syndrome. JAMA network open, 6(10), pp.e2338707-e2338707. https://doi.org/10.1001/jamanetworkopen.2023.38707
4. Lunova, T., Komorovsky, R. and Klishch, I., 2023. Gender differences in treatment delays, management and mortality among patients with acute coronary syndrome: a systematic review and meta-analysis. Current Cardiology Reviews, 19(1), pp.111-126. https://doi.org/10.2174/1573403x18666220630120259
5. Cader, F.A., Banerjee, S. and Gulati, M., 2022. Sex differences in acute coronary syndromes: a global perspective. Journal of Cardiovascular Development and Disease, 9(8), p.239. https://doi.org/10.3390/jcdd9080239
6. De Rosa, R., Morici, N., De Luca, G., De Luca, L., Ferri, L.A., Piatti, L., Tortorella, G., Grosseto, D., Franco, N., Misuraca, L. and Sganzerla, P., 2021. Association of sex with outcome in elderly patients with acute coronary syndrome undergoing percutaneous coronary intervention. The American Journal of Medicine, 134(9), pp.1135-1141. https://doi.org/10.1016/j.amjmed.2021.03.025
7. Huber, E., Le Pogam, M.A. and Clair, C., 2022. Sex related inequalities in the management and prognosis of acute coronary syndrome in Switzerland: cross sectional study. BMJ medicine, 1(1), p.e000300. https://doi.org/10.1136/bmjmed-2022-000300
8. Lv, J., Ni, L., Liu, K., Gao, X., Yang, J., Zhang, X., Ye, Y., Dong, Q., Fu, R., Sun, H. and Yan, X., 2021. Clinical characteristics, prognosis, and gender disparities in young patients with acute myocardial infarction. Frontiers in Cardiovascular Medicine, 8, p.720378. https://doi.org/10.3389/fcvm.2021.720378
9. Gauthier, V., Montaye, M., Ferrières, J., Kai, S.H.Y., Biasch, K., Moitry, M., Amouyel, P., Dallongeville, J. and Meirhaeghe, A., 2022. Sex differences in time trends in acute coronary syndrome management and in 12-month lethality: data from the French MONICA registries. International Journal of Cardiology, 361, pp.103-108. https://doi.org/10.1016/j.ijcard.2022.05.040
10. Negrea, M.O., Zdrenghea, D., Teodoru, M., Neamțu, B., Cipăian, C.R. and Pop, D., 2022. Gender particularities and prevalence of atypical clinical presentation in non-ST elevation acute coronary syndrome. Journal of Cardiovascular Development and Disease, 9(3), p.84. https://doi.org/10.3390/jcdd9030084
11. Weininger, D., Cordova, J.P., Wilson, E., Eslava, D.J., Alviar, C.L., Korniyenko, A., Bavishi, C.P.,

Hong, M.K., Chorzempa, A., Fox, J. and Tamis-Holland, J.E., 2022. Delays to hospital presentation in women and men with ST-segment elevation myocardial infarction: a multi-center analysis of patients hospitalized in New York City. Therapeutics and Clinical Risk Management, pp.1-9. https://doi.org/10.2147/tcrm.s335219

12. Occhipinti, G., Greco, A., Angiolillo, D.J. and Capodanno, D., 2023. Gender differences in efficacy and safety of antiplatelet strategies for acute coronary syndromes. Expert Opinion on Drug Safety, 22(8), pp.669-683. https://doi.org/10.1080/14740338.2023.2245331
13. Hyun, K., Negrone, A., Redfern, J., Atkins, E., Chow, C., Kilian, J., Rajaratnam, R. and Brieger, D., 2021. Gender difference in secondary prevention of cardiovascular disease and outcomes following the survival of acute coronary syndrome. Heart, Lung and Circulation, 30(1), pp.121-127. https://doi.org/10.1016/j.hlc.2020.06.026
14. Sotorra-Figuerola, G., Ouchi, D., García-Sangenís, A., Giner-Soriano, M. and Morros, R., 2022. Pharmacological treatment after acute coronary syndrome: baseline clinical characteristics and gender differences in a population-based cohort study. Atencion Primaria, 54(1), p.102157. https://doi.org/10.1016/j.aprim.2021.102157
15. Kytö, V., Sipilä, J., Rautava, P. and Gunn, J., 2021. Sex differences in outcomes following acute coronary syndrome treated with coronary artery bypass surgery. Heart, Lung and Circulation, 30(1), pp.100-107. https://doi.org/10.1016/j.hlc.2020.02.009