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Sex-based differences in presentation, treatment, and complications among middle-aged and older adults hospitalized for acute myocardial infarction: a cross-sectional study

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Abstract

Background: Sex-related differences in acute myocardial infarction (AMI) may involve clinical presentation, infarction phenotype, treatment, and short-term outcomes, with potential variation across age groups. This study evaluated sex-based differences among middle-aged and older patients hospitalized with AMI.

Methods: This observational study included 1,312 patients hospitalized with AMI between 4 May 2021 and 3 January 2024. Demographic characteristics, presenting symptoms, AMI subtype, Killip class, clinical variables, treatment, revascularization, and in-hospital outcomes were compared between women and men. Analyses were additionally stratified by age group. Categorical variables were analyzed using chi-square or Fisher's exact tests, and continuous variables using independent-samples *t*-tests or Mann–Whitney U tests, as appropriate. Effect estimates with 95% confidence intervals (CIs) were reported.

Results: Of 1,312 patients, 409 (31.2%) were women and 903 (68.8%) were men. Women more frequently presented with respiratory symptoms, other discomfort, gastrointestinal symptoms, and weakness/fatigue, whereas primary chest pain was more frequent among men. NSTEMI was more frequent among women than men (86.8% vs. 56.0%; OR 5.16, 95% CI 3.76–7.07; $P<0.001$), while STEMI was more frequent among men. Higher Killip classes were more frequently observed among women ($P<0.001$). Women also demonstrated higher GRACE scores and lower eGFR. Treatment patterns differed between sexes, and primary PCI among STEMI patients was more frequently documented among men. In-hospital mortality did not differ significantly between women and men (6.1% vs. 5.3%; OR 1.16, 95% CI 0.70–1.91; $P=0.560$). Age-stratified analyses demonstrated heterogeneous sex differences.

Conclusion: Sex-based differences in AMI were evident across presentation, infarction subtype, clinical risk profile, and treatment patterns, but were not associated with a significant difference in in-hospital mortality.

Keywords: Acute Myocardial Infarction; Age Factors; Cardiovascular Diseases; Sex Factors; Sex Characteristics

Background

Acute myocardial infarction (AMI) remains a major cause of morbidity and mortality worldwide, including in Pakistan. Sex-based differences in the clinical presentation, management, complications, and outcomes of patients hospitalized with AMI have been reported in previous studies. Women generally have a greater burden of comorbidities and may present with a broader range of symptoms than men. Differences have also been reported in the use and timing of reperfusion strategies, cardiac catheterization, and other evidence-based therapies, as well as in the occurrence of complications such as major bleeding and vascular access-related complications. Differences in management and outcomes have partly been attributed to the older age and greater comorbidity burden commonly observed among women presenting with AMI (1, 2).

Evidence from different populations has demonstrated variation in sex-based differences in clinical presentation and outcomes. The KAMIR-NIH multicenter study enrolled 13,104 patients with AMI across young and older age groups. Most participants were older patients (70.7%) and men. Among young patients, women had a higher rate of all-cause mortality than men (2.7% vs. 1.2%; adjusted HR, 3.305; 95% CI, 1.211–9.019; $p = 0.020$) (3). Other studies have reported varying findings with respect to clinical presentation and outcomes, suggesting that observed sex differences may vary across populations and clinical settings (4).

Clinical presentation represents an important component of AMI recognition. In a study of 225 patients presenting for the first time with AMI, chest pain was the most common symptom in both men and women, whereas non-specific symptoms, including nausea, back pain, dizziness, and palpitations, were more frequently reported among women (5). Similarly, the VIRGO study involving 2,985 patients presenting to emergency departments with acute coronary syndrome found that chest pain was the most common presenting complaint in both sexes, while women more frequently reported epigastric pain, palpitations, and shortness of breath. Women also reported a greater mean number of symptoms than men (6). In the ACI-TIPI multicenter study, chest pain remained the primary presenting symptom in both sexes, although women were older than men at presentation (7). These findings indicate that although chest pain remains a common feature of AMI in both sexes, differences may exist in the accompanying symptom profile.

Sex-based differences have also been described in the management of AMI. Previous studies have reported that women were less likely than men to receive certain established medical therapies, including aspirin and beta-blockers during hospitalization and statins at discharge. Differences have also been reported in the use of cardiac catheterization, thrombolysis, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG) (8). Although more recent studies have suggested improvements in some of these differences, the extent to which sex-based differences persist and the factors associated with them remain incompletely characterized. Age, comorbidities, socioeconomic status, race/ethnicity, clinical presentation, quality of care, and biological coronary vascular characteristics have been suggested as potential factors (9).

Age is an important consideration when evaluating sex-based differences in AMI. Older patients may have multiple comorbid conditions that can influence clinical presentation, treatment, and outcomes. Previous studies have reported substantial mortality among older patients with AMI despite advances in reperfusion and medical treatment (10). A four-year nationwide German study involving 875,735 patients with STEMI and NSTEMI reported that men constituted approximately 70% of the study population, while women accounted for approximately 30%. Women had higher in-hospital mortality in both STEMI and NSTEMI groups. Sex-specific cardiovascular risk factors in women, including early menopause, gestational diabetes, preeclampsia, eclampsia, and polycystic ovarian syndrome, have also been described in relation to cardiovascular risk (11).

Despite the available evidence, comparative assessment of sex-based differences in clinical presentation, treatment, and complications across middle-aged and older patients with AMI remains limited. Existing studies have frequently focused on specific age groups, individual clinical presentations, or particular aspects of treatment and outcomes. Consequently, the relationship between sex and these clinical characteristics across middle-aged and older patients remains incompletely characterized.

Evidence from Pakistan regarding sex-based differences in AMI is also limited in this specific population. Although previous studies have examined acute coronary syndromes and myocardial infarction in Pakistani patients, comparative information regarding clinical presentation, treatment, and complications among middle-aged and older men and women hospitalized with AMI remains insufficient. Therefore, this study aimed to determine sex-based differences in clinical presentation, treatment, and complications among middle-aged and older

adults hospitalized with acute myocardial infarction at Liaquat University Hospital, Hyderabad/Jamshoro, Pakistan.

Methods

Study design and setting

This hospital-based observational study was conducted in the Department of Cardiology, Liaquat University of Medical & Health Sciences, Hyderabad/Jamshoro, Pakistan. Patients hospitalized with acute myocardial infarction (AMI) were evaluated during the study period from 4 May 2021 to 3 January 2024. The study was designed to assess sex-based differences in clinical presentation, treatment, and in-hospital complications among middle-aged and older patients hospitalized with AMI.

Study population and patient selection

This evaluation was conducted per pre-specified inclusion-exclusion criteria for patients presenting to the cardiology department with acute myocardial infarction over the study period. A total of 1,312 patients constituted the final analytical dataset. The study design included patients of either gender with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI).

Patients were separated into two pre-ordained age groups: younger patients between 45–64 years and older patients between 65 and 85 years of age. This yielded a final cohort of 999 middle-aged and 313 older patients.

Patients were selected through consecutive non-probability sampling. Eligibility was defined according to the original study design, including patients ≥45 years of age with a new-onset AMI and who gave informed consent. Patients with a history of previous myocardial infarction, established cardiomyopathy or valvular heart disease, and those who had undergone coronary artery bypass grafting previously were excluded. Those patients with pregnancy, anemia, malignancy, chronic renal failure, chronic obstructive pulmonary disease, and chronic liver disease were also excluded because they can affect study outcomes. **Figure 1.**

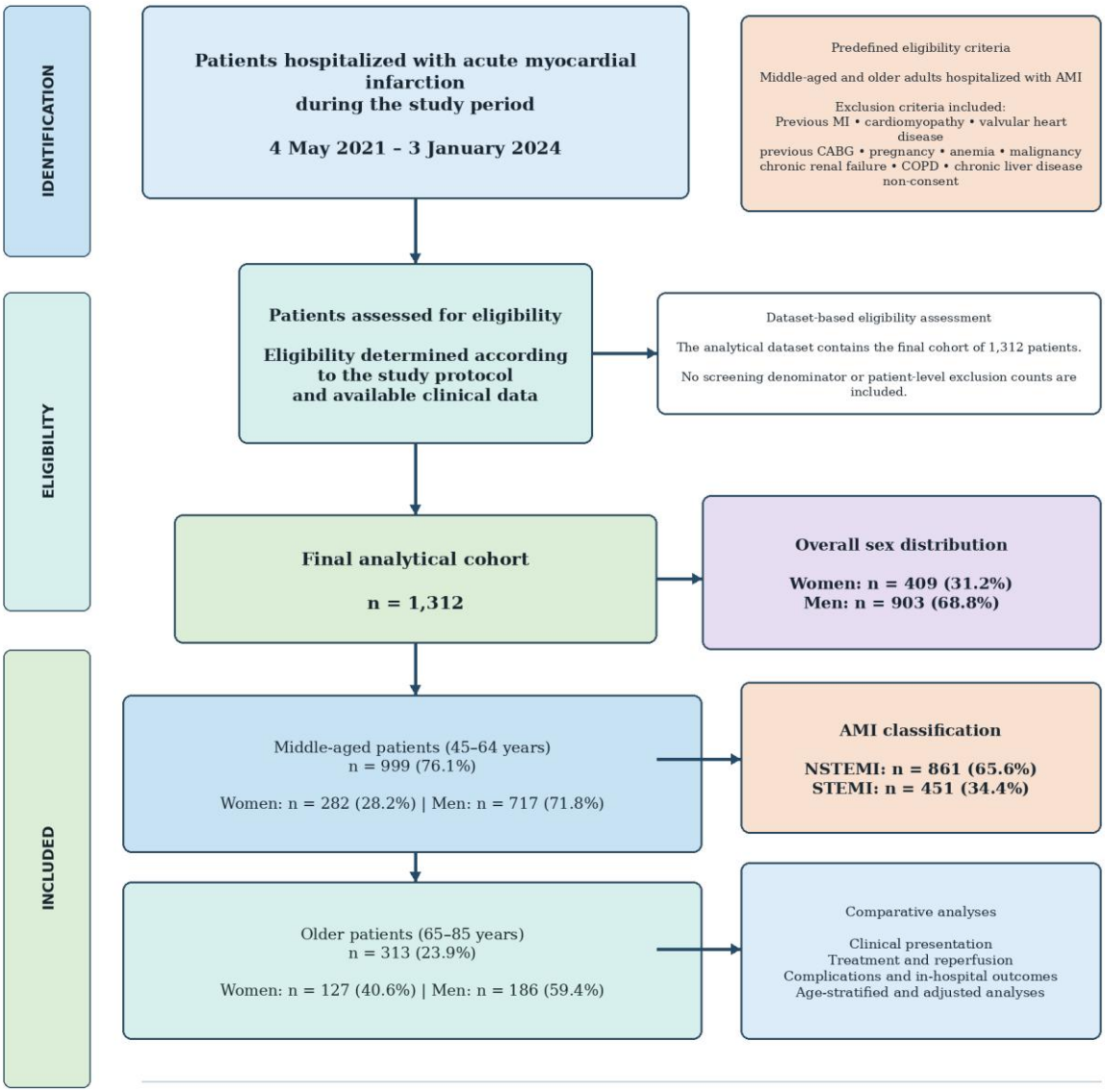


Figure 1. Flow diagram of patient inclusion

Diagnostic assessment

AMI was diagnosed according to the Fourth Universal Definition of Myocardial Infarction. The diagnostic assessment incorporated the clinical presentation, electrocardiographic findings, including ST-segment elevation or depression, and cardiac biomarker assessment, including troponin I and troponin T, as specified in the study protocol. Patients were classified as having STEMI or NSTEMI.

The study dataset additionally recorded STEMI subtype, including anterior, extensive anterior, inferior, high-lateral, and other documented STEMI patterns. Clinical severity at presentation

was assessed using Killip class, while TIMI and GRACE scores were recorded as measures of risk stratification.

Data collection and study variables

Data were collected with a structured data-collection instrument. The final dataset available for analysis comprised demographic characteristics; anthropometric measurements; cardiovascular risk factors; clinical presentation (chest pain, dyspnoea, palpitations); type of AMI (STEMI or NSTEMI); clinical severity (Killip class) and laboratory parameters including acute inflammatory markers such as CRP, procalcitonin and presence of leukocytosis at presentation; pharmacological treatment in-hospital; revascularization procedure adopted during index admission [percutaneous coronary intervention (PCI)(yes/no), CABG(yes/no)], left ventricular ejection fraction (LVEF)% assessed prior to discharge post-MI complications and in-hospital outcome.

The data on demographic variables included age, sex, residence, socioeconomic status, ethnicity and educational status. Hypertension, diabetes mellitus, dyslipidaemia, tobacco use (cigarette smoking and other documented addiction behaviours such as alcohol use) were considered cardiovascular risk factors.

Clinical presentation was assessed using the presenting symptoms recorded at admission, including chest pain, respiratory symptoms, gastrointestinal symptoms, other discomfort, and weakness or fatigue. Hemodynamic variables included systolic blood pressure, diastolic blood pressure, and heart rate. Laboratory variables included serum creatinine, estimated glomerular filtration rate (eGFR), troponin I, and random blood sugar. The dataset also included TIMI and GRACE scores and echocardiographic ejection fraction.

Anthropometric and laboratory assessment

Weight and height were recorded and used to calculate body mass index (BMI). BMI was categorized according to the predefined categories used in the study protocol. Estimated glomerular filtration rate was calculated using the Cockcroft–Gault formula.

For biochemical assessment, a 5-mL venous blood sample was obtained using a sterile disposable syringe by a senior laboratory technologist. Biochemical investigations included serum creatinine, troponin I, and random blood glucose.

Treatment and revascularization

Treatment administered during hospitalization was recorded for each patient. The dataset included aspirin, P2Y12 inhibitors, anticoagulation, nitrates, statins, beta-blockers, and angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or angiotensin receptor-neprilysin inhibitors.

Among patients with STEMI, the dataset recorded the revascularization strategy as primary percutaneous coronary intervention (PPCI), pharmacological reperfusion, or conservative management.

Clinical outcomes

The study evaluated in-hospital outcomes and post-MI complications. In-hospital outcome was categorized according to the patient's status at the end of hospitalization, including discharge without a documented post-MI complication, discharge with a post-MI complication, or in-hospital death.

The dataset additionally contains a dedicated post-complication variable and a categorical complication variable, allowing the occurrence and type of documented in-hospital complications to be evaluated.

Statistical analysis

Statistical analysis

Statistical analysis was performed using the complete dataset of 1,312 patients. Continuous variables were summarized as mean ± standard deviation or median with interquartile range according to data distribution, while categorical variables were presented as frequencies and percentages. Sex-based comparisons were performed using the independent-samples *t*-test or Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. All tests were two-sided, with $p < 0.05$ considered statistically significant.

Multivariable logistic regression analysis was performed for clinically relevant treatment and in-hospital outcome variables to estimate adjusted odds ratios (aORs) with 95% confidence intervals (CIs). Sex was evaluated as the primary explanatory variable, with clinically relevant

demographic and clinical covariates included in the models. Analyses were additionally stratified by age group (45–64 and 65–85 years). A sex-by-age-group interaction term was evaluated to determine whether the association between sex and in-hospital complications differed according to age group. Missing data were assessed before modelling, and no imputation was performed; patients with missing outcome data were excluded from the corresponding analysis. Model assumptions and potential multicollinearity were assessed before interpretation of regression estimates.

Ethical considerations

The study was approved by the Research Ethics Committee of Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro, Pakistan (Approval No. LUMHS/REC/-87; dated 3 May 2021). The committee reviewed the research protocol, REC application, and informed consent form before approving. Written informed consent was obtained from participants or their accompanying attendants before enrollment. Any subsequent changes to the research protocol or extension of the study period were subject to notification to the Research Ethics Committee, in accordance with the approval conditions.

Results

Study population

A total of 1,312 patients hospitalized with acute myocardial infarction (AMI) were included in the final analysis. The study population comprised 409 women and 903 men. The patient selection process and progression from the eligible hospital cohort to the final analytical population are presented in Figure 1. All subsequent analyses were performed using the available observations in the final dataset.

Baseline and demographic characteristics

The baseline characteristics demonstrated substantial differences in the demographic and clinical profile of women and men. The distribution of socioeconomic status, area of residence, ethnicity, educational level, body mass index categories, comorbid conditions, and addiction-related characteristics differed between the two sexes. Women had a greater representation of several cardiometabolic comorbidities, whereas addiction-related characteristics were more

frequently documented among men. These differences provide the demographic and risk-factor context for the subsequent comparison of clinical presentation and management. **(Table 1)**

Clinical presentation and type of myocardial infarction

Marked sex-based differences were observed in the presenting phenotype of AMI. Women more frequently presented with respiratory symptoms, other forms of discomfort, gastrointestinal symptoms, and weakness or fatigue, whereas chest pain as the primary presenting symptom was more frequently documented among men. The distribution of AMI subtype also differed substantially: NSTEMI predominated among women, whereas STEMI was considerably more frequent among men. At admission, women were also more frequently represented in the higher Killip classes, with the distribution across Killip I–IV differing significantly between the sexes. **(Table 2)**

Admission clinical characteristics and risk profile

The comparison of admission parameters showed relatively similar systolic and diastolic blood pressure and heart rate between women and men overall, although differences were observed for selected laboratory and risk-stratification variables. Women had lower estimated glomerular filtration rate and higher TIMI and GRACE risk scores, indicating differences in the clinical risk profile at presentation. Troponin I and random blood glucose did not demonstrate statistically significant overall sex-based differences. **(Table 2)**

Medical treatment and revascularization

Differences were also observed in the distribution of acute medical therapies. Women were more frequently treated with nitrates, β-blockers, and ACE inhibitor/ARB/ARNI therapy, whereas aspirin, P2Y12 inhibitors, and anticoagulation were more frequently documented among men. Statin use did not differ significantly between the sexes. Among patients with STEMI, primary PCI was more frequently documented among men, while a larger proportion of women had no documented revascularization. These findings describe differences in treatment patterns within the study cohort and do not by themselves establish whether sex independently determined treatment selection. **(Table 3)**

In-hospital outcomes

Regarding in-hospital outcomes, most patients were discharged without a documented post-MI complication, while a smaller proportion were discharged with complications or died during hospitalization. The overall distribution of these outcome categories did not demonstrate a statistically significant difference between women and men. In-hospital mortality was 6.1% among women and 5.3% among men, with no statistically significant sex-based difference. Similarly, the proportion discharged with a documented post-MI complication was not significantly different between the two groups. **(Table 4)**

Age-stratified clinical profile

Age-stratified analyses demonstrated that sex differences were not uniform across the middle-aged and older groups. Among middle-aged patients, women had higher rates of hypertension and higher TIMI and GRACE scores, whereas men had higher BMI, serum creatinine, eGFR, troponin I, and addiction-related measures. Among older patients, women continued to demonstrate higher hypertension prevalence and higher GRACE scores, while men had higher BMI, eGFR, troponin I, random blood glucose, and TIMI scores. The magnitude and direction of several clinical differences therefore varied according to age group. **(Table 5)**

The age-stratified comparison further demonstrated distinct patterns in clinical presentation and AMI subtype. Among middle-aged patients, women had substantially higher odds of presenting with respiratory symptoms, other discomfort, and weakness/fatigue, while NSTEMI was more frequently observed among women and STEMI among men. Similar differences in symptom presentation persisted among older patients, particularly for chest pain, other discomfort, respiratory symptoms, and gastrointestinal symptoms. The corresponding effect estimates and confidence intervals are presented graphically in the age-stratified forest plot. **(Figure 2)**

Discussion

This study demonstrated that sex-based differences among patients hospitalized with acute myocardial infarction were expressed across clinical presentation, infarction phenotype, admission risk profile, treatment patterns, and age-stratified characteristics, while the overall difference in in-hospital mortality was not statistically significant. Importantly, the findings do

not support a simple interpretation in which one sex uniformly experiences poorer outcomes. Rather, the pattern was heterogeneous and differed according to age and clinical presentation.

Women in our cohort more frequently presented with respiratory symptoms, other discomfort, gastrointestinal symptoms, and weakness/fatigue, whereas men more commonly presented with chest pain as the primary symptom. This finding is consistent with contemporary evidence showing that women with acute coronary syndromes may have a broader symptom profile than men, although substantial overlap exists between the sexes. A systematic review and meta-analysis similarly found lower odds of chest pain among women but emphasized that the traditional distinction between “typical” and “atypical” symptoms may be misleading because many symptoms are shared by both sexes (12). A Pakistani study from Karachi also reported greater frequencies of nausea/vomiting, backache, palpitations, and epigastric pain among women with ACS, demonstrating that differences in symptom presentation are relevant within the local population (13).

The substantially higher proportion of NSTEMI among women in our cohort is also compatible with findings from contemporary registries. In the European Society of Cardiology ACVC-EAPCI NSTEMI registry, women with type 1 NSTEMI were older, had a greater burden of comorbidity, and were more frequently categorized as having higher ischemic risk (14). Similarly, a large Chinese registry demonstrated persistent sex differences in cardiovascular risk factors and invasive management among patients with NSTEMI, although differences in mortality changed substantially after accounting for age and other characteristics (15). These observations reinforce the importance of interpreting sex differences together with the underlying clinical phenotype rather than considering sex in isolation.

A notable finding in the present study was the higher representation of women in the more advanced Killip classes and the higher GRACE score among women. These findings suggest a greater measured burden of acute clinical risk at presentation. Contemporary work has questioned whether commonly used risk tools perform identically across sexes. In a very large multinational analysis, the GRACE 2.0 score underestimated in-hospital mortality risk in women with NSTE-ACS, and incorporation of sex-specific information improved risk classification in the updated GRACE 3.0 model (16). Earlier validation work also demonstrated sex-related differences in GRACE discrimination, particularly among women with STEMI (17). Thus, the higher GRACE scores observed among women in our cohort should be

interpreted as part of a broader difference in admission risk profile rather than as evidence of an inherently worse prognosis attributable to sex alone.

The treatment findings require particularly careful interpretation. Women were more frequently documented as receiving nitrates, β-blockers, and ACE inhibitor/ARB/ARNI therapy, whereas aspirin, P2Y12 inhibitors, and anticoagulation were more frequently documented among men. Among patients with STEMI, primary PCI was more frequently documented among men. These findings differ in some respects from reports from other healthcare systems, where women have been less likely to receive invasive management and guideline-based therapies. For example, contemporary NSTEMI data have demonstrated lower rates of angiography and PCI among women, while an Australian STEMI registry similarly reported lower odds of coronary angiography, revascularization, timely vascularization, and primary PCI among women (18). A nationwide German analysis likewise reported lower PCI use among women with both STEMI and NSTEMI (11). However, these external findings should not be directly interpreted as evidence that women in the present cohort received inferior care, because treatment selection may reflect differences in infarction type, clinical risk, contraindications, presentation characteristics, and other factors not fully captured by the present analysis.

The age-stratified findings provide an important additional dimension. The direction and magnitude of several sex differences changed between the middle-aged and older groups. Women had higher hypertension prevalence in both age groups, while differences in BMI, renal function, troponin, glucose, TIMI score, and GRACE score varied according to age. The clinical presentation also remained heterogeneous across age strata. These observations are consistent with large population-based analyses demonstrating that the relationship between sex and AMI outcomes is age-dependent rather than constant across the life course. In a national analysis involving more than 6.7 million AMI hospitalizations, sex differences in management were observed across age groups, while the magnitude and direction of mortality differences varied by age and MI subtype (19). Similarly, contemporary Japanese registry data involving more than 250,000 patients showed sex-specific differences in mortality and process-of-care measures across middle-aged, older, and oldest-old patients (20).

The present study also found that in-hospital mortality did not differ significantly between women and men despite the observed differences in presentation, Killip class, risk scores, and treatment patterns. This finding is important because previous literature has not produced a uniform direction of sex differences in mortality. In a large German real-world analysis, higher

crude mortality among women was substantially related to differences in age and cardiovascular risk profile (11). Conversely, other cohorts have reported higher female mortality after AMI, particularly in selected STEMI populations (21). A recent dual-cohort analysis further demonstrated that women undergoing primary PCI could have greater myocardial salvage and smaller infarct size despite being older and having a less favorable conventional risk profile (22). Taken together, these studies support caution against interpreting crude sex-based mortality differences as evidence of a uniform biological or treatment-related disadvantage.

Our findings should also be considered in the context of the distinction between observed treatment differences and causal disparities. Several contemporary analyses have demonstrated sex-related differences in invasive management, particularly among NSTEMI patients (18). However, individual-patient data from randomized trials evaluating invasive timing in NSTE-ACS found no significant sex difference in the primary composite of death or MI after early or delayed invasive strategies, emphasizing that sex-treatment relationships are complex and strongly dependent on clinical context (23). Therefore, the lower documentation of selected therapies or revascularization among women in our cohort should be regarded as an observed association requiring further investigation rather than proof of discriminatory or inappropriate care.

The study has several strengths. It included a relatively large real-world cohort of 1,312 consecutive hospitalized AMI patients, incorporated socioeconomic and demographic variables alongside clinical characteristics, and evaluated both treatment and in-hospital outcomes. The age-stratified analysis is particularly relevant because it demonstrates that sex differences were not homogeneous across the studied age groups. The combination of effect estimates and confidence intervals also provides greater interpretability than reliance on statistical significance alone.

Several limitations should nevertheless be acknowledged. The observational, single-center design limits generalizability and precludes causal inference. The analysis was based on variables available in the study dataset, and residual confounding cannot be excluded. Although the study demonstrated differences in treatment patterns, it was not designed to determine whether these differences resulted from sex itself, clinical indication, contraindication, disease severity, timing of presentation, or other unmeasured factors. Furthermore, the available analysis did not include adjusted regression modelling or imputation-based missing-data

analysis; consequently, the reported associations should be interpreted as unadjusted comparative findings. Finally, the study assessed in-hospital outcomes and therefore does not address longer-term mortality, recurrent infarction, or subsequent cardiovascular events.

Conclusion

In this cohort of 1,312 patients with acute myocardial infarction, sex-based differences were evident in presenting symptoms, infarction subtype, admission risk profile, treatment patterns, and age-stratified clinical characteristics, but not in overall in-hospital mortality. The findings emphasize that sex differences in AMI are heterogeneous and strongly influenced by age and clinical presentation. Further multicenter studies incorporating longitudinal outcomes and adjusted analyses are warranted to determine which observed differences represent independent associations and which reflect differences in baseline clinical risk.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethical Review Committee of Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro/Hyderabad, Pakistan (Approval No. LUMHS/REC/-1043). Written informed consent was obtained from all participants before enrollment.

Consent for publication

Not applicable.

Clinical trial number

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZIA contributed to the conception and design of the study, data collection, data organization, statistical analysis, manuscript drafting, and critical review. **AGM** contributed to study supervision, clinical oversight, methodological guidance, interpretation of findings, and critical revision of the manuscript. **SHM** contributed to clinical supervision, participant recruitment, interpretation of clinical findings, and critical revision. **MKS** contributed to study supervision, clinical data collection, interpretation of results, and critical revision. **NR** contributed to participant recruitment, clinical data collection, data organization, and manuscript review. **FM** contributed to clinical supervision, interpretation of findings, and critical revision. **MZB** contributed to clinical data collection, interpretation of findings, and critical revision. **SZ** contributed to data entry, data cleaning, and critical review of the manuscript. All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Authors' information

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Abbreviations

ACEi: Angiotensin-converting enzyme inhibitor
AMI: Acute myocardial infarction
ARB: Angiotensin II receptor blocker
ARNI: Angiotensin receptor–neprilysin inhibitor
BMI: Body mass index
CI: Confidence interval
eGFR: Estimated glomerular filtration rate

GRACE: Global Registry of Acute Coronary Events

LUMHS: Liaquat University of Medical & Health Sciences

NSTEMI: Non-ST-segment elevation myocardial infarction

OR: Odds ratio

PCI: Percutaneous coronary intervention

STEMI: ST-segment elevation myocardial infarction

TIMI: Thrombolysis in Myocardial Infarction

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Table 1. Baseline demographic, socioeconomic, anthropometric, comorbidity, and addiction characteristics of the study population stratified by sex (N =1,312)

Variable	Overall (N=1,312)	Women (n=409)	Men (n=903)	Effect estimate*	95% CI	*P* value
Demographic characteristics						
Age, years	57.5 ± 8.5	59.9 ± 9.0	56.4 ± 8.1	MD 3.51	2.67–4.35	<0.001
Age group, n (%)						<0.001
45–64 years	999 (76.1)	336 (82.2)	663 (73.4)	Ref.	—	
65–85 years	313 (23.9)	73 (17.8)	240 (26.6)	0.60	0.45–0.80	
Area of residence, n (%)						0.040
Rural	475 (36.2)	131 (32.0)	344 (38.1)	Ref.	—	
Urban	837 (63.8)	278 (68.0)	559 (61.9)	1.31	1.01–1.70	
Ethnicity, n (%)						<0.001
Sindhi	633 (48.2)	228 (55.7)	405 (44.9)	Ref.	—	
Urdu-speaking	406 (30.9)	122 (29.8)	284 (31.5)	0.76	0.58–1.00	
Punjabi	112 (8.5)	27 (6.6)	85 (9.4)	0.56	0.36–0.88	
Pashto	68 (5.2)	9 (2.2)	59 (6.5)	0.27	0.14–0.54	
Other	93 (7.1)	23 (5.6)	70 (7.8)	0.58	0.36–0.95	
Socioeconomic status, n (%)†						0.999
Lower socioeconomic class	550 (41.9)	171 (41.8)	379 (42.0)	Ref.	—	
Lower-middle class	388 (29.6)	121 (29.6)	267 (29.6)	1.00	0.76–1.33	
Middle class	342 (26.1)	107 (26.2)	235 (26.0)	1.01	0.75–1.35	
Upper class	31 (2.4)	10 (2.4)	21 (2.3)	1.06	0.49–2.29	
Level of education, n (%)						<0.001
Illiterate	692 (52.7)	297 (72.6)	395 (43.7)	Ref.	—	
Primary	311 (23.7)	80 (19.6)	231 (25.6)	0.46	0.34–0.63	
Secondary	178 (13.6)	23 (5.6)	155 (17.2)	0.20	0.13–0.32	
≥Bachelor	131 (10.0)	9 (2.2)	122 (13.5)	0.10	0.05–0.19	
BMI, kg/m²	25.6 ± 4.1	24.4 ± 4.4	26.1 ± 3.9	MD −1.70	−2.18–−1.21	<0.001
BMI category, n (%)						<0.001
Underweight	46 (3.5)	9 (2.2)	37 (4.1)	Ref.	—	
Normal weight	604 (46.0)	286 (69.9)	318 (35.2)	3.70	2.57–5.34	
Overweight	502 (38.3)	69 (16.9)	433 (48.0)	0.66	0.45–0.97	
Obese	160 (12.2)	45 (11.0)	115 (12.7)	1.61	1.05–2.47	
Comorbid conditions						
Hypertension, n (%)	772 (58.8)	323 (79.0)	449 (49.7)	3.80	2.90–4.98	<0.001
Diabetes mellitus, n (%)	574 (43.8)	196 (47.9)	378 (41.9)	1.28	1.01–1.62	0.047
Dyslipidemia, n (%)	265 (20.2)	88 (21.5)	177 (19.6)	1.12	0.84–1.50	0.468
Addiction and substance-use characteristics						
Addiction habit, n (%)	398 (30.3)	41 (10.0)	357 (39.5)	0.17	0.12–0.24	<0.001
Type of addiction, n (%)						<0.001
No addiction	1,042 (79.4)	377 (92.2)	665 (73.6)	Ref.	—	
Tobacco only	252 (19.2)	32 (7.8)	220 (24.4)	0.26	0.18–0.38	<0.001
Alcohol only	9 (0.7)	0 (0.0)	9 (1.0)	—	—	0.041
Tobacco + alcohol	9 (0.7)	0 (0.0)	9 (1.0)	—	—	0.041
Tobacco use, n (%)	261 (19.9)	32 (7.8)	229 (25.4)	0.25	0.17–0.37	<0.001

Alcohol consumption, n (%)	18 (1.4)	0 (0.0)	18 (2.0)	—	—	0.009

Abbreviations: BMI, body mass index; CI, confidence interval; MD, mean difference; OR, odds ratio; Ref., reference category.

* Effect estimates represent women compared with men. For continuous variables, the effect estimate is the mean difference; for categorical variables, odds ratios are reported relative to the stated reference category.

† Socioeconomic-status counts are based on the socioeconomic distribution previously provided for the full cohort and the sex-specific allocation established in the preceding analysis. Because the original socioeconomic variable was not present in the uploaded Excel dataset, these sex-specific values should be verified against the source records before final submission.

Table 2. Clinical presentation and admission characteristics of patients with acute myocardial infarction according to sex (N = 1,312)

Variable	Overall (N=1,312)	Women (n=409)	Men (n=903)	Effect estimate*	95% CI	*P* value
Clinical presentation						
Chest pain, n (%)	430 (32.8)	179 (43.8)	251 (27.8)	2.02	1.58–2.58	<0.001
Chest pain as primary symptom, n (%)	759 (57.8)	160 (39.1)	599 (66.3)	0.33	0.26–0.42	<0.001
Other discomfort, n (%)	250 (19.1)	145 (35.5)	105 (11.6)	4.17	3.13–5.56	<0.001
Respiratory symptoms, n (%)	305 (23.2)	176 (43.0)	129 (14.3)	4.53	3.46–5.94	<0.001
Gastrointestinal symptoms, n (%)	160 (12.2)	70 (17.1)	90 (10.0)	1.87	1.33–2.61	<0.001
Weakness/fatigue, n (%)	94 (7.2)	68 (16.6)	26 (2.9)	6.73	4.21–10.75	<0.001
Type of acute myocardial infarction						
NSTEMI, n (%)	861 (65.6)	355 (86.8)	506 (56.0)	5.16	3.76–7.07	<0.001
STEMI, n (%)	451 (34.4)	54 (13.2)	397 (44.0)	0.19	0.14–0.27	<0.001
Killip class at admission						
Class I, n (%)	992 (75.6)	211 (51.6)	781 (86.5)	Ref.	—	
Class II, n (%)	223 (17.0)	146 (35.7)	77 (8.5)	7.01	5.18–9.48	<0.001
Class III, n (%)	76 (5.8)	39 (9.5)	37 (4.1)	3.90	2.39–6.36	<0.001
Class IV, n (%)	21 (1.6)	13 (3.2)	8 (0.9)	6.02	2.39–15.18	<0.001
Overall Killip-class comparison	—	—	—	—	—	<0.001
Admission clinical variables						
Systolic blood pressure, mmHg	137.1 ± 24.8	137.4 ± 25.1	137.0 ± 24.7	MD 0.4	−2.3–3.1	0.77
Diastolic blood pressure, mmHg	84.0 ± 14.6	83.9 ± 14.6	84.1 ± 14.6	MD −0.2	−1.8–1.4	0.81
Heart rate, beats/min	88.1 ± 18.2	89.0 ± 18.7	87.8 ± 18.0	MD 1.2	−0.8–3.2	0.24
Serum creatinine, mg/dL	1.14 ± 0.47	1.15 ± 0.47	1.14 ± 0.48	MD 0.01	−0.04–0.06	0.68
eGFR, mL/min/1.73 m²	74.5 ± 29.1	72.2 ± 29.7	75.6 ± 28.8	MD −3.4	−6.7–−0.1	0.042
Troponin I, ng/mL	7.35 ± 8.03	7.63 ± 8.24	7.22 ± 7.93	MD 0.41	−0.47–1.29	0.36
TIMI score	3.67 ± 1.49	3.95 ± 1.48	3.54 ± 1.48	MD 0.41	0.23–0.59	<0.001
GRACE score	109.1 ± 23.7	114.1 ± 23.8	106.8 ± 23.1	MD 7.3	4.5–10.1	<0.001
Random blood glucose, mg/dL	181.0 ± 83.0	187.5 ± 86.4	178.1 ± 81.2	MD 9.4	−0.1–18.9	0.053

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; MD, mean difference; NSTEMI, non-ST-segment elevation myocardial infarction; OR, odds ratio; Ref., reference category; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.
* Effect estimates represent women compared with men. For categorical variables, ORs are presented; for continuous variables, mean differences represent women minus men. Killip class I was used as the reference category. The overall Killip-class *P* value represents the omnibus comparison across all four classes.

Table 3. Medical therapies on admission and revascularization among patients with acute myocardial infarction according to sex (N = 1,312)

Variable	Overall (N=1,312)	Women (n=409)	Men (n=903)	Effect estimate*	95% CI	*P* value
Medical therapies on admission						
Nitrates, n (%)	434 (33.1)	175 (42.8)	259 (28.7)	1.86	1.46–2.37	<0.001
Aspirin, n (%)	1,258 (95.9)	373 (91.2)	885 (98.0)	0.21	0.12–0.38	<0.001
P2Y12 inhibitor, n (%)	1,071 (81.6)	288 (70.4)	783 (86.7)	0.36	0.27–0.49	<0.001
Anticoagulation, n (%)	878 (66.9)	253 (61.9)	625 (69.2)	0.72	0.56–0.92	0.009
Statin, n (%)	430 (32.8)	138 (33.7)	292 (32.3)	1.07	0.83–1.37	0.616
β-blocker, n (%)	440 (33.5)	166 (40.6)	274 (30.3)	1.57	1.23–2.00	<0.001
ACE inhibitor/ARB/ARNI, n (%)	255 (19.4)	97 (23.7)	158 (17.5)	1.47	1.10–1.95	0.008
Revascularization among STEMI patients	**Overall STEMI (n=451)**	**Women (n=54)**	**Men (n=397)**			
No revascularization/conservative management, n (%)	111 (24.6)	31 (57.4)	80 (20.2)	5.12	2.83–9.27	<0.001
Primary PCI, n (%)	299 (66.3)	23 (42.6)	276 (69.5)	0.29	0.16–0.52	<0.001
Pharmacological revascularization, n (%)	28 (6.2)	0 (0.0)	28 (7.1)	—	—	0.036
Missing revascularization data, n (%)	13 (2.9)	0 (0.0)	13 (3.3)	—	—	—

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; CI, confidence interval; OR, odds ratio; PCI, percutaneous coronary intervention; Ref., reference; STEMI, ST-segment elevation myocardial infarction.
* Effect estimates represent women compared with men. For medical therapies, ORs represent the odds of receiving each treatment among women relative to men. For STEMI revascularization, ORs were calculated for each treatment category relative to all other documented revascularization categories. Revascularization analyses were restricted to the 451 patients with STEMI.

Table 4. In-hospital outcomes and post-myocardial infarction complications according to sex (N = 1,312)

Variable	Overall (N=1,312)	Women (n=409)	Men (n=903)	Effect estimate*	95% CI	*P*value
In-hospital outcome						
Improved and discharged without post-MI complication, n (%)	754 (57.5)	245 (59.9)	509 (56.4)	Ref.	—	
Discharged with post-MI complication, n (%)	485 (37.0)	139 (34.0)	346 (38.3)	0.83	0.65–1.06	0.132
In-hospital death, n (%)	73 (5.6)	25 (6.1)	48 (5.3)	1.16	0.70–1.91	0.560
Overall comparison of in-hospital outcomes						0.198
Post-MI complication status†						
No post-MI complication, n (%)	754 (57.5)	245 (59.9)	509 (56.4)	Ref.	—	
Post-MI complication present, n (%)	485 (37.0)	139 (34.0)	346 (38.3)	0.83	0.65–1.06	0.132
Mortality						
Survived to discharge, n (%)	1,239 (94.4)	384 (93.9)	855 (94.7)	Ref.	—	
In-hospital death, n (%)	73 (5.6)	25 (6.1)	48 (5.3)	1.16	0.70–1.91	0.560

Abbreviations: CI, confidence interval; MI, myocardial infarction; OR, odds ratio; Ref., reference category.
* Effect estimates represent women compared with men. ORs were calculated using patients who improved and were discharged without a post-MI complication as the reference for complication status, and survivors to discharge as the reference for mortality.
† Post-MI complication status was available for patients who survived to discharge; patients who died in hospital were not included in this binary comparison.

Figure 2. Age-stratified sex differences in clinical presentation, infarction type, revascularization, and in-hospital mortality

Legend: Forest plot demonstrating sex-based differences in selected clinical characteristics and outcomes separately among middle-aged and older patients with acute myocardial infarction. Effect estimates represent women compared with men within each age group. Odds ratios are presented with corresponding 95% confidence intervals; the vertical reference line represents an odds ratio of 1.0. The figure highlights differences in presenting symptoms, AMI subtype, STEMI revascularization, and in-hospital mortality across the two age groups.

Table 5. Age-stratified differences in clinical risk profile and severity markers according to sex

Variable	Middle-aged women (n=282)	Middle-aged men (n=717)	Effect estimate (95% CI)	*P*value	Older women (n=127)	Older men (n=186)	Effect estimate (95% CI)	*P*value
Anthropometric and haemodynamic variables								
BMI, kg/m²	24.39 ± 4.73	26.08 ± 4.07	−1.69 (−2.31 to −1.06)	<0.001	24.42 ± 3.70	26.17 ± 3.11	−1.75 (−2.54 to −0.96)	<0.001
Systolic BP, mmHg	141.47 ± 28.12	135.26 ± 24.19	6.21 (2.47–9.95)	0.001	130.89 ± 22.43	142.07 ± 21.41	−11.18 (−16.17 to −6.19)	<0.001
Diastolic BP, mmHg	87.16 ± 13.83	84.65 ± 13.99	2.51 (0.60–4.43)	0.010	79.92 ± 13.06	79.61 ± 17.24	0.31 (−3.06–3.69)	0.855
Heart rate, beats/min	92.31 ± 18.12	88.02 ± 17.88	4.29 (1.80–6.79)	<0.001	87.19 ± 23.46	82.95 ± 13.88	4.24 (−0.33–8.81)	0.069
Renal and biochemical markers								

Serum creatinine, mg/dL	1.06 ± 0.27	1.18 ± 0.57	−0.12 (−0.17 to −0.07)	<0.001	1.12 ± 0.29	1.13 ± 0.36	−0.01 (−0.08–0.06)	0.773
eGFR, mL/min/1.73 m²	62.64 ± 22.06	84.19 ± 29.31	−21.54 (−24.90 to −18.19)	<0.001	47.58 ± 14.82	73.69 ± 26.77	−26.11 (−30.76 to −21.46)	<0.001
Troponin I, ng/mL	6.75 ± 7.37	8.39 ± 8.58	−1.64 (−2.71 to −0.57)	0.003	3.94 ± 4.98	6.56 ± 7.66	−2.62 (−4.03 to −1.21)	<0.001
Random blood glucose, mg/dL	167.06 ± 71.67	179.47 ± 80.02	−12.41 (−22.65 to −2.18)	0.018	174.66 ± 68.95	212.39 ± 107.79	−37.73 (−57.39 to −18.06)	<0.001
Risk and severity scores								
TIMI score	3.80 ± 1.35	3.20 ± 1.36	0.60 (0.41–0.78)	<0.001	4.21 ± 1.48	4.93 ± 1.31	−0.72 (−1.04 to −0.40)	<0.001
GRACE score	107.37 ± 25.73	100.27 ± 16.84	7.11 (3.85–10.36)	<0.001	139.73 ± 21.18	124.79 ± 18.96	14.94 (10.34–19.55)	<0.001
Ejection fraction, %	47.52 ± 8.30	48.21 ± 9.48	−0.69 (−1.88–0.50)	0.257	48.78 ± 9.59	48.44 ± 9.12	0.34 (−1.79–2.47)	0.755
Comorbid conditions and risk behaviours								
Hypertension, n (%)	213 (75.5)	407 (56.8)	3.83 (2.81–5.22)	<0.001	110 (86.6)	123 (66.1)	2.86 (1.57–5.20)	<0.001
Diabetes mellitus, n (%)	139 (49.3)	332 (46.3)	1.49 (1.13–1.97)	0.005	57 (44.9)	86 (46.2)	0.78 (0.50–1.23)	0.282
Dyslipidemia, n (%)	53 (18.8)	132 (18.4)	0.94 (0.66–1.33)	0.717	35 (27.6)	41 (22.0)	1.64 (0.96–2.80)	0.068
Addiction habit, n (%)	14 (5.0)	273 (38.1)	0.07 (0.04–0.13)	<0.001	27 (21.3)	83 (44.6)	0.54 (0.32–0.91)	0.020
Tobacco use, n (%)	14 (5.0)	217 (30.3)	0.15 (0.09–0.27)	<0.001	18 (14.2)	48 (25.8)	0.47 (0.26–0.86)	0.013

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; eGFR, estimated glomerular filtration rate; GRACE, Global Registry of Acute Coronary Events; OR, odds ratio; TIMI, Thrombolysis in Myocardial Infarction.
Notes: Continuous variables are presented as mean ± standard deviation, with mean differences calculated as women minus men within each age group. Categorical variables are presented as *n* (%), with odds ratios comparing women with men within the corresponding age group. The middle-aged group comprised patients aged 45–64 years, while the older group comprised patients aged 65–85 years. Analyses were based on the available observations for each variable; no imputation was performed.

Graphical Abstract: Sex-based differences in clinical presentation, management, and in-hospital outcomes among middle-aged and older patients with acute myocardial infarction.
The illustration summarizes the principal findings from 1,312 patients, including differences in presenting symptoms, AMI subtype, clinical severity, treatment patterns, revascularization, and in-hospital mortality according to sex. Age-stratified analyses demonstrated heterogeneous sex differences across middle-aged and older patients.