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Sex differences in acute myocardial infarction: clinical characteristics, management practices, and outcomes for patients in a large tertiary hospital from Palestine

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ABSTRACT

Several studies have shown gender variations in acute coronary syndrome's clinical presentation, diagnosis, therapy, and outcomes. Both immediate and long-term outcomes were worse for women with the acute coronary syndrome than men. This study investigates the influence of sex differences on the clinical presentations, treatment approaches, and patient outcomes of acute myocardial infarction at a large tertiary hospital in Palestine. A retrospective cohort study included all patients with acute myocardial infarction who presented to An-Najah National University Hospital from January 2018 to December 2020. Of the 422 patients in this study, 96 (22.7%) were women. Compared to men, women were older (p <0.001) and had significantly higher rates of diabetes mellitus (p <0.001) and hypertension (p <0.001). Additionally, women had greater chances of complaining of atypical cardiac chest pain (p = 0.012). Furthermore, non-ST segment elevation myocardial infarction was more prevalent among women (p = 0.017). Regarding the hospital course, the median number of stents was statistically significant in men (p = 0.029), but women had significantly higher in-hospital mortality (p = 0.013) and a higher rate of blood transfusion (p = 0.026). Myocardial infarction presents differently in males and women. Women were older, had more comorbid conditions than men, had atypical presentations, and had higher in-hospital mortality rates. As a result, while evaluating and treating patients suspected of having a myocardial infarction, healthcare practitioners must account for these discrepancies to reduce the mortality rate among women.

Keywords: Palestine; Myocardial Infarction; Sex Differences; Presentation; Management; Outcome.

INTRODUCTION

Cardiovascular disease is the world's leading cause of morbidity and mortality [1, 2]. Acute coronary syndrome (ACS) is a term used to describe a spectrum of clinical presentations that result from acute myocardial ischemia. It includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). It constitutes a major element of ischemic heart disease [3]. Mortality due to ACS has declined in recent decades due to advances in therapy, lifestyle improvements, and an emphasis on primary prevention, yet high rates remain [4, 5]. Emerging evidence has revealed sex-specific variations in coronary function and anatomy, baseline risk factors, ACS clinical characteristics, pathogenesis, diagnosis, therapeutic efficiency, and outcomes in women [6-11]. Women's underrepresentation exacerbates these significant disparities in cardiovascular clinical studies [12-14].

Women's epicardial coronary arteries are smaller, resulting in increased endothelial shear stress, which might account for gender differences in susceptibility to CAD [15-17]. Low endothelial shear stress has been linked to plaque instability, pathological remodeling,

and local lipid accumulation [18]. Furthermore, the phenotype of low vascular resistance and anti-inflammatory activity mediated by estrogen protects against CVD. [19, 20]. Compared to men, women with ACS had even worse short- and long-term results [21-23]. Some predictors include old age at presentation, higher comorbid conditions, and atypical complaints. These atypical complaints might be attributed to delays in diagnosis and treatment, resulting in poor clinical outcomes [8, 9]. However, the mechanisms behind these variations remain largely unexplored [10, 11].

In Palestine, there are insufficient data studying sex differences in acute myocardial infarction. As a result, we opted to investigate the association between sex variations, clinical presentations, treatment processes, and patient outcomes in MI in a large Palestinian tertiary hospital. This study provides new information to help improve morbidity and mortality in our community.

METHODS

Study design, settings, and population

This retrospective study was conducted between January 2018 and December 2020 at An-Najah National University Hospital (NNUH), a large tertiary referral hospital. Its cardiology department is one of the main cardiology centers in the north of West Bank, with three interventional cardiology consultants providing continuous primary percutaneous coronary intervention (PCI) services day and night for patients from all over Palestine. The sample size was all MI patients admitted to An-Najah National University Hospital from January 2018 to December 2020. Age, sex, smoking history, STEMI, NSTEMI, comorbidities (e.g., hypertension, diabetes mellitus, chronic renal disease, cerebrovascular disease, dyslipidemia, and coronary artery disease), prior PCI, and previous coronary artery bypass graft (CABG) were collected and analyzed. The final study group consisted of 422 eligible patients.

Inclusion and exclusion criteria

Inclusion criteria

– Patients were over 18 years old.

– Meet MI criteria.

– Patients have presented or transferred to a large tertiary hospital with the required facilities.

Exclusion criteria

Patients who had MI during hospitalization.

Data collection

We designed a three-section data collection form.

– Section 1 includes demographic characteristics, including age, sex, and smoking status.

– Section 2 includes the type of MI, patient comorbidities, medication, PCI history, and CABG history.

– Section 3 includes clinical presentation, type of intervention made, in-hospital complications related to MI, and in-hospital mortality.

Ethical considerations

The research protocol, which includes the use and access of patient clinical data, was approved by the *Institutional Review Boards (IRB) of An-Najah National University* and the regional health authorities. We confirm that the information gathered was only utilized for clinical research.

Statistical analysis

The data were entered and analyzed using IBM-SPSS version 21, a widely used statistical software package. The data are presented as continuous variables' means and standard deviations (SD), while categorical variables are expressed as frequencies and percentages. The medians were used to represent nonnormally distributed variables (lower-upper quartiles). The variables' normality was then verified using the Kolmogorov–Smirnov test. To examine the significance between categorical variables, exact chi-square or Fisher exact tests were performed as needed. Next, the Kruskal–Wallis or Mann–Whitney tests were used for median differences between categories. A p-value of 0.05 was used to determine the significance threshold.

RESULTS

Four hundred twenty-two patients were enrolled in this study over two years, of whom

96 (22.7%) were women. The baseline features are shown in Table 1, stratified by sex. Compared to men, women were older (mean age 67 vs. 60 years; $p < 0.001$), were significantly less likely to use tobacco (2 vs. 63%: $p < 0.001$), and had significantly more diabetes mellitus (67 vs. 47%: $p < 0.001$) and hypertension (75 vs. 50%: $p < 0.001$). However, there was no substantial disparity in dyslipidemia between men and women (5 vs. 3%: $p < 0.319$), chronic renal disease (15 vs. 13%: $p < 0.653$), congestive heart failure (8 vs. 10%: $p < 0.547$), or stroke (5 vs. 4%: $p < 0.603$). Regarding the history of CABG and PCI, there were no notable disparities between women and men (6 vs. 9%: $p < 0.283$ and 27 vs. 30%: $p < 0.573$, respectively). More commonly, women who presented to the hospital had atypical chest pain (44 vs. 31%; $p = 0.012$).

Table (1): Baseline characteristics of patients with myocardial infarction according to sex.

Variable	Male (n=326), n (%)	Female (n=96), n (%)	*P* value, n (%)
Age, (mean±SD, years)	60.02±10.870	67.85±10.703	<0.001
Risk Factors			
Smoking	206 (63.2)	2 (2.1)	<0.001
DM	154 (47.2)	65 (67.7)	<0.001
Hypertension	166 (50.9)	72 (75)	<0.001
Dyslipidemia	10 (3.1)	5 (5.2)	0.319
History of CABG	32 (9.8)	6 (6.3)	0.283
History of PCI	98 (30.1)	26 (27.1)	0.573
Medical History			
CKD	45 (13.8)	15 (15.6)	0.653
CHF	34 (10.4)	8 (8.3)	0.547
Stroke	13 (4)	5 (5.2)	0.603
Chest pain character			
Typical	225 (69)	53 (55.2)	0.012
Atypical	101 (31)	43 (44.8)	0.012
Time , median (Q1-Q3) *	24 (4-48)	24 (18-48)	0.003
Type of MI			
STEMI	117 (35.9)	22 (22.9)	0.017
NSTEMI	209 (64.1)	74 (77.1)	0.017
Medication history			
Aspirin	204 (62.6)	53 (55.2)	0.193
Clopidogrel	47 (14.4)	11 (11.5)	0.459
B blocker	74 (22.7)	27 (28.1)	0.273
Statin	102 (31.3)	30 (31.3)	0.994
ACE-I	97 (29.8)	27 (28.1)	0.758
ARB	41 (12.6)	12 (12.5)	0.984
Anticoagulant	7 (2.1)	4 (4.2)	0.281
Laboratory Result			
Creatinine, median (Q1-Q3)	0.92 (0.8-1.3)	0.9 (0.7-1.3375)	0.181
Troponin, median (Q1-Q3)	1.7 (0.4-7.2)	1.285 (0.6-3.335)	0.412
Echocardiography			
LVEF, median (Q1-Q3)	50 (40-55)	45 (40-55)	0.582

Abbreviations: DM, diabetes mellitus; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; CKD, chronic kidney disease; CHF, congestive heart failure; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction.

*Time from symptoms to the presentation (hours).

Regarding the in-hospital course shown in Table 2, men had a significantly higher median number of stents used than women (p = 0.029). In contrast, women were significantly more likely to receive a blood transfusion (4 vs. 0.6%: p = 0.026). There were no statistically relevant variations in recurrent angina (0 vs. 0.6%: p > 0.999), reinfarction (1 vs. 0.6%: p = 0.54), cardiogenic shock (4 vs. 1%: p = 0.245), bleeding (1 vs. 0.6%: p = 0.54), renal impairment (5 vs. 3%: p = 0.408), or cardiac arrest (4 vs. 3%: p = 0.767). Women's in-hospital mortality rates were significantly higher than men's (7 vs. 2%: p = 0.013).

Table (2): In-hospital course of patients with myocardial infarction according to sex.

Variable	Male (n=326), n(%)	Female (n=96), n (%)	P value, n (%)
Number of coronary vessels, median (Q1-Q3)*	2 (1-3)	2 (1-3)	0.923
Number of stents, median (Q1-Q3)	1 (0-2)	1 (0-1)	0.029
Complications			
Recurrent angina	2 (0.6)	0 (0)	>0.999
Reinfarction	2 (0.6)	1 (1)	0.540
Cardiogenic shock	6 (1.8)	4 (4.2)	0.245
Bleeding	2 (0.6)	1 (1)	0.540
Transfusion	2 (0.6)	4 (4.2)	0.026
Renal impairment	11 (3.4)	5 (5.2)	0.408
Cardiac arrest	12 (3.7)	4 (4.2)	0.767
In-hospital mortality	7 (2.1)	7 (7.3)	0.013

*Number of major coronary vessels with significant lesions.

DISCUSSION

Emerging studies over the last decade have revealed sex variations in the clinical manifestations, diagnosis, pathogenesis, and therapy of ACS in women. ACS women were older and had many more comorbidities. They had atypical angina more commonly than men and took far longer to seek medical help. Furthermore, women are more prone to MI-related in-hospital complications and mortality [8, 24-27].

Several agencies have recently advocated for more women to be included in clinical trials investigating gender differences [28-30]. The proportion of women in clinical trials has increased recently, yet sex-specific analyses are still insufficiently undertaken[30]. In our study, the female proportion was 22.7%, less than that of other global studies, reaching almost 38.2% [31].

In this investigation, women with myocardial infarction were older, as in previous research [25, 32, 33]. This might be explained by estrogen's ability to protect against coronary vascular disease, presumably through anti-inflammatory effects and by producing low vascular resistance in blood vessels [19, 20]. Furthermore, women have increased endothelial shear stress, which protects against CVD by reducing lipid buildup and plaque instability [16-18].

Women reported significantly greater diabetes and hypertension than men in our study, consistent with previous research [8, 34, 35]. This is supported by the fact that there is evidence to suggest that women, on average, may experience more socioeconomic disadvantages and psychosocial stressors than men, which can lead to poorer physical and mental health outcomes and lower quality of life [36, 37]. This is consistent with the observation that women's psychological stress has grown dramatically over the previous two decades as their economic contribution and educational attainment have increased [38].

As in previous research, women are more likely to present with atypical angina and wait longer to seek medical attention [25, 39, 40]. Women are more likely to experience atypical symptoms during a heart attack, such as nausea, vomiting, back or jaw pain, shortness of

breath, or extreme fatigue, which may be mistakenly attributed to other conditions. This can lead to delays in seeking medical attention and receiving appropriate treatment for a heart attack. Additionally, women are more likely to downplay their symptoms or dismiss them as stress- or anxiety-related, which can delay seeking help. Both women and healthcare providers must be aware of these atypical symptoms and take them seriously to ensure timely and appropriate care [41]. As a result, women are at a higher risk of receiving an inaccurate diagnosis and delayed intervention, as proven by multiple studies finding significant system delays in women [42-44]. Furthermore, in some regions of our society, women may have reduced access to healthcare services, which can contribute to delayed presentation. As a result, women presenting with noncardiac symptoms, particularly those with cardiovascular risk factors, require attentive care.

Women are more likely to have NSTEMI as the primary diagnosis and require less angioplasty for therapy with fewer stents, consistent with prior research [42, 43, 45]. Women have a lower proportion of obstructive coronary artery disease and are more likely than men to develop microvascular angina [46, 47]. Others contend that the lack of sex recommendations and the significant proportion of women having nontypical symptoms and comorbid conditions contribute to women's lower likelihood than men of undergoing invasive cardiac intervention [48, 49].

The gender difference in the current study substantially influenced in-hospital complications such as blood transfusion and in-hospital mortality, which are greater in women. This finding is consistent with earlier research [25, 33, 43, 50-52]. Higher blood transfusion rates in women have been linked to advanced age, comorbidities, body weight, and homeostasis variations due to the menstrual cycle, hormonal contraceptives or hormonal replacement therapy (HRT), menopause, and pregnancy [53, 54]. Furthermore, estrogen's direct inhibitory action on platelet aggregation may contribute to women's higher bleeding risk [46, 47, 55].

Multiple factors might contribute to in-hospital mortality. For instance, women with ACS are often older and have more concomitant diseases than males. Furthermore, women are less likely than males to have chest pain, diagnostic electrocardiograph (ECG) abnormalities, or elevated troponin levels on arrival, resulting in an incorrect diagnosis and treatment delay [56-58]. Finally, women have more mental stress after ACS than men, which leads to worse results [47, 59-61].

This emphasizes the need for social health practitioners to perform more comprehensive assessments in hospitals and after discharge to enhance the psychosocial domain [47].

Study limitations

This study was carried out at a single center (NNUH), and the study population was comparatively small to examine all variables. Our data are based on an observational retrospective registry and did not include patients with acute myocardial infarction who had not been admitted to the hospital. Moreover, the female proportion in our study was less than that in other global studies, which could affect the results of our study. Other demographic characteristics, such as education level, geographical area, and economic status, were not considered. However, well-designed registry data will provide valid results.

CONCLUSIONS

Myocardial infarction manifests differently in men and women. Women had more comorbidities than males with an initial diagnosis of myocardial infarction. Women were often older than males and had higher in-hospital mortality rates. This increase in female mortality rates may be due to women having more atypical symptoms, resulting in misdiagnosis and undertreatment. We advocate that healthcare practitioners consider these disparities when diagnosing and treating patients suspected of having a myocardial infarction to reduce the fatality rate among women. We also suggest that future studies on myocardial infarction be performed in Palestine, given that there are preliminary studies on this life-threatening condition.

Ethics approval and consent to participate

The administrator of An-Najah National University Hospital and the institution's institutional review board (IRB) approved this study. The study methodologies were all carried out under the required laws and guidelines. Since we used retrospective data, An-

Najah National University's IRB omitted the requirement for informed consent.

Consent to publish

Not applicable

Availability of data and materials

Because of the ethical approval requirements regarding patient data and confidentiality, the datasets created and/or analyzed during the current research are not publicly available but accessible from the corresponding author upon justifiable inquiry. The abstract was released as part of institutional repositories' self-archiving initiatives (i.e., university repository).

Competing interests

The authors state that they have no conflicts of interest.

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None

Authors' contributions

MSJ, OSM, and YNA performed data collection, data analysis, and manuscript drafting after reviewing the literature. MA and YD participated in the study's design, assessed patients for eligibility, reviewed the literature, and provided an important manuscript revision. AAT drafted the manuscript, was responsible for the integrity of the data, and conducted a critical assessment of the research to improve its intellectual quality. The research was developed and designed by SHZ, who also oversaw, coordinated, and analyzed the data, provided critical feedback on interpreting the findings, and helped with the final manuscript writing. The final manuscript was then read by all authors and approved. This paper was included in a graduation project for the Doctor of Medicine program at An-Najah National University.

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