

## ORIGINAL ARTICLE

# The Insight into the Sex Differences in the Patients Diagnosed with Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention

HUMA NAEEM TAREEN<sup>1</sup>, AKHTAR SHER<sup>2</sup>, FOUZIA GOHER<sup>3</sup>, IFTIKHAR HUSSAIN<sup>4</sup>, MOHSIN SAIF<sup>5</sup>, MUHAMMAD REHAN KHAN<sup>6</sup>

<sup>1</sup>Interventional Cardiology Trainee, AFIC / NIHD, Rawalpindi

<sup>2</sup>Consultant Cardiologist/ Assistant Professor Cardiology, DHQ Teaching Hospital / GKMC, Swabi

<sup>3</sup>Assistant Professor Cardiology, Cardiac Complex, Bahawalpur

<sup>4</sup>Assistant Professor Cardiology, Niazi Medical and Dental College, Sargodha

<sup>5</sup>Classified Cardiologist, AFIC / NIHD, Rawalpindi

<sup>6</sup>Assistant Professor Cardiology, DHQ Hospital, DI Khan

Corresponding author: Akhtar Sher, Email:-dr\_akhtarsher@yahoo.com

## ABSTRACT

**Background:** The limited knowledge is present about the outcomes associated with the patients diagnosed with acute coronary syndrome (ACS). The insufficient data about the sex difference in the post-interventions outcomes and disparities in management is available.

**Objective:** This study aim was to determine the sex-related differences in the patient diagnosed with ACS. This study also aimed to determine how these differences have perished in a time span of one year.

**Study design:** It is a retrospective study with the statistical approaches.

**Material and Methods:** The data of the 1000 patients that visited to AFIC Rawalpindi was collected. The duration of the study was 6 months, from August 2021 to January 2022. The patients were diagnosed with the non-ST-segment elevation acute coronary syndrome were selected. The ethical and review board committee of the hospital approved the study. The patients were further grouped to ACS I and ACS II.

**Results:** Out of the 1000 patients taken, there were 650 patients that had acute coronary syndrome I while there were 350 patients that had acute coronary syndrome II. Among the 650 patients of ACS I there were 430 males and 220 were female patients. And among the 350 ACS II there were 230 males and 120 were female. The study indicate that the older women have the higher cases with reported history of heart failure and hypertension. The higher mortality cases were also observed in the females. The association between coronary angiography in-hospital use and female gender was very weak. The physicians underestimate the risk associated with the diagnosed patients that leads to less use of invasive strategies for treatment of the men and women.

**Conclusion:** Due to underestimation of the risks associated with the ACS patients the conservative methods are used for the treatment of the women. The poor in-hospital outcome are associated with the female gender. It was found that women are less likely to undergo coronary artery angioplasty and other cardiac procedures as compared to the male patients. Awareness is needed for both male and female to eliminate this gender disparity.

**Keywords:** Coronary angiography, acute coronary syndrome, percutaneous coronary intervention, post-interventions outcomes and heart failure.

## INTRODUCTION

Cardiovascular diseases are the major cause of increasing mortality rates worldwide. These are one of the global issue. The data has indicated that the incidence of the cardiovascular diseases are higher in the women than men. The prognosis of chronic diseases is also worst in the women. The proportion of the women affected by CVD is rising every day with the increase in the life expectancy<sup>1,2</sup>. The older women are more prone to the development of the CVD as compared to the older men. Similarly women share the higher burden of ischemic heart diseases. The higher mortality rates and worst baseline cardiovascular profile are observed in the women presented with the ACS undergoing PCI at hospital. The PCI is the first line of the treatment for the patients diagnosed with the ST-elevation myocardial infarction (STEMI)<sup>3,4</sup>. Although PCI procedure are observed to be less protective in women but their frequent use can be beneficial for the women.

The STEMI patient who undergoing PCI are highly recommended with the implantation of drug-eluting stents (DES). It is safe and beneficial procedure for patients. Few studies have suggested that the DES-based PCI in patients with ACS produce conflicting results<sup>5</sup>.

The gender related disparities are highly observed in the patients diagnosed with ACS. It is still remain questionable that do the sex related disparities of ACS management truly persist in the patients or not. The proportion of the fatal and non-fatal ischemic complications can be reduced in the patients diagnosed with ACS by invasive investigations and revascularization<sup>6</sup>. Because of the gender disparities in treatment strategies of ACS patients there is the lower proportion of women who undergo revascularization. This is a multifactorial problem. There is the higher prevalence of the comorbidities associated with the women diagnosed with ACS.

The incidence of the risk factors i.e diabetes hypercholesterolemia and hypertension are also higher in the women diagnosed with ACS as compared to the men<sup>7,8</sup>. The revascularization by percutaneous coronary intervention is seemed less suitable for the women as compared to the men because of the smaller coronary vessel women have.

The study aimed to determine the sex related disparities evidences in treatment and outcomes of the ACS diagnosed patients<sup>9</sup>.

## MATERIAL AND METHOD

The data of ACS I, ACS II was obtained from the hospital. The data of the 1000 patients who visited to AFIC Rawalpindi was collected. It is a prospective observational study. The duration of the study is from August 2021 to January 2022. The patients were diagnosed with the non-ST-segment elevation acute coronary syndrome were selected. The patients older than 18 years were selected for further study. The patients with incomplete data were excluded from the study.

The inclusion criteria was applied on the patients. The patients must have ACS and his electrocardiogram changes must be consistent with ACS. The history of coronary artery disease of every participants must be documented. The patient with ST-segment elevation  $\geq 0.1$  mV in  $\geq 2$  contiguous leads were excluded from the study. The patients observed with any other disease after final diagnosis were also excluded. The ethical and review board committee of the hospital approved the study. The patients were further grouped to ACS I and ACS II. The demographic features were reported and studied.

## RESULTS

The 1000 patient's data was taken for the study. Among 1000 patients taken, there were 650 patients that had acute coronary syndrome I. and there were 350 patients suffering from acute coronary syndrome II. The baseline features of all the admitted patients are described in table no.1. Among the 650 patients of ACS I there were 430 males and 220 were female patients. And among the 350 ACS II there were 230 males and 120 were female.

The age of the male patients was from 55-73 in case of ACS I and in case of ACS II it was from 56-78. The age of female patients was average 72 in case of ACS I and ACS II as well. The women in this study were significantly older as compared to male members therefore they had more chances to suffer from angina and related heart issues as compared to male. Women were seen to be showing less chances to have revascularization either by using PCI or CABG as compared to men.

Table 1: Baseline features of the patients as per their gender

| ACS I (n=650)                              |               |                | ACS II (n=350) |               |                |
|--------------------------------------------|---------------|----------------|----------------|---------------|----------------|
| Features                                   | Male (n= 430) | Female (n=220) | P value        | Male (n= 230) | Female n=(120) |
| Age                                        | 65 (55-73)    | 72 (62-79)     | -              | 63 (56-74)    | 72 (62-78)     |
| Medical history                            |               |                |                |               |                |
| Angina                                     | 62.8          | 62.7           | 0.05           | 58.0          | 53.4           |
| Heart failure                              | 12.2          | 14.3           | 0.010          | 23.4          | 20             |
| PCI                                        | 19.2          | 11.4           | 0.001          | 23.5          | 11             |
| Diabetes                                   | 26.6          | 31.9           | 0.002          | 27            | 29.7           |
| Hypertension                               | 45.7          | 62.7           | 0.001          | 56.7          | 68.2           |
| Clinical features at the time of admission |               |                |                |               |                |
| Heart rate                                 | 73 (62-90)    | 73 (63-90)     | 0.001          | 74 (65-94)    | 79 (69-94)     |
| Systolic BP                                | 148 (130-167) | 151 (132-171)  | 0.001          | 147 (129-167) | 151 (131-174)  |
| Abnormal initial biomarker                 | 41.8          | 37.2           | 0.019          | 52.5          | 54.3           |

The incidence of angina was reported by the patients and the data showed that there were 62% male patients that reported angina pain among the participants and same percentage was found for female of this group as well where 62.8% patients reported about the angina pain. Women had less chances to undergo coronary angioplasty than male members according to data shown in table 2 with the passage of time the coronary angiography usage by both male and female increased overall. The multivariable analysis showed that the female members of the study was kept as predictor (independent) of the mortality in the hospital.

Table 2: Medication usage within 24h by the male and female participants

| ACS I n= 650                   |           |              |         | ACS II n=350 |            |         |
|--------------------------------|-----------|--------------|---------|--------------|------------|---------|
| Features                       | Men n=430 | Women n= 220 | P value | Men n=230    | Women= 120 | P value |
| Medicines used within 24 hours |           |              |         |              |            |         |
| Aspirin                        | 90%       | 89%          | 0.001   | 93%          | 90%        | 0.005   |
| Heparin                        | 88%       | 90%          | 0.005   | 80%          | 60%        | 0.005   |
| In hospital procedures         |           |              |         |              |            |         |
| PCI                            | 16%       | 12%          | 0.005   | 13%          | 6%         | 0.001   |
| CABG                           | 6%        | 3%           | 0.005   | 34%          | 23%        | 0.001   |
| Coronary angioplasty           | 40%       | 35%          | 0.005   | 67%          | 61%        | 0.001   |

## DISCUSSION

Coronary artery disease is one of the most leading causes of death worldwide with every 1 in 4 deaths, if left untreated. Here in this study the gender base differences among patients that suffer from acute coronary syndrome was studied and the data of the patients was analyzed to look for the variations that exist between these two genders linked with coronary artery disease. The gender disparities exist among patients when it comes to early prognosis and prolonged treatment<sup>10-11</sup>. As per recent studies there were very few female patients that were treated with medicines like heparin, GPIIb/IIIa inhibitor as compared to the male patients.

As far as in-hospital angioplasty is concerned there are more number of male patients that carry out coronary angioplasty as compared to female. There was independently low percentage of female found for in hospital angioplasty. It was found that the underestimation of the risk is main reason why this ratio is less in female as compared to male<sup>12</sup>.

There were more mortalities of female in hospital due to coronary artery disease as compared to men. And this study was irrespective of age of the patient. Likewise, the disparities were commonly found in other management patterns as well<sup>13-14</sup>.

As per previous studies the baselines feature of male and female characteristics showed variations in NSTEMI-acute coronary syndrome. In this study the average age of women was found to be more than men. The incidence of diseases like hypertension, diabetes, heart failure was more commonly found among female patients as compared to male. However as per studies the incidence of PCI and CABG was found to be less in case of women<sup>15</sup>.

Irrespective of the fact that baseline characteristics show variation, the female members also showed same response to the medication like aspirin, anticoagulants etc. these studies reveal that the use of GPIIb/IIIa inhibitor can prove to be excellent to treat high risk patients. there were very few women that were treated with medications like heparin, thienopyridine etc as compared to the men. And previous studies support these findings. It was reported that women reported more dosing errors as compared to men, and because these dosing errors ultimately lead to bleeding issues with the use of anticoagulants prove to be one of the reasons of disparity among male and female members<sup>16</sup>.

Our study also shows that the men undergo coronary angioplasty more than female. Such findings were also found in previous studies as well where the gender base differences were found between male and female patients in case of coronary artery angioplasty.

There was negative prediction for angioplasty in case of female as compared to male and previous studies also supported this data. There were many hypotheses that tried to explain why there exists a gender based disparity between male and female patients in case of coronary artery disease management<sup>17-18</sup>.

One of the hypothesis included the appearance of vasospastic diseases and the occurrence of atypical symptoms in case of women because of which their diagnosis becomes even harder by the doctors. Women may also be presenting with non-obstructive coronary artery disease. Therefore, the physicians become reluctant in recommending the catheterization treatment for heart in case of women there is quite high cost of the treatment and there is uncertainty that either there is coronary obstructive lesion or not<sup>19</sup>.

As per studies recently it is suggested by the physicians that the younger female is less likely to be cared for by cardiac surgeon that prove to be one of the reasons of underutilization of certain evidence based treatment. However, in this study all the patients showed ACS and they will be given treatment under same consideration<sup>20</sup>.

This study has uniqueness as the data mentioned is the actual data taken from treating doctor's rationale so that a comparative and observational study can be carried out. The most common reason that was cited by physician and the patient was that the risk was not high enough to undertake the coronary angioplasty. And same remarks were given by both female and male participants. By using large files of data this study was able to explore trends that were changing with the passage of time. But this study was not completely adjusted for all kinds of confounders which can be one of the limitations of this study<sup>21,22</sup>.

## CONCLUSION

This study analyzed the gender differences among the patients with coronary artery syndrome that undergo percutaneous intervention. It was found that women are less likely to undergo coronary artery angioplasty and other cardiac procedures as compared to the male patients. great awareness is needed for both male and female to eliminate this gender disparity.

## REFERENCES

- Heer T, Hochadel M, Schmidt K, Mehilli J, Zahn R, Kuck KH, Hamm C, Böhm M, Ertl G, Hoffmeister HM, Sack S. Sex differences in percutaneous coronary intervention—insights from the coronary angiography and PCI registry of the German Society of Cardiology. *Journal of the American Heart Association*. 2017 Mar 20;6(3):e004972.
- Potts J, Sirker A, Martinez SC, Gulati M, Alasnag M, Rashid M, Kwok CS, Ensor J, Burke DL, Riley RD, Holmvang L. Persistent sex disparities in clinical outcomes with percutaneous coronary intervention: insights from 6.6 million PCI procedures in the United States. *PLoS one*. 2018 Sep 4;13(9):e0203325.
- Dey S, Flather MD, Devlin G, Brieger D, Gurfinkel EP, Steg PG, FitzGerald G, Jackson EA, Eagle KA, GRACE investigators. Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the Global Registry of Acute Coronary Events. *Heart*. 2009 Jan 1;95(1):20-6.
- Lu HT, Nordin R, Ahmad WA, Lee CY, Zambahari R, Ismail O, Liew HB, Sim KH, NCVD Investigators. Sex differences in acute coronary syndrome in a multiethnic Asian population: Results of the Malaysian National Cardiovascular Disease database—Acute Coronary Syndrome (NCVD-ACS) registry. *Global heart*. 2014 Dec 1;9(4):381-90.
- Blomkalns A.L., Chen, A.Y., Hochman, J.S., Peterson, E.D., Trynosky, K., Diercks, D.B., Brogan, G.X., Boden, W.E., Roe, M.T., Ohman, E.M. and Gibler, W.B., 2005. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) national quality improvement initiative. *Journal of the American College of Cardiology*, 45(6), pp.832-837.
- Sabbag A, Matetzky S, Porter A, Iakobishvili Z, Moriel M, Zwas D, Fefer P, Asher E, Beigel R, Gottlieb S, Goldenberg I. Sex differences in the management and 5-year outcome of young patients (< 55 years) with acute coronary syndromes. *The American Journal of Medicine*. 2017 Nov 1;130(11):1324-e15.
- Gudnadottir GS, Andersen K, Thrainsdottir IS, James SK, Lagerqvist B, Gudnason T. Gender differences in coronary angiography, subsequent interventions, and outcomes among patients with acute coronary syndromes. *American Heart Journal*. 2017 Sep 1;191:65-74.
- Josiah A, Farshid A. Gender is not a predictor of mortality or major adverse cardiovascular events in patients undergoing percutaneous coronary intervention for acute coronary syndromes. *Heart, Lung and Circulation*. 2019 May 1;28(5):727-34.
- Kumbhani DJ, Shishehbor MH, Willis JM, Karim S, Singh D, Bavry AA, Zishiri E, Ellis SG, Menon V. Influence of Gender on Long-Term Mortality in Patients Presenting With Non-ST-Elevation Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention. *The American journal of cardiology*. 2012 Apr 15;109(8):1087-91.
- Worrall-Carter L, MacIsaac A, Scruth E, Rahman MA. Gender difference in the use of coronary interventions for patients with acute coronary syndrome: experience from a major metropolitan hospital in Melbourne, Australia. *Australian Critical Care*. 2017 Jan 1;30(1):3-10.
- Ndrepepa G, Kufner S, Mayer K, Cassese S, Xhepa E, Fusaro M, Hasimi E, Schüpke S, Laugwitz KL, Schunkert H, Kastrati A. Sex differences in the outcome after percutaneous coronary intervention—a propensity matching analysis. *Cardiovascular Revascularization Medicine*. 2019 Feb 1;20(2):101-7.
- Borovac, J.A., Kwok, C.S., Mohamed, M.O., Fischman, D.L., Savage, M., Alraies, C., Kalra, A., Nolan, J., Zaman, A., Ahmed, J. and Bagur, R., 2021. The predictive value of CHA2DS2-VASc score on in-hospital death and adverse periprocedural events among patients with the acute coronary syndrome and atrial fibrillation who undergo percutaneous coronary intervention: a 10-year National Inpatient Sample (NIS) analysis. *Cardiovascular Revascularization Medicine*, 29, pp.61-68.
- Naito R, Miyauchi K, Konishi H, Tsuboi S, Ogita M, Dohi T, Kasai T, Tamura H, Okazaki S, Isoda K, Daida H. Gender difference in long-term clinical outcomes following percutaneous coronary intervention during 1984–2008. *Atherosclerosis*. 2016 Apr 1;247:105-10.
- Otten AM, Maas AH, Ottervanger JP, Kloosterman A, van't Hof AW, Dambrink JH, Gosselink AM, Hooftje JC, Suryapranata H, de Boer MJ, Zwolle Myocardial Infarction study Group. Is the difference in outcome between men and women treated by primary percutaneous coronary intervention age dependent? Gender difference in STEMI stratified on age. *European Heart Journal: Acute Cardiovascular Care*. 2013 Dec 1;2(4):334-41.
- Lee CY, Liu KT, Lu HT, Mohd Ali R, Fong AY, Wan Ahmad WA. 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*. 2021 Feb 8;16(2):e0246474.
- Pendyala LK, Torguson R, Loh JP, Kitabata H, Badr S, Dvir D, Barbash IM, Sattler LF, Pichard AD, Waksman R. Comparison of adverse outcomes after contemporary percutaneous coronary intervention in women versus men with acute coronary syndrome. *The American Journal of Cardiology*. 2013 Apr 15;111(8):1092-8.
- Tan YC, Sinclair H, Ghoorah K, Teoh X, Mehran R, Kunadian V. Gender differences in outcomes in patients with acute coronary syndrome in the current era: A review. *European Heart Journal: Acute Cardiovascular Care*. 2016 Nov 1;5(7):51-60.
- Mueller C, Neumann FJ, Roskamm H, Buser P, Hodgson JM, Perruchoud AP, Buettner HJ. Women do have an improved long-term outcome after non-ST-elevation acute coronary syndromes treated very early and predominantly with percutaneous coronary intervention: a prospective study in 1,450 consecutive patients. *Journal of the American College of Cardiology*. 2002 Jul 17;40(2):245-50.
- Lempereur M, Magne J, Cornelis K, Hanet C, Taeymans Y, Vrolix M, Legrand V. Impact of gender difference in hospital outcomes following percutaneous coronary intervention. Results of the Belgian Working Group on Interventional Cardiology (BWGIC) registry. *EuroIntervention: Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology*. 2014.
- Kim C, Redberg RF, Pavlic T, Eagle KA. A systematic review of gender differences in mortality after coronary artery bypass graft surgery and percutaneous coronary interventions. *Clinical Cardiology: An International Indexed and Peer-Reviewed Journal for Advances in the Treatment of Cardiovascular Disease*. 2007 Oct;30(10):491-5.
- Zhao Q, Zhang TY, Cheng YJ, Ma Y, Xu YK, Yang JQ, Zhou YJ. Triglyceride-glucose index as a surrogate marker of insulin resistance for predicting cardiovascular outcomes in nondiabetic patients with non-ST-segment elevation acute coronary syndrome undergoing percutaneous coronary intervention. *Journal of Atherosclerosis and Thrombosis*. 2021 Nov 1;28(11):1175-94.
- Hu C, Zhang J, Liu J, Liu Y, Gao A, Zhu Y, Zhao Y. Discordance between the triglyceride glucose index and fasting plasma glucose or HbA1C in patients with acute coronary syndrome undergoing percutaneous coronary intervention predicts cardiovascular events: a cohort study from China. *Cardiovascular diabetology*. 2020 Dec;19(1):1-3.