

**Review Article****Coronary artery disease in women in Pakistan: A systematic review analysis**

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**ABSTRACT**

Pakistani populations have one of the highest risks of coronary artery disease (CAD) in the world. Apart from smoking, women had more CAD risk factors (diabetes, hypertension, obesity, dyslipidaemia) than men. It is recognized that a better understanding of the topics is necessary for a meaningful communication between public, patients, and healthcare professionals. The aim of this paper will be to review the literature on the subject of CVD in women. The review will be in four sections, the first section will focus on contributions on mechanisms of pathophysiology, diagnosis, and treatment. In conclusion, this is the first large-scale population-based study from the Indo-Pakistan subcontinent, home to one-sixth of the world's population, on gender differences in CAD and its determinants. Our findings indicate that one in four subjects aged ≥40 years may have underlying CAD in urban Pakistan.

**Keywords:** CVD, Women, Diseases

**INTRODUCTION**

Coronary heart disease (CHD) is the leading cause of death world-wide. Although men have higher rates than women at all ages, and coronary disease occurs up to 10 years later in women CHD is a major cause of death for both sexes: the World Health Organisation estimates that 3.8 million men and 3.4 million women around the world die from it each year. Despite recent improvements, the mortality rate in the UK remains amongst the highest in the world and coronary prevention is a priority.<sup>1</sup>

In recent years, gender issues have received increasing attention in international health policy. For example, the recognition that medical research was largely based on the experiences of young white men led to initiatives to make research more gender sensitive in the United States, Canada, Australia and South Africa. It is therefore important that those caring for patients with CHD

have an understanding of the gendered nature of health and illness.<sup>2</sup> Even though women have a higher frequency of chest pain/angina than men, the incidence of obstructive CAD in the female population is lower when compared with men with similar symptoms. In addition, it would appear that young women with obstructive CAD have a worse prognosis after acute myocardial infarction (AMI), whereas older women in similar circumstances often present with larger number of comorbidities that adversely influence the outcome, when compared to men. Women with acute coronary syndromes (ACS) are also less likely to receive rapid effective diagnosis and treatment than are men.<sup>3</sup>

Regarding the North American population, the Women's Ischemic Syndrome Evaluation (WISE) study workshop from the National Heart, Lung and Blood Institute (NHLBI) released in 2004 an

executive summary in which a strategy for cardiovascular research and education for women must be developed. A number of targets were set in a few different areas, such as improving understanding of pathology and pathophysiology of gender differences in ischemic heart disease (IHD), improving understanding of symptom description and diagnostic tools, conducting gender-specific clinical investigation, investigating mechanisms for adverse cardiovascular events in an early phase of hormone replacement therapy (HRT) and promotion of translation research—approaches into actual practice.<sup>4</sup>

It is recognized that a better understanding of the topics is necessary for a meaningful communication between public, patients, and healthcare professionals. The aim of this paper will be to review the literature on the subject of CVD in women. The review will be in four sections, the first section will focus on contributions on mechanisms of pathophysiology, diagnosis, and treatment. The second section will concentrate on well known risk factors and novel risk markers. This will be followed by a section emphasizing new recommendations for clinical practice. Subsequently, attention will turn to preventive strategies recently established and recommendations for future research. The literature here reviewed leads to a request for future research regarding all steps of CVD evaluation, treatment and prevention focused on the female population.<sup>5-6</sup>

### **Objectives of the study**

Our aim is to analyse the risk factor of coronary heart disease in woman in Pakistani population by using past data and literature.

### **Coronary artery disease in female**

As far as we know, this is the first report of a large population-based study of gender differences in the prevalence and determinants of CAD in adults from an urban setting in the Indo-Pakistan subcontinent using doctors' reports and electrocardiographic criteria. The prevalence of CAD, whichever definition was used, and especially the non-Q wave major ECG changes, was remarkably higher in this urban population

than in populations of European origin,<sup>13</sup> and rural populations in the Indo-Pakistan subcontinent.<sup>8</sup>

We confirm that definite CAD, based on a doctor's report and Q waves on ECG, was twice as prevalent in men as in women. However, unlike populations of European origin, we not only show that ischemic or major ECG changes were highly prevalent in our population, but that the prevalence was twice as high in women as in men. Others indicate either similar or only a modestly increased prevalence of such ECG changes.<sup>9</sup>

The greater prevalence of CAD in the Indo-Pakistan population is likely to be due to a greater susceptibility to the metabolic syndrome; around a third to a half of these middle-aged men and women, respectively, were classified as positive for the metabolic syndrome using current criteria. The greater prevalence of definite CAD in men is largely due to the effect of smoking exposure, which owing to its substantially higher prevalence in men, overwhelms the impact of the greater prevalence of the metabolic syndrome in women.<sup>10</sup>

Previous studies in the Indo-Pakistan subcontinent have generally reported combined definite and probable CAD prevalence, and thus not demonstrated marked gender differences.<sup>7</sup> However, in a study from South India, the prevalence of T-wave changes was markedly higher in women than in men (11% vs 2%), reflecting our own observations of a substantially greater prevalence of ischemia and major changes on ECG in women.<sup>6</sup> These changes are not benign, and are thought to be indicative of myocardial ischemia, conduction abnormalities and early repolarization reflective of structural heart disease. We show that they are strongly and equally related to the metabolic syndrome in men and women, in particular the hypertensive and dysglycaemic components. In addition, previous studies show that these changes strongly predict events and mortality, with around a twofold increased risk, even on multivariate adjustment for the presence of hypertension, diabetes, overweight and obesity, dyslipidemia, and smoking status.<sup>11</sup> That the risk prediction is similar in Blacks and Whites suggests that these

abnormalities may well be important mortality predictors in other ethnic groups such as Indo-Pakistani populations.<sup>12</sup> Moreover, the identification of similar risk factors for definite CAD as well as ischemia on ECG in our study suggests that a common underlying mechanism may be responsible for these abnormalities in this population. Thus, we suggest that ECG changes are not benign in women, and indicate that CAD may be being underdiagnosed in Indo-Pakistani women, as evident by the discrepancy between gender differences in doctor-diagnosed heart attack and ECG changes suggestive of ischaemia.<sup>13</sup>

We sought to account for the greater prevalence of these changes in women by adjustment for their greater prevalence of the metabolic syndrome. However, surprisingly this made little difference to the odds ratio. Possible explanations for this are that we have either not properly accounted for our measured risk factors, or that there is some other unmeasured CVD risk factor, also highly prevalent in women which makes a stronger contribution. Support from the former hypothesis comes from two directions. In the UK, metabolic syndrome, and specifically insulin resistance, did not account for the greater CAD mortality in Indo-Pakistani migrants to the UK than in the general population. But an interaction was also noted between dysglycaemia and ethnicity on CAD mortality, such that diabetes increased CAD mortality by 2.78 times in Indo-Pakistanis, and only 1.46 times in Europeans.<sup>14</sup> The sample was too small in that study to explore these relationships further. It is also interesting to note that among the components that constitute the metabolic syndrome, hypertension appears to be most closely related to definite CAD as well as ECG changes, particularly in women. Possibly, the duration of hypertension, in particular untreated hypertension, which has been shown to be greater in women than men, accounts for some of the greater risk of CAD in women. This is consistent with data from China which suggests that hypertension has the highest attributable risk of cardiovascular mortality in women.<sup>15</sup>

Our study has potential limitations. First, we did not measure the presence of atherosclerosis or infarct directly. In addition, doctor-diagnosed heart attacks were not adjudicated. However, use of ECG is a well-established and validated method for assessment of ischemic heart disease in population-based studies.<sup>13</sup> Second, ECG coding for CAD based on Minnesota coding has not been specifically validated in Indo-Pakistani populations. This requires long-term cohort data in such populations. However, correlations of these ECG changes with angiographic evidence of CAD, and with mortality have been well documented in other populations.<sup>14</sup> Third, our study was limited to the population residing in Karachi, an urban area, and therefore, may not represent the rural population of Pakistan. However, the epidemic of heart disease is likely to emerge in urban areas first, and attempts to document and stem the epidemic should begin here.<sup>24</sup> Further, our findings are consistent with the recent INTERHEART study, which identified a high prevalence of CAD in this population.<sup>25</sup> Our study adds to INTERHEART and other facility-based studies as our study methodology of a door to door population-based approach ensured subject selection unbiased by health seeking behaviour on the part of the subject, or by selective detailed medical evaluation on the part of the healthcare provider.<sup>16</sup> Thus, we believe our rigorous study design, and the stringent, objective criteria used to define CAD maximize the generalizability, validity and reproducibility of our findings.

## CONCLUSION

In conclusion, this is the first large-scale population-based study from the Indo-Pakistan subcontinent, home to one-sixth of the world's population, on gender differences in CAD and its determinants. Our findings indicate that one in four subjects aged  $\geq 40$  years may have underlying CAD in urban Pakistan. Increasing age, history of smoking, and the metabolic syndrome are strongly associated with CAD, and women are at greater risk than men. Doctors should be alerted to the

high probability of this condition in Indo-Pakistani women, and further research conducted on why these women are at especially high risk. Concerted efforts are needed to reduce the burden of conventional risk factors for CAD, including hypertension, diabetes, dyslipidaemia, physical inactivity, tobacco use, unhealthy diets and obesity in this population, and must target both women and men.

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