Editorial

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Ischemic Heart Disease in Women-changing Perspective

Meenakshi Kadiyala*

Department of Cardiology, Saveetha Medical College, Chennai, Tamilnadu, India

***Corresponding author:** Kadiyala M, Department of Cardiology Saveetha Medical College, Chennai, Tamilnadu, India, Tel: +91 9840161911; E-mail: drmeenaram@gmail.com

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Editorial

The weaker albeit the stronger sex, at least before menopause was once thought to be immune to the vagaries of atherosclerotic heart disease, but this thinking is changing, though slowly over the years. At every age, more women die of heart disease than Cancer and a 50-year-old woman has a 46% risk of having IHD and 31% risk of dying from it whereas her chances of having or dying of breast cancer are 10% and 3% respectively [1]. The mortality for CAD has been decreasing in both sexes but there is some semblance to stagnation in women, reasons being multifactorial. A plethora of risk factors can predispose to IHD in women, ranging from Diabetes and Hypertension to Dyslipidemia to smoking and Obesity and the Stress of a multi-faceted and simultaneous multi-tasking personality, typical of a woman. Emerging and nontraditional risk of Ischemic cardiovascular disease in the woman, years after a pre-term delivery(PTD), hypertension of pregnancy and gestational diabetes(GDM) are gaining momentum, and to be added to the growing list on the side of the female gender are auto immune diseases like Rheumatoid arthritis(RA) and The Lupus syndrome(SLE). The Last but not the least is the side effects of breast cancer therapy which has offset the improved longetivity caused by therapeutic advancement of the same.1. Black women are 35% more likely to suffer from IHD than their white counterparts and a family history of CAD at a young age of <65 for women, and < 55 for men increases risk of the same in the offspring. In diabetic women, the relative risk of CAD was 44% greater when compared to diabetic men and 3 fold higher in contrast to non-diabetic women. Myocardial infarction (MI) occurred earlier and had a higher mortality and there was decreased long term survival after revascularization than in diabetic men. Although fewer adult women than men smoke, there is a 25% increased risk for CAD by cigarette smoking in women, compared with men and twice the risk of MI, compared with women nonsmokers irrespective of the intensity of smoking. The combination of smoking and the Oral Contraceptive Pill is formidable. The prevalence of obesity is higher among women than men and the impact of obesity on CAD development is also greater in women. According to Framingham Heart Study, obesity increased the risk of CAD by 64% in women and 46% in men. The National Health Interview Survey (NHIS) 2011 in adults reported that Inactivity was higher among women than men and that it increased with age from 26.1% at 18 y to 52.4% at ≥75 years. This is surprising because at a younger age, they who play the role of a carrier woman and home maker cannot be inactive and probably the lack of time did not enable them to meet The Physical Activity Guidelines of 150 minutes/week of moderate-intensity aerobic activity or 75 minutes/week of vigorous-intensity aerobic activity. Isolated systolic Hypertension occurs in approximately 30% of women >65 y resulting in an elevated risk of death from stroke or CAD. Blood pressure is also less well controlled in women than men and 23% of women and 38% of men above the age of 80 y have BP less than 140/90 mm Hg. Dyslipidemia has the highest risk among women compared with all other known risk factors for CAD. Low HDL is a better risk predictor in woman than in men and Lp(a) and Triglycerides can be more predictive in younger and older women respectively. Advanced lipid testing in the prediction of CAD events in women is promising particularly in the setting of continuing morbidity and near normal lipid levels. Even after treatment with conventional therapies, premenopausal women with CAD have dyslipidemia and significantly elevated levels of emerging risk factors such as ApoB, ApoB/ApoA1 ratio, hsCRP, lipoprotein (a), uric acid, T4, fibrinogen, and total leukocyte count as compared to controls ($p < 0.05$). Preterm delivery complicates 5% to 12.7% of deliveries and is considered an independent risk factor for subsequent long-term Cardiac related morbidity and hospitalizations. Meta-analysis with 198252 preeclamptic women revealed a 2.16-fold relative risk for IHD after 12 years [2]. Soluble Flt1 and soluble Endoglin (anti angiogenic factors) increasingly secreted by the placenta in pre eclampsia produce endothelial dysfunction, and whether this could this be extrapolated to the coronary micro vascular dysfunction (CMD) occurring later has to be further studied [3]. Gestational Diabetes mellitus increases the risk of developing DM by 7-fold and MI by 4-fold. An association between inflammatory diseases and coronary micro vascular disease is seen in both men and women. As the incidence of RA and SLE are more common in females, they may be considered as female specific risks for CAD. Radiation for breast cancer can lead to CAD few yrs to 20 yrs after exposure. Women with preexisting cardiac risk factors and radiation of left breast have a higher predilection. Women on breast cancer Chemotherapy like Capecitabine and Cisplatin can present with classic symptoms of angina or MI due to vascular spasm [4]. Stress is a powerful CAD risk factor,

especially in young women because they have to cope with work and home stress. Marital stress is a harbinger of unfavorable outcomes after a CAD event. Menopause portends overall increase in IHD risk due to the reduction in the hormones leading to dyslipidemia, hypertension and central obesity. Menopausal hormone therapy (MHT) may offer relief from menopausal symptoms in the short term, but over long-term, the harms outweigh the benefits and should never be prescribed for the purpose of preventing CVD. The results of the Women's Heart Initiative (WHI), the HERS study to name a few and meta-analysis of >39 000 women enrolled in 23 trials led to dramatic declines in the use of MHT worldwide. Lower bone mineral density, subclinical hypothyroidism and migraine also occur in women with CAD, and whether it's a cause or an association needs to be studied further. IHD in women includes atherosclerotic obstructive CAD, MI associated with non-obstructive coronary arteries (MINOCA), Spontaneous coronary artery dissection, cardiac syndrome X due to micro vascular dysfunction, Stress induced cardiomyopathy (Takotsubo Syndrome) and heart failure with preserved ejection fraction. Almost 64% of women who die suddenly of CAD have no previous symptoms. Any kind of symptom can be associated with MI in woman but according to The Framingham study, chest pain occurred more often than in men. Women are usually 7-10 years older at the time of MI and tend to wait longer than men before calling for help. 38% of women with an Ac MI will die within one year compared to 25% of men and 35% of women MI survivors will have another heart attack compared to 18% of men. STEMI is less common and bleeding was more common with thrombolysis in women. Mechanical complications occur more in women possibly because of less collaterals and more advanced micro vascular disease. They tend to have more skeletal muscle complaints with statin and the JUPITER trial revealed that women taking rosuvastatin had a greater increase in their HbA1c compared with placebo; however the benefits of statins outweigh the risk of diabetes. On discharge for NSTEMI, women were 3% less likely to receive Aspirin and β-blockers and 13% less likely to receive statin compared to men. They underwent fewer cholesterol screenings, fewer referrals for cardiac rehabilitation and women constituted only 25% in all heart related research studies. Twenty years after Bernadene Healy used the term Yentl Syndrome in 1991 to call attention to under diagnosis and under treatment of IHD in women, Dr. Noel Bairey Merz wrote an editorial for the European Heart Journal that "The Yentl syndrome is alive and well !, where she quoted two studies which brought out gender differences in treatment [5]. Women underwent fewer interventions in the acute phase but stable patients underwent more repeat angiograms. Primary and secondary prevention and treatment should be no different from that in men and more women than are now, should be referred for cardiac rehabilitation.

To conclude, at every age more women die of CAD than cancer and preventing, identifying and treating conventional and female specific risk factors has become a major focus to accomplish this goal. CVD presentations that are more prevalent or unique to women should be recognized and gender-specific approaches to research, with appropriate representation of women in cardiovascular trials is mandatory. The Yentl syndrome is still alive and well they say, but hopefully its end is not too far.

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