SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 6.
Issue: 4
Page N. 132-136
Year: 2022

Original Article www.wjahr.com

CORONARY ARTERY DISEASE IN DIABETIC WOMEN AND MEN –PROSPECTIVE STUDY AT TERTIARY CARE HOSPITAL FROM NORTH INDIA

Premshanker Singh*[1], Jyoti Verma[2], Himanshu Sharma[3], Granth Kumar[4] and Vidya Sagar[5]

[1]FMR Prof, Head Medicine & Dean, UP University of Medical Sciences (UPUMS) India.
[2]Assoc Prof Medicine, Dr RML Institute of medical Sciences Lucknow.
[3]Senior Resident Medicine, UPUMS, India.
[4,5]Assoc Prof Medicine, UPUMS, India.

Received date: 08 January 2022 **Revised date:** 28 February 2022 **Accepted date:** 20 March 2022

***Corresponding Author: Premshanker Singh**

FMR Prof, Head Medicine & Dean, UP University of Medical Sciences (UPUMS) India.

ABSTRACT

Previous analyses have shown that women with diabetes are at substantially increased risk of Coronary Heart Disease (CHD) compared with men. Several larger studies have been published on the sex-specific associations between diabetic women and men for incident CHD. We performed this study to provide the most reliable evidence of any sex difference in the effect of diabetes on subsequent risk of CHD This prospective population-based study was carried out at UP University of Medical Sciences, India wef 07 Apr 2006 t0 07 Apr 2017(11 yrs) years The diabetes have more than a 40% greater risk of incident CHD in women as compared with men. Data from Single center, including 858,5 individuals and 28,2 incident CHD events, were included. The RR for incident CHD associated with diabetes compared with no diabetes was 2.82 (95% CI 2.35, 3.38) in women and 2.16 (95% CI 1.82, 2.56) in men. The multiple-adjusted RRR for incident CHD was 44% greater in women with diabetes than in men with diabetes (RRR 1.44 [95% CI 1.27, 1.63]) with no significant heterogeneity between studies Coronary artery disease (CAD) is the leading cause of cardiovascular mortality worldwide Despite a recent decline in developed countries, both CAD mortality and the prevalence of CAD risk factors continue to rise rapidly in developing countries.

KEYWORDS: Coronary Heart Disease, Diabetes, Coronary Artery Disease.

INTRODUCTION

A lack of sex-specific data from early epidemiological studies has typically led to the assumption that the associations between risk factors and disease outcomes are equivalent in women and men. But, increasingly, evidence to support the existence of clinically meaningful sex differences in the relationships between certain risk factors, such as smoking and diabetes.[1,2,3,4,5] with chronic disease is becoming apparent, often with more detrimental effects of such risk factors in women than in men. Sex differences in risk factor–disease associations would not only have implications for patient management and treatment, but would also have repercussions on efforts to quantify the burden of disease due to specific risk factors, as most such studies use only a single estimate of risk that is uniformly applied to both men and women.[6,7,8,9] In 2006, a systematic review of 37 cohort studies of the sex-specific effects of diabetes on risk of fatal CHD suggested that women with diabetes had a near 50% greater excess risk compared with their male equivalents, even after consideration of differences in baseline levels of other major risk factors.[10,11,12,13,14] Since that report, estimates from a number of large and more contemporary cohort studies have been published, with many reporting incident as well as fatal CHD outcomes.[15,16,17,18,19]

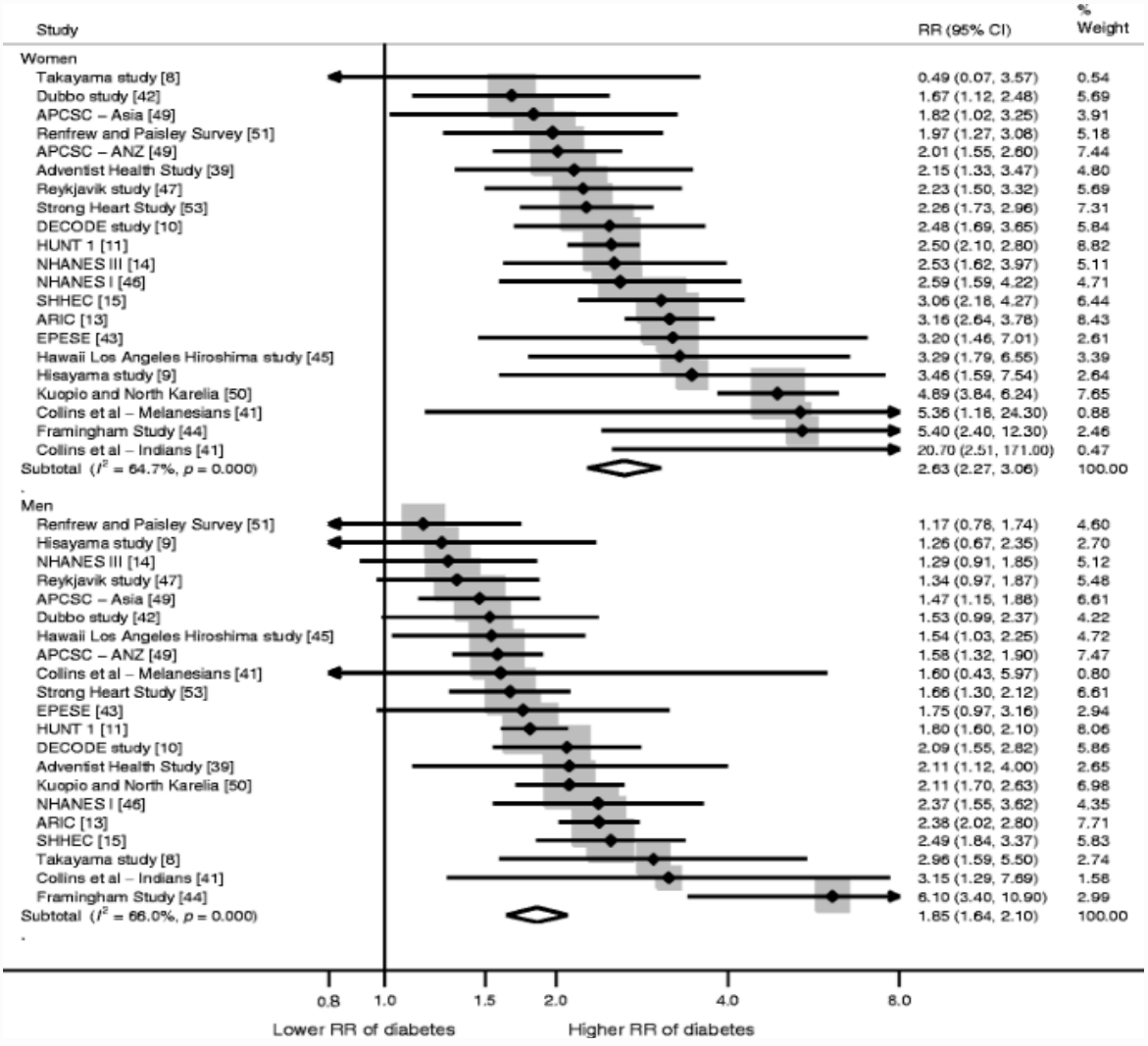
METHOD: We performed this study to provide the most reliable evidence of any sex difference in the effect of diabetes on subsequent risk of CHD This prospective population-based study was carried out at Medicine Dept of UP University of Medical Sciences India wef 07 Apr 2006 t0 07 Apr 2017(11 yrs) years Prospective population-based studies were included if they had provided RRs (or equivalents) for the associations between diabetes and CHD in men and women. Studies were excluded if they had not adjusted for at least age or did not provide information on the variability around the point estimate. The search strategy and items for data extraction were defined and agreed by all authors. For

each study, we obtained the sex-specific RRs for individuals with diabetes vs individuals without diabetes and 95% CIs through extraction of RRs from the published manuscripts or through new statistical analyses on the available individual participant data. We subsequently used these RRs to estimate the women-to-men ratio of RRs (RRR) and 95% CIs.[20,21,22] The primary endpoint was incident CHD (either fatal or non-fatal) and the secondary endpoint was fatal CHD, to facilitate comparison with previous reviews. Multiple-adjusted results were used in our primary analyses. The set of multiple adjustments made were allowed to vary by study, but had to include at least one other risk factor in addition to age. After natural log transformation of study-specific estimates, pooled estimates across studies were obtained using random-effects meta-analysis. The inverse of the variance of the log RR and of the log RRR were used to weight studies according to an estimate of statistical size.[23,24,25]

Sensitivity analyses were performed by age (≤60 vs >60 years), region and baseline year of data collection. The statistic was used to estimate the percentage of variability between studies.[26,27,28,29,30]

RESULT

Overall, data including 858,5 individuals (42% women) and 28,2 incident CHD events, were available. Individuals were between 20 and 80 years of age at baseline and the duration of follow-up ranged from 5 to 11 years. The average prevalence of diabetes at baseline was 3.4% among women and 4.8% among men.The overall summary RR for incident CHD associated with diabetes compared with no diabetes was 2.82 (95% CI 2.35, 3.38) in women and 2.16 (95% CI 1.82, 2.56) in men The statistic for heterogeneity between studies was 83% in women and 86% in men indicating substantial between-study heterogeneity. Exclusion of the four studies with only age-adjusted results reduced the between-study heterogeneity to 65% in women and 66% in men and mildly attenuated the RR estimates (RR 2.63 [95% CI 2.27, 3.06] in women and 1.85 [95% CI 1.64, 2.10] in men



Multiple-adjusted RR for incident CHD, comparing individuals with diabetes with those without diabetes.

The multiple-adjusted women-to-men RRR for incident CHD was 1.44 (95% CI 1.27, 1.63) Visual inspection of

the funnel plot showed minimal evidence for publication bias adjustment for which did not alter the results. There was no evidence that the pooled RRR varied materially by important study characteristics, namely: duration of study follow-up (p for heterogeneity = 0.16); the proportion of CHD events within each study ($p = 0.76$); the women-to-men ratio of the CHD event rate ($p = 0.93$); the prevalence of diabetes ($p = 0.58$); or the women-to-men ratio of diabetes prevalence ($p = 0.84$) In the sensitivity analysis there was no evidence that the multiple-adjusted RRRs for incident CHD differed materially by age or region (p value for interaction, 0.26 and 0.78, respectively); however, there was a borderline significant effect of year of study baseline on the RRR (p value for interaction = 0.048) Pooled estimates and RRR for the diabetes-related risk of fatal CHD In an analysis that included data including 7829 (91%) individuals and at least 16,9 fatal CHD events, the pooled multiple-adjusted RR estimates for fatal CHD associated with diabetes were 2.83 (95% CI 2.25, 3.54) in women and 2.04 (95% CI 1.72, 2.43) in men The corresponding women-to-men RRR was 1.44 (95% CI 1.20, 1.73) There was variation in the confounders that were adjusted for in the individual studies but, aside from age, most adjusted for blood pressure, cigarette smoking, BMI and lipids. Adjustment for major cardiovascular risk factors had only a small effect and attenuated the age-adjusted RR of diabetes for CHD to a similar extent in women (12%) and men (11%).

DISCUSSION

Thi study confirms the greater excess risk of CHD in women with diabetes compared with men with diabetes. The current estimate of 44% greater RR for incident CHD in women with diabetes compared with their male counterparts is comparable with the previous estimate of 46% excess risk for fatal CHD reported in a meta-analysis that was restricted to 37 cohorts and fatal CHD events, with about one-third the number of events available in the current study The sex difference in diabetes-related risk for CHD was consistent across subgroups defined by age and region and remained unchanged after excluding non-fatal CHD events. Furthermore, as the level of attenuation of the age-adjusted summary risk estimates was both moderate and equivalent in women and men the observed sex difference is unlikely to be driven by residual confounding. Recently, we have shown that the excess risk of stroke in individuals with diabetes is more than 25% greater in women than in men taken together with these current data, there is convincing evidence that.[28,29,30,31,32] diabetes poses a greater relative risk for cardiovascular diseases in women than men.

There is considerable uncertainty as to the mechanisms responsible for the observed greater coronary hazard conferred by diabetes in women compared with men. It has long been speculated that there is a widespread sex disparity in the management and treatment of cardiovascular risk factors in individuals with diabetes, to the detriment of women. Historically, women with diabetes were more likely to have a more adverse cardiovascular risk profile and were less likely to achieve the recommended levels of risk factors compared with male counterparts; in particular, this may have affected the sex-specific estimates from the older cohort studies that were established when there were significant disparities in treatment between sexes.[31,32,33] Even though treatment has become more equitable between the sexes, when treated similarly, diabetic women are still less likely than men to achieve target values for cardiovascular risk factors.[33,34,35] This might suggest that it is not the higher levels of cardiovascular risk factors or the relative under treatment in women alone that account for all of the excess risk of CHD induced by diabetes in women.

Alternatively, sex differences in diabetes-related changes in the levels of cardiovascular risk factors may play an important role. Indeed, there is accumulating evidence to support the hypothesis that women's metabolic and vascular risk factor profile has to deteriorate to a greater extent, i.e. that women have to 'travel further', than men to become diabetic. Several studies have shown that the difference in both traditional and novel cardiovascular risk factor levels in people with and without diabetes is significantly greater in women than in men.[31,32,33,34,35] Furthermore, in the prediabetic state where glucose tolerance may already be impaired but does not meet all diagnostic criteria of diabetes, risk factor levels are more elevated in women than in men.[31,32] Several studies have suggested that men develop diabetes at a lower BMI compared with women,[31,35] For example, in the UK General Practice Research Database, the BMI of individuals at the time of diabetes diagnosis was, on average, 1.8 kg/m^2 higher in women than in men,[32] Similarly, data from the UK Prospective Diabetes Study indicated that men with newly diagnosed diabetes were significantly less obese compared with newly diagnosed women.[34,35] It is conceivable, therefore, that the diabetes-related excess risk of CHD in women is not due to significant sex differences in the physiological effects and complications of diabetes. Rather, we hypothesise that the excess risk in women is due to a combination of both a greater deterioration in cardiovascular risk factor levels and a chronically elevated cardiovascular risk profile in the prediabetic state, driven by greater levels of adiposity in women compared with men. If confirmed, the implementation of sex-specific interventions before diabetes becomes manifest—such as increased screening for prediabetes, especially in women, combined with more stringent follow-up of women at high risk for diabetes, such as women with a history of gestational diabetes—could have a substantial impact on the prevention of CHD. Moreover, physicians may be more likely to recognise the early symptoms of CHD in men than women because of men's higher absolute risk, and thus sex differences in medication use and risk factor control may still exist. Greater awareness of early symptoms of CHD in women and sex-specific

therapeutic risk factor management, irrespective of the presence of diabetes, is optimal for improving clinical outcomes in both women and men.

CONCLUSION

Diabetes confers a significantly greater relative risk of incident CHD in women than in men. Higher levels of cardiovascular risk factors and relative under treatment in women compared with men are unlikely to account for all of the excess risk observed in women. Instead, we propose that a greater deterioration in cardiovascular risk profile combined with more prolonged exposure to adverse levels of cardiovascular risk factors among prediabetic women compared with their male equivalents, possibly driven by greater levels of adiposity, may be responsible for the excess risk of diabetes-related CHD in women.

Abbreviation

APCSC
Asia Pacific Cohort Studies Collaboration.

ARIC
Atherosclerosis Risk in Communities Study.

Nhanes III
National Health and Nutrition Examination Survey III.

RRR
RR ratio.

Shhec
Scottish Heart Health Extended Cohort Study.

Funding: None.

Conflict Of Interest: None.

Ethical Clearance: Taken from ethical committee of University.

REFERENCE

1. Peters SA, Huxley RR, Woodward M Smoking as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 81 cohorts, including 3,980,359 individuals and 42,401 strokes. Stroke, 2013; 44: 2821–2828.
2. Martiniuk AL, Lee CM, Lam TH et al The fraction of ischaemic heart disease and stroke attributable to smoking in the WHO Western Pacific and South-East Asian regions. Tob Control, 2006; 15: 181–188.
3. Oba S, Nagata C, Nakamura K, Takatsuka N, Shimizu H Self-reported diabetes mellitus and risk of mortality from all causes, cardiovascular disease, and cancer in Takayama: a population-based prospective cohort study in Japan. J Epidemiol, 2008; 18: 197–203.
4. Woodward M, Barzi F, Martiniuk A et al Cohort profile: the Asia Pacific Cohort Studies Collaboration. Int J Epidemiol, 2006; 35: 1412–1416.
5. The ARIC investigators The Atherosclerosis Risk in Communities (ARIC) study: design and objectives. Am J Epidemiol, 1989; 129: 687–702.
6. CDC (1994) Plan and operation of the Third National Health and Nutrition Examination Survey, 94. Series 1: programs and collection procedures. Vital Health Stat, 1988; 1: 1–407.
7. Woodward M, Brindle P, Tunstall-Pedoe H Adding social deprivation and family history to cardiovascular risk assessment: the ASSIGN score from the Scottish Heart Health Extended Cohort (SHHEC). Heart, 2007; 93: 172–176.
8. Penno G, Solini A, Bonora E et al Gender differences in cardiovascular disease risk factors, treatments and complications in patients with type 2 diabetes: the RIACE Italian multicentre study. J Intern Med, 2013; 274: 176–191
9. Franzini L, Ardigo D, Cavalot F et al Women show worse control of type 2 diabetes and cardiovascular disease risk factors than men: results from the MIND.IT Study Group of the Italian Society of Diabetology. Nutr Metab Cardiovasc Dis, 2013; 23: 235–241.
10. Kramer HU, Raum E, Ruter G et al Gender disparities in diabetes and coronary heart disease medication among patients with type 2 diabetes: results from the DIANA study. Cardiovasc Diabetol, 2012; 11: 88.
11. Winston GJ, Barr RG, Carrasquillo O, Bertoni AG, Shea S Sex and racial/ethnic differences in cardiovascular disease risk factor treatment and control among individuals with diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). Diabetes Care, 2009; 32: 1467–1469.
12. Evans RW, Orchard TJ Oxidized lipids in insulin-dependent diabetes mellitus: a sex-diabetes interaction? Metabolism, 1994; 43: 1196–1200.
13. J.C. Pickup.Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes Diabetes Care, 2004; 27(3): 813-823.
14. E. Eren, N. Yilmaz, O. Aydin.Functionally defective high-density lipoprotein and paraoxonase: a couple for endothelial dysfunction in atherosclerosis Cholesterol, 2004; 2013: 792090.
15. Y. Yan, Q. Chang, Q. Li, L. Li, S. Wang, R. Du, *et al.*Identification of plasma vascular endothelia-cadherin as a biomarker for coronary artery disease in type 2 diabetes mellitus patientsInt J Clin Exp Med, 2015; 8(10): 19466-19470.
16. M. Laakso.Cardiovascular disease in type 2 diabetes from population to man to mechanisms: the Kelly West Award Lecture Diabetes Care, 2010; 33(2): 442-449.
17. T.W. Jax, A.J. Peters, G. Plehn, F.C. Schoebel.Hem ostatic risk factors in patients with coronary artery disease and type 2 diabetes – a two year follow-up of 243 patientsCardiovasc Diabetol, 2009; 8: 48.

18. B. García-Fontana, S. Morales-Santana, C. Navarro, P. Rozas-Moreno, O. Genilloud, F. Pérez, *et al*.Metabolomic profile related to cardiovascular disease in patients with type 2 diabetes mellitus: a pilot study Talanta, 2016; 148: 96.
19. Z. Wang, H.Y. Song, M.M. An, L.L. Zhu Association of serum SPARC level with severity of coronary artery lesion in type 2 diabetic patients with coronary heart diseaseInt J Clin Exp Med, 2015; 8(10): 19290-19296.
20. S.K.P. Palazhy, D.M. Vasudevan Elevated oxidative stress among coronary artery disease patients on statin therapy: a cross sectional study Indian Heart J, 2015; 67: 227-232.
21. L. Guariguata, D.R. Whiting, I. Hambleton, J. Beagl ey, U. Linnenkamp, J.E. Shaw Global estimates of diabetes prevalence for 2013 and projections for 2035Diabetes Res Clin Pract, 2014; 103(2): 137-149.
22. D.R. Whiting, L. Guariguata, C. Weil, J. ShawIDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030Diabetes Res Clin Pract, 2011; 94(3): 311-321.
23. M.M. Al-Nozha, M.A. Al-Maatouq, Y.Y. Al-Mazrou, S.S. Al-Harthi, M.R. Arafah, M.Z. Khalil, *et al*.Diabetes mellitus in Saudi ArabiaSaudi Med J, 2004; 25(11): 1603-1610.
24. M.M. Al-Nozha, M.R. Arafah, Y.Y. Al-Mazrou, M.A. Al-Maatouq, N.B. Khan, M.Z. Khalil, *et al*.Coronary artery disease in Saudi Arabia Saudi Med J, 2004; 25(9): 1165-1171.
25. Garaulet M, Perex-Llamas F, Fuente T, Zamora S, Tebar FJ Anthropometric, computed tomography and fat cell data in an obese population: relationship with insulin, leptin, tumor necrosis factor-alpha, sex hormone-binding globulin and sex hormones. Eur J Endocrinol, 2000; 143: 657–666.
26. Howard BV, Cowan LD, Go O et al Adverse effects of diabetes on multiple cardiovascular disease risk factors in women. The Strong Heart Study. Diabetes Care, 1998; 21: 1258–1265.
27. Mansfield MW, Heywood DM, Grant PJ Sex differences in coagulation and fibrinolysis in white subjects with non-insulin-dependent diabetes mellitus. Arterioscler Thromb Vasc Biol, 1996; 16: 160–164.
28. Ossei-Gerning N, Wilson IJ, Grant PJ Sex differences in coagulation and fibrinolysis in subjects with coronary artery disease. Thromb Haemost, 1998; 79: 736–740.
29. Steinberg HO, Paradisi G, Cronin J et al Type II diabetes abrogates sex differences in endothelial function in premenopausal women. Circulation, 2000; 101: 2040–2046.
30. Wannamethee SG, Papacosta O, Lawlor DA et al Do women exhibit greater differences in established and novel risk factors between diabetes and non-diabetes than men? The British Regional Heart Study and British Women's Heart Health Study. Diabetologia, 2012; 55: 80–87.
31. Donahue RP, Rejman K, Rafalson LB et al Sex differences in endothelial function markers before conversion to pre-diabetes: does the clock start ticking earlier among women? The Western New York Study. Diabetes Care, 2007; 30: 354–359.
32. Haffner SM, Miettinen H, Stern MP Relatively more atherogenic coronary heart disease risk factors in prediabetic women than in prediabetic men. Diabetologia, 1997; 40: 711–717.
33. UK Prospective Diabetes Study IV. Characteristics of newly presenting type 2 diabetic patients: male preponderance and obesity at different ages. Multi-center Study. Diabet Med, 1988; 5: 154–159.
34. Logue J, Walker JJ, Colhoun HM et al Do men develop type 2 diabetes at lower body mass indices than women? Diabetologia 54:3003–3006 34.Paul S, Thomas G, Majeed A, Khunti K, Klein K (2012) Women develop type diabetes at a higher body mass index than men. Diabetologia, 2011; 55: 1556–1557.
35. Coronary heart disease in the prospective Dubbo Study of Australian elderly. Atherosclerosis, 117: 107–118.