

# CORONARY HEART DISEASE TOGETHER WITH DIABETES POSES A SERIOUS HEALTH THREAT

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## ABSTRACT

Among various risk factors, the most important is diabetes and its prime form, type 2 diabetes mellitus (T2DM), and has idiosyncratic connection with coronary heart disease (CHD). Diabetes patients have two- to four-fold higher threat of developing coronary disease than the people without diabetes, and cardio-vascular disease (CVD) is responsible for an irresistible 65-75 per cent of deaths in people with diabetes. Moreover considerably the age and sex-adjusted mortality risk in diabetic patients without pre-existing coronary artery disease was found to be equal to that of non-diabetic individuals with prior myocardial infarction (MI). These incredible results concerning higher risk of mortality have led to doubt that widespread precursors predispose to diabetes and CHD with subsequent implications that insulin resistance, visceral adiposity, and excess inflammation cause the pathophysiology of thrombogenesis. In addition, a complex mix of mechanistic processes such as oxidative stress, enhanced atherogenicity of cholesterol particles, abnormal vascular reactivity, augmented haemostatic activation, and renal dysfunction have been proposed as features characteristic of T2DM that may confer excess risk of coronary heart disease.

**KEY WORDS:** Idiosyncratic; Pathophysiology; Thrombogenesis; Atherogenicity Visceral Adiposity.

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## INTRODUCTION

Coronary heart disease (CHD) is at present the foremost basis of death all-inclusive and together with diabetes, poses a severe health threat, predominantly in the population of sub-continent. The risk issue management has evolved significantly with the continued emergence of new and challenging evidence. The flow of laboratory and population based research findings as well as uncertain controversies may pose dilemmas and contradictory impulses in most clinicians and even in more well-informed patients. Cardiovascular diseases (CVD), CHD and cerebro-vascular diseases, are currently the leading cause of death globally, accounting for 21.9% of total deaths, and are projected to increase to 26.3% by 2030.<sup>1</sup> The ubiquity of smoking, dyslipidaemia, obe-

sity, diabetes, and hypertension has been gradually escalating and are thought to be the driving influence behind the epidemic of heart disease faced today. Population of sub-continent descent makes over a fifth of the world's population. This population refers to an amalgamation of clinical (larger waist-to-hip and waist-to-height ratios signaling excess visceral adiposity), biochemical (insulin resistance, lower adiponectin, and higher C-reactive protein levels) and metabolic abnormalities (raised triglycerides, low high-density lipoprotein (HDL) cholesterol) that are more prevalent in individuals of South Asian origin and predispose this group to developing diabetes and premature CHD.<sup>2,3</sup> The absolute numbers of individuals with diabetes in Pakistan, Bangladesh and India, make three of the top ten countries worldwide and together, the region with the highest number of diabetes-related deaths currently.<sup>4</sup> The proportion of coronary disease patients with diabetes varies across countries, but approximately one-fifth of clinical trial (18%) and registry patients (15.1-21.4%) are documented as known diabetes patients. South Asians have higher prevalence of cardiovascular risk factors,<sup>5,6</sup> higher prevalence of T2DM, and earlier

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onset of CHD despite a normal body mass index (BMI), the premise that this population is more susceptible to diabetes and CVD, that these conditions are conceivably interlinked.<sup>2,5,7,8</sup> Though previously CHD and T2DM were considered mainly diseases of affluence, reversal of socio-economic gradient in these diseases is starting as lower socio-economic groups in South Asia are exhibiting ever-increasing risk.<sup>9</sup> In addition, characteristic disparities (rural-urban split, public-private health care and low awareness) that are pervasive across the region, combined with chronicity and asymptomatic nature (silent killer) of non-communicable risk factors and diseases, perpetuate delays in diagnosis, inertia to seek care, and effective self-management of risks. T2DM increases the risk of CHD events at least by two-to-three fold in type 2 diabetic subjects compared with nondiabetic subjects.<sup>10</sup> In type 2 diabetic women the relative risk is even greater. The reasons for this increased risk are largely unknown but could be related at least in part to more adverse changes in cardiovascular risk factors among diabetic women compared with diabetic men. Although the incidence of CHD events in non-diabetic subjects has considerably decreased during the last decades, this is not true for T2DM diabetic patients, particularly for women.<sup>9</sup>

## DISCUSSION

Broadly speaking, established CVD risk factors most often do not occur in isolation, and addition of associated morbidities results in multiplicative, rather than additive, amplification of risk.<sup>10</sup> Once any individual factor is identified, systematic, comprehensive, and regular assessments should be undertaken to identify the development of co-existing risks or target organ complications, and treatment plus monitoring should be diligently instituted.<sup>11</sup> Driven by physician eagerness, haste, and to some extent, pharmaceutical sector interests<sup>12,13</sup> and persuasion,<sup>14</sup> there has been strong emphasis on medication usage in managing dyslipidaemia, hypertension, and diabetes. This has detracted somewhat from the significant benefits that can be gleaned from alteration in lifestyle (nutrition,<sup>15</sup> weight, physical activity and tobacco use<sup>16</sup>) that occurs upstream of metabolic disturbances.

There is robust evidence that lifestyle modification (regular, moderate physical activity and healthy dietary habits) has a sustained effect on reducing incidence of diabetes<sup>17</sup>, and helps reduce the occurrence and mortality of CVD events in people with and without established CHD.<sup>18</sup> In patients with diabetes, where excess CVD risk has already been

demonstrated, the relationship between glycaemia itself and CVD should not, theoretically, be in doubt. Even studies in non-diabetic subjects<sup>19,20</sup> including a meta-regression analysis combining data from >95000 participants have shown an association between fasting blood glucose and CVD. Firstly, diabetes is still the leading cause of adult-onset blindness, end-stage renal disease, and non-traumatic lower-extremity amputations worldwide<sup>21,22</sup> and glycaemic control overwhelmingly reduces these microvascular complications.<sup>23,24</sup> Therefore, blood glucose management remains a vital component of preventing disabling and fatal target organ damage in both type 1 diabetes mellitus (T1DM) and T2DM. Secondly, optimal glycaemic targets have been chosen based on this evidence from microvascular risk reduction and should at least be deemed appropriate considering the increased risks of hypertension, dyslipidaemia, and hyperhomocysteinaemia - themselves strong risks for CVD - which are associated with renal insufficiency.<sup>25</sup> However, in the broader context of CVD prevention and considering the severity of chronic kidney disease, these targets may need to be customized according to individual risk.<sup>26</sup> A final and very convincing point is that glycaemia is not the sole consideration in CVD risk, but rather plays a role in the confluence of multi-factorial influences.<sup>27</sup> Glycogenic control is still exceedingly important in reducing micro-vascular complications and ensuing morbidity.

Diabetes is one of a multitude of risks associated with CVD and increases mortality independently of other factors. Therefore: (i) Comprehensive, multi-factorial risk factor control is necessary and beneficial for risk, morbidity, and mortality reduction. (ii) Although various drug trials are continuously ongoing, trials investigating alternative treatment strategies in populations of people with diabetes may offer novel clues regarding the mechanism of glycogenic involvement in cardio-metabolic risk (iii) Glycogenic control according to recommended targets ( $HbA1c \leq 7.0\%$ ) may need to be individualized<sup>26</sup>, for patients based on age, baseline level of control, co-existing morbidities, overall risk of diabetes-related complications and weighed against the risk of hypoglycaemia. Lifestyle modification provides low-cost, effective and pre-emptive benefits upstream of metabolic disturbances and therefore should remain a first-line or parallel intervention in all diabetes patients.<sup>27</sup> Patients face many challenges in managing the various components of care required in diabetes, therefore empowering patients to better self-manage and co-ordinate clinical aspects of patient care are significant steps to better care. Monitoring performance through audits and quality of care indicators will both improve diabetes care

but also motivate local standards of care, quality improvement and encourage physicians to strive to enhance their reputations. CVDs are slowly reaching out to all sections of the society. The estimates indicate a pattern of increase in the incidence of CVD amongst various age groups and across genders having diabetes. Therefore, a more detailed and continuous check on the prevalence of heart diseases is suggested to know the progress of the epidemic so that appropriate measure can be taken for prevention and control. Diabetes is a metabolic disease whose incidence and prevalence has significantly increased in recent decades, mainly because of an increase in T2DM, which represents almost 90% of all cases of diabetes. The World Health Organization estimates that, by 2025, there will be 300 million diabetic patients (5.4% of the world population).<sup>28</sup> Older patients are most affected by diabetes, as the disease prevalence increases with age, at least up until 75 years. The progressive aging of the global population could explain about half of the predicted increase of diabetic patients in the near future.<sup>28</sup> Macrovascular disease (CHD, stroke, and peripheral vascular disease) is responsible for the majority of morbidity and mortality associated with T2DM. In the United Kingdom prospective diabetes study (UKPDS)<sup>29</sup> the 10 year risk of all macrovascular complications was four times that of microvascular complications. Coronary artery disease is the leading cause of death among diabetic patients, and women have a higher cardiovascular risk than men. Diabetics have a worse prognosis after an acute coronary syndrome than non-diabetic patients. The Framingham heart study has also shown a higher mortality rate, as well as re-infarction and heart failure rates, in diabetic patients, both during the acute phase and in the post-infarction period, even after data adjustment for other risk factors. Diabetic patients may, therefore, derive a greater benefit from therapies shown to be effective in treating ischemic heart disease. In recent years, the importance of diabetes as a cardiovascular risk factor has increased. The myocardial metabolism of diabetic patients is significantly impaired, due to several factors that determine a significant decrease in the mechanisms that protect the heart from insults, such as preconditioning, in regard to ischemia/reperfusion injury. In order to change this reality, recent emphasis has been placed on optimizing diabetes treatment (namely using insulin and cardio protective oral hypoglycaemic drugs), as well as anti-ischemic therapy. In the near future, knowledge from basic research namely, improvement strategies for pro-survival pathways may offer diabetic patients a significant improvement in cardio protection, thus

decreasing the morbidity and mortality associated with diabetes.<sup>29</sup>

## CONCLUSION

Glycogenic and CVD risk factors control can be challenging in any context, not least in the sub-continent. If the quality of diabetes care is optimal in a region where dedicated, diligent follow up of diabetes patients has priority, results in low risks of CVD. Focused, context-specific research and careful analyses that integrate medication therapy and preventative lifestyle choices may cover the way for alignment of resources with needs, health systems development, and consequent reductions in morbidity and mortality.

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#### CONFLICT OF INTEREST

Authors declare no conflict of interest.

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None declared.