The Journal Of The International Federation Of Clinical Chemistry And Laboratory Medicine

eJIFCC

8 DIABETES MELLITUS AND CARDIOVASCULAR DISEASE

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Diabetes mellitus is chronic disease which has been described as a state of raised blood glucose associated with premature mortality. Diabetes is becoming a world pandemic. Both type 1 and type 2 diabetes are spreading rapidly across the globe. Globally there are already over 150 million people with diabetes, and this is conservatively predicted to double by 2025 [1]. Type 2 diabetes accounts for most of the current and forecasted figures. Less developed countries are shouldering most of the burden and, by 2025, one third of all people with diabetes will live in India or China alone [1]. In addition to these alarming absolute rises in numbers, there is also a worsening trend for the disease to affect younger age groups. In developed countries the sharpest increases affect the over 65s, unlike the situation in developing countries where most new cases occur in those between 44 and 65 years of age. Of particular concern is the worldwide emergence of type 2 diabetes in the very young, including children and adolescents. This downward shift, in the age at which diabetes develops, has serious implications for the development of complications. Diabetes complications, including cardiovascular disease (CVD), become more probable with the longer duration of diabetes, and are also more likely to develop at an earlier age.

8.1 Cardiovascular disease: the number one killer

CVD such as coronary heart disease, cerebrovascular disease and peripheral vascular disease are a major worldwide public health problem. It is the number one cause of death in industrialized countries. It is also set to overtake infectious diseases as the most common cause of death in many parts of the less developed world [1].

Although the problems associated with CVD are severe in all parts of the world, differences in patterns can be identified. In China, Japan and many Africans countries for example, stroke is more common than coronary heart disease whereas, among Caucasian populations, coronary heart disease is more common. In some developed nations, such as the USA, Australia and Europe, where coronary heart disease rates were previously very high, mortality has fallen in recent decades [1]. However in other areas such as Eastern Europe and the Middle East, the opposite is true. The “top ten” countries for both coronary and cerebrovascular disease mortality rates are now mainly from Eastern Europe and the former Soviet Union [1].

8.2 A ticking time bomb

As can be seen from the preceding paragraphs, both diabetes and CVD are major health problems. Since people with diabetes are at increased risk of CVD, the two situations when taken together constitute a “double jeopardy”. People with diabetes are two to four times more likely to develop CVD than people without diabetes, making it the most common complication of diabetes. When we consider that the number of people with diabetes around the world is predicted to double over the coming decades, the outlook for CVD becomes even more alarming.

In short, the predicted escalation in the prevalence of diabetes is likely to contribute to a CVD epidemic, particularly in the developing world - unless preventive measures are taken as a matter of urgency.

Diabetes is already consuming up to 10% of total national healthcare budgets in many countries. About half of this expense can be attributed to the costs of managing the complications of diabetes. Cardiovascular complications account for the bulk of this [2], as reflected in the patterns of hospital admission for the treatment of complications,

8.3 How does diabetes lead to cardiovascular disease?

Diabetes predisposes to CVD in a number of ways. People with diabetes are at increased risk of atherosclerosis, and, to make matters worse, atherosclerosis in people with diabetes is accelerated in development, more widespread and more severe.

High blood pressure is also at least twice as common in people with diabetes, and is also more frequent in people with impaired glucose tolerance [3].

Diabetes also has other effects on blood vessels, notably the specific complications of microangiopathy and neuropathy, together with damage to blood vessel walls. These complications not only produce specific diabetes-related problems such as retinopathy and nephropathy, but also synergize with atherosclerosis and hypertension to produce an ongoing cycle of blood vessel damage throughout the arterial system, affecting all sizes of vessel.

The causal link between hyperglycaemia and microangiopathy has been emphasized by a number of recent clinical trials, all of which show that the microangiopathic complications of diabetes are the most readily preventable with good glycaemic control [4, 5]. Endothelial dysfunction is an important component of both macroangiopathy and microangiopathy, but can also appear early in the course of diabetes before the onset of detectable vascular disease. The presence of these additional factors helps to explain why people with diabetes suffer more severe consequences from individual events such as heart attacks and strokes.

The presence of coexisting nerve damage in diabetes can affect the ability to feel pain. Thus, conditions such as heart attack and angina may go unrecognized because the sufferer feels no pain and the condition is "silent".

8.4 The cardiovascular disease triad in diabetes

In practice the most important clinical manifestations of diabetic vascular disease can be divided into the same three groups:

- those affecting the coronary circulation
- those affecting the cerebral circulation
- those affecting the lower limb

8.4.1 Coronary Heart Disease

Angina: When autonomic neuropathy is present, the typical pain of angina which is usually associated with ischemia may not be experienced, leading to silent ischemia.

Heart attack: People with type 2 diabetes have the same risk of heart attack as people without diabetes who have already had a heart attack [6]. People with diabetes can have a heart attack without even realizing it. Also, since people with diabetes often have widespread vascular disease, the consequences of a heart attack are often more severe than in people without diabetes, resulting in greater difficulty with emergency treatments. For these and other reasons, people with type 2 diabetes have a higher risk of death following a heart attack [7].

Sudden death: Men with diabetes are also more prone to sudden death compared to other people of a similar age, and this is particularly marked in women [8].

Heart failure: People with diabetes have a two to three-fold greater risk of heart failure when compared with non-diabetic people.

8.4.2 Cerebrovascular Disease

Stoke: Strokes occur twice as often in people with diabetes and hypertension as in those with hypertension alone [8].

Transient ischemic attack: Transient ischemic attack occurs between two and six times more frequently in people with diabetes [8].

Dementia: The additive effects of multiple small strokes, together with microangiopathy affecting the small blood vessels to the brain, lead to an increased likelihood of dementia in people with diabetes.

8.4.3 Peripheral Vascular Disease

Atherosclerosis of the arteries in the lower limbs together with nerve damage explains the very high risk of lower-limb amputation in people with diabetes, which is increased 15-40 fold compared to the general population [8].

The impact of diabetes is further emphasized by data from USA, where CVD mortality rates are falling in the general population. In men with diabetes they are also falling but to a much lesser extent and in women with diabetes the rates go against the trend and continue to rise [9].

As we have seen, diabetes can lead to cardiovascular damage in a number of ways. These processes do not develop independently, as each may accelerate or worsen the others. This means that when people with diabetes develop for example a heart attack or stroke, the prognosis is worse than for people without diabetes because of the vicious cycle caused by the combined vascular abnormalities associated with diabetes. Indeed, cardiovascular disease is the leading cause of death in people with diabetes in developed countries [8].

8.5 Why the increased risk?

About half of the excess risk in diabetes is explained by the fact that people with diabetes have a higher prevalence of many other CVD risk factors, such as hypertension, disturbances of blood fat levels and obesity [10]. These risk factors are interrelated and are more prominent in type 2 diabetes than in type 1.

Diabetes belongs to a special risk category as it so markedly the risk of cardiovascular disease [11]. The United Kingdom Prospective Study (UKPDS) has shown that there is a significant linear correlation between haemoglobin A1c and macrovascular events in type 2 diabetes [12]. This is also seen in people with more minor disturbances of blood glucose metabolism such as impaired fasting glycaemia (IFG) and impaired glucose tolerance (IGT) [13].

People with type 1 diabetes over the 30 years have a coronary heart disease risk similar to people with type 2 diabetes. People with type 1 diabetes who suffer from diabetic nephropathy, regardless of age, should be treated as being at particularly high risk.

It is important to emphasize that the presence of multiple cardiovascular risk factors has a multiplicative and not an additive effect upon the incidence of coronary heart disease in the general population [14]. The situations is even more serious in people with diabetes as, for each risk factor present, cardiovascular mortality is about thee times greater than in the general population [15].

Microalbuminuria, lipoprotein (a), homocysteine and C-reactive protein have also been shown to be risk factors for cardiovascular disease in people with diabetes [16, 17, 18].

Due to the higher prevalence and impact of cardiovascular risk factors, as well as the role of hyperglycaemia, people with diabetes without overt cardiovascular complications merit an intervention against risk factors similar to that which would normally be provided for individuals with established cardiovascular disease.

8.6 Diabetes care and management

The devastating complications of diabetes, such as CVD, kidney failure and blindness, are imposing a huge burden on health care services. It is estimated that diabetes accounts for between 5% stand 10% of a nation's health budget [2]. The human and economic costs of diabetes could be significantly reduced by investing in prevention, particularly early detection, to avoid the onset of diabetic complications.

There is good evidence from a number of recent clinical trials to show that control of blood pressure, blood lipids and blood glucose levels can all reduce substantially the risk of CVD events and diabetes-related death [19, 20, 21]. The figures vary according to the risk factor and the design of the study, but the percentage drops ranging from 30-60% are clearly well within reach. Despite these findings, a recent US study revealed that while cardiovascular disease mortality and particularly coronary heart disease related deaths have declined in those without diabetes, in men with diabetes the decrease has been a modest 13%, while in women with diabetes the rates have actually increased by 23% [9]. This suggests that approaches proven to reduce cardiovascular disease in people with diabetes are frequently not implemented in clinical practice.

Targets for common cardiovascular risk factors in people with diabetes:

Dyslipidaemia:

- Decrease LDL cholesterol levels (< 115 mg/dl or 3 mmol/L)
- Raise HDL cholesterol levels (>46 mg/dl or 1.2 mmol/L)
- Lower triglycerides (<150 mg/dl or 1.7 mmol/L)

Hypertension:

- Lower blood pressure (<135/85 mm Hg)

Hyperglycaemia:

- Reduce hyperglycaemia (HbA1c<7%)

These levels are based on IDF Europe's guidelines [22].

Once diabetes has become established in an individual there is a lot that can be done to prevent CVD and minimize risk. Once CVD has developed, and events such as heart attack or stroke have occurred, the aggressive application of modern treatments can still lead to improved outcomes. Measures such as insulin therapy, aspirin, certain drugs such as ß-blockers, hypolipaemic agents (statins, fibrates or a combination of the two), angiotensin converting enzyme (ACE) inhibitors, AT1 receptor blockers, calcium channel blockers, clot dissolving agents, and modern revascularization procedures can all improve outcome.

The major difficulty here is the provision of adequate resources, particularly in poorer countries. It also has to be remembered that many people may not survive an acute event to receive the benefit of these treatments. This serves to emphasize the importance of prevention, including both the primary prevention of diabetes and the secondary prevention of CVD in people who have already developed diabetes. Investment in primary and secondary prevention strategies is potentially the most effective measure in the long term, in both human and economic terms.

The major lifestyle measures - diet and physical activity - need to be emphasized in national diabetes and CVD programmes. These programmes can be integrated or linked with other health or environmental programmes. The message should be transmitted to all sectors of society, and ideally should be addressed to whole populations rather than just to high-risk groups.

Engagement of governments is essential if these programmes are to have maximal effect, and this is where the influential role of international organizations such as IDF and WHO becomes very important.

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