Diabetes and CVD in South Asians: A review

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Article points

1. Diabetes is up to 6 times more common and mortality rates from cardiovascular disease 150% greater in South Asians than that observed in local Caucasians.
2. In addition to diabetes, South Asians have a higher prevalence of metabolic syndrome, microalbuminuria and an unfavourable lipid profile that may account for the increased CV risk.
3. Current treatment targets and risk engines underestimate the risk among South Asians.
4. Poor access to healthcare, social and cultural factors may complicate care delivery, and newer initiatives targeted to the needs of this community may be needed to improve outcomes.

Key words

- South Asians
- Cardiovascular disease
- Novel healthcare strategies

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The worldwide prevalence of diabetes is expected to rise significantly over the next decade (King et al, 1998) and the biggest impact will be in developing countries. Sedentary lifestyles, urbanisation and increasing obesity have been largely implicated in this rise, but other factors such as migration and increased life expectancy have also been major contributors (Lipscombe and Hux, 2007). The UK has a large South Asian population comprising migrants from Bangladesh, India and Pakistan. The prevalence of diabetes among South Asian adults in the UK is estimated to be approximately 20% compared with 3–4% in Caucasians (Barnett et al, 2006). The purpose of this review is to examine the literature on diabetes and CVD in South Asians and to discuss novel options for improving health care in this high-risk population.

The prevalence of diabetes and cardiovascular disease in this population is disproportionately high: diabetes is almost six times greater (Mather and Keen, 1985) and mortality from CVD nearly twice as common compared with the local Caucasian population (Chaturvedi and Fuller, 1996). Epidemiological studies have shown that this excess risk is due to a higher prevalence of insulin resistance and an unfavourable CV risk profile more commonly seen in South Asians (McKeigue et al, 1991). This is further compounded by economic deprivation, poor access to healthcare, and cultural practices that make it difficult to deliver optimal care. This is thought to be due to a combination of genetic and environmental factors (Reddy and Yusuf, 1998).

The genetics of type 2 diabetes is complex and involves interaction of several genes with the environment (Barroso, 2005; Ramachandran et al, 1992). Although no single gene has been implicated in the causation of type 2 diabetes, better understanding of the pathogenesis and improved techniques of genetic testing have allowed identification of several susceptibility genes associated with the condition (Grant et al, 2006; Ramachandran et al, 2006). Most of these studies have been in Caucasians and until recently there have been very few genetic studies in South Asians. Despite the widely-held belief that South Asians may be genetically different to other ethnic populations, studies involving South Asians have so far not demonstrated any significant differences between the ethnic groups. On the other hand, features of insulin resistance have been identified in early childhood in South Asians suggesting a possible genetic predisposition (Krishnaveni et al, 2005).

In contrast, evidence for environmental

influence is much stronger. Studies comparing prevalence of diabetes between migrants and native South Asians have shown a much higher prevalence in migrants (Dhawan et al, 1994; Bhatnagar et al, 1995). Studies from India (Ramachandran et al, 1992; Ramachandran et al, 1997) have shown significantly greater prevalence in those residing in urban compared with rural areas. These studies support the assertion that environmental influences play an important role in the pathogenesis of type 2 diabetes. In addition to the increased prevalence, diabetes occurs at least a decade earlier in South Asians with substantially greater rates of microvascular complications such as nephropathy and retinopathy even at diagnosis (Burden et al, 1992). The burden of long-term complications, therefore, is much higher in this ethnic group.

The higher rates of CVD in South Asians parallel the high prevalence of diabetes. In the UK, for example, mortality from cardiovascular causes is 40–50 % greater among South Asians compared with the local Caucasian population (Chaturvedi and Fuller, 1996). The difference in risk is further exaggerated in individuals with diabetes with mortality rates as much as three times that seen in Caucasians. This pattern persists even in second generation migrants. In one study comparing South Asians with six other racial groups, mortality from CHD was highest among South Asians (Palaniappan et al, 2004). Another study found a much higher prevalence of sub-clinical atherosclerosis (Anand et al, 2000). The precise reasons for this excess cardiovascular risk are not fully understood, but it is widely believed that the increased prevalence of diabetes and adverse metabolic risk factors commonly seen in this ethnic group are (at least in part) responsible. In fact, the relationship between CHD and diabetes is so strong that there may be a common pathogenic mechanism linking the two (Lebovitz, 2006).

The relationship between diabetes and CHD can be further explored through studies of the metabolic syndrome. Originally described by Reaven (1988), this syndrome comprises the co-existence of insulin resistance, hypertension, raised triglycerides and low HDL-c in an individual. Several alternative definitions of the metabolic syndrome have since been proposed (IDF, 2007; Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001; see *Table 1*). Subtle differences exist between the definitions but increased waist circumference or BMI, hypertension, dyslipidaemia and glucose intolerance are common to most of them. The prevalence of metabolic syndrome is considerably higher among South Asians than in Europeans using both the WHO and the NCEP ATP III criteria (Tillin et al, 2005). In another study using the ATP III criteria the prevalence of metabolic syndrome was reported to be as high as 41 % in urban Indians with the figures rising to over 70 % in those with diabetes (IDF, 2007). This potentially ominous combination of diabetes and metabolic risk factors in an individual could well be the reason for the high CHD risk in South Asians.

Role of traditional risk factors

The contribution of conventional risk factors to the excess cardiovascular risk in South Asians has been investigated in several epidemiological studies. Most of these have compared migrant South Asians with local Caucasians. Other studies have included comparisons between the migrant and indigenous South Asian populations. These have highlighted important differences between the ethnic groups as discussed below.

Hypertension

Studies comparing the prevalence of hypertension in Caucasians and South Asians have shown varying results (Cruickshank et al, 1983; Agyemang and Bhopal, 2002; Lane et al, 2002). While some studies have reported higher blood pressures in South Asians, others have reported lower values. A review of the cross-sectional data on blood pressure (Agyemang and Bhopal, 2002) in South Asians found that there was considerable variation in the blood pressure values reported. In men, seven of twelve studies reported a lower mean systolic blood pressure; while six of nine studies reported a lower systolic blood pressure in women. Relatively higher diastolic pressures were

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1. The higher rates of cardiovascular disease in South Asians parallel the high prevalence of diabetes.
2. The relationship between CHD and diabetes is so strong that there may be a common pathogenic mechanism linking the two.
3. The prevalence of metabolic syndrome is considerably higher amongst South Asians than in Europeans.

Page points

1. In general it is accepted that the blood pressure values in South Asians are slightly lower or similar to that observed in Caucasians.
2. Despite the reportedly lower or similar levels of total cholesterol, South Asians have a more atherogenic lipid profile than Caucasians.
3. South Asians have a lower BMI than their European counterparts. Even at lower BMI, however, South Asians have been found to have a higher percentage of visceral fat and features of insulin resistance.

reported in both South Asian men and women than in Caucasians.

A multi-ethnic comparison of risk factors among people recruited to the UKPDS showed that South Asians had lower blood pressures compared with Afro-Caribbeans but similar values to that observed in Caucasians (UKPDS Group, 1994). In general, however, it is accepted that the blood pressure values in South Asians are slightly lower or similar to that observed in Caucasians. Despite this, South Asians have a much higher prevalence of microalbuminuria and nephropathy (Fischbacher et al, 2003). There is also evidence to suggest that this increased prevalence of microalbuminuria persists even in individuals with blood pressures considered to be within the 'normal' range (Dixon et al, 2006). This may be an argument to have lower thresholds for intervention and to aim for lower blood pressure targets in South Asians.

Dyslipidaemia

Despite the reportedly lower or similar levels of total cholesterol, South Asians have a more atherogenic lipid profile than Caucasians. Higher levels of triglycerides and lower HDL-c levels have been observed among South Asians (Kulkarni et al, 1999) – features frequently associated with insulin resistance and the metabolic syndrome. This pattern of dyslipidemia appears to be further exaggerated in migrants suggesting a strong environmental influence (Bhatnagar et al, 1995). South Asians also have smaller and denser LDL-c particles and altered apoA:apoB ratio which may help explain their propensity for early atherosclerosis (Bhalodkar et al, 2004).

Table 1. IDF and NCEP ATP III definitions of the metabolic syndrome. (Adapted from: Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001; IDF, 2007).

IDF definition of metabolic syndrome using ethnic-specific values for South Asians
The presence of central obesity defined as waist circumference > 90cm in males and > 80 cm in females
plus any two of the following:
Raised triglyceride level: >150mg/dl (1.70 mmol/l) or specific treatment for it
Reduced HDL-c: <40mg /dl (1.03mmol/l) in males and <50mg/dl(1.29mmol/l) in females or specific treatment for it
Raised blood pressure: systolic blood pressure >130mmHg or diastolic blood pressure >85mmHg, or treatment of previously diagnosed hypertension
Raised fasting plasma glucose (FPG) >100mg/dl (5.60mmol/l), or previously diagnosed type 2 diabetes
NCEP ATP III criterion for the diagnosis of metabolic syndrome
The diagnosis of metabolic syndrome using the ATP III (2001) criterion in a person requires at least three of the following:
Central obesity: waist circumference >102cm (male), >88cm (female)
Dyslipidaemia: triglycerides >1.70mmol/l (150mg/dl)
Dyslipidaemia: HDL-c <40mg/dl (male), <50mg/dl (female)
Blood pressure: >130/85 mmHg
Fasting plasma glucose: >6.1mmol/l (110mg/dl)

Lifestyle

Diet and Exercise

There is now considerable evidence to suggest that poor diet and lack of exercise are also major contributors to increased cardiovascular risk in South Asians. South Asians have been shown to less physically active than their Caucasian counterparts (Fischbacher et al, 2004). Similarly, use of saturated fats, such as ghee, and practices that involve excessive cooking of vegetables may, in part, explain the increased tendency to insulin resistance. South Asians have a lower BMI than their European counterparts. Even at lower BMI, however, South Asians have been found to have a higher percentage of visceral fat and features of insulin resistance. The cut-off values for obesity in South Asians have therefore been revised by the WHO with a BMI greater than 25 kg/m^2 considered obese in this group and greater than 23 kg/m^2 as overweight (WHO Expert Consultation, 2004).

Smoking

While the overall rates of smoking in South Asian and Caucasian men are comparable, smoking rates in South Asian women are particularly low (Anand et al, 2000). Within South Asians, smoking is more common among Bangladeshis than in Indians and Pakistanis.

South Asians in the UK population have lower blood pressures and total cholesterol and lower rates of smoking (particularly in women) than Caucasians. Treatment targets based on studies in other ethnic populations may therefore not be applicable to South Asians. Moreover, the conventional risk engines such as Framingham and FINRISK, largely based on studies in non-

Asian individuals, grossly underestimate the true risk in South Asians resulting in under treatment of these individuals (Bhopal et al, 2005). It is important to recognise that despite the relatively lower values of traditional risk factors such as blood pressure and cholesterol these still account for nearly 80 % of the risk of CHD (Joshi et al, 2007). These risk factors must be identified and aggressively treated in all individuals (*Table 2*).

Novel risk factors

The fact that the excess cardiovascular risk observed in South Asians may not be fully explained by traditional risk factors has led to increased attention on novel risk factors. These include adipocytokines, prothrombotic factors and inflammatory markers and some of these are of particular interest.

Adiponectin is an adipocytokine known to have insulin sensitising, anti-atherogenic and anti-inflammatory properties. Low levels of adiponectin are associated with insulin resistant states and strongly correlate with visceral adiposity. Studies comparing adiponectin levels in Caucasians and South Asians have shown consistently low levels of adiponectin in the latter (Snehalatha et al, 2003). There also appears to be a correlation between low HDL-c levels and adiponectin (Valsamakis et al, 2003). These features are present even in patients with impaired glucose tolerance and may explain the propensity of South Asians to early cardiovascular disease (Valsamakis et al, 2003). Similarly, higher levels of C-reactive protein, homocysteine, plasminogen activator inhibitor and fibrinogen and impaired endothelium dependent vasodilatation have been reported in South Asians (Anand et al, 2004; Hughes and Ong, 2000). While there is considerable interest in these novel risk factors, they have not been evaluated in prospective studies and their potential role in the pathogenesis of cardiovascular disease is not fully established.

Cultural and socio-economic issues

Healthcare delivery can be affected by many other factors such as access, economic background and cultural practices. In the UK, many South Asians live in inner city areas with high deprivation indices (Simmons et al, 1989). Communication difficulties arising out of inability to speak or read English may also impact on the understanding of illness and education. There is also evidence to suggest that South Asians are likely to seek help much later than their Caucasian counterparts (Shakut et al, 1993). Poor adherence to medication, and practices such as religious fasting may contribute to the difficulties in achieving good results. Understanding these needs is therefore essential to deliver good quality care.

Table 2. Comparison of risk factors for acute myocardial infarction in individuals from South Asia and other countries – the INTERHEART study. Adapted from: Joshi et al, 2007.

Risk factor	Cases (%)	Controls (%)	Odds ratio (95% CI)
ApoB:ApoA			
Other Countries	48.3	31.8	3.01 (2.77 to 3.26)
South Asia	61.5	43.8	2.57 (2.03 to 3.26)
Smoking (Current and Former)			
Other Countries	65.7	49.4	2.22 (2.09 to 2.36)
South Asia	61.6	40.8	2.57 (2.22 to 2.96)
Hypertension			
Other Countries	40.5	23.6	2.44 (2.30 to2.60)
South Asia	29.6	12.7	2.92 (2.46 to 3.48)
Diabetes			
Other Countries	18.2	7.2	3.20 (2.93 to 3.50)
South Asia	20.2	9.5	2.52 (2.07 to 3.07)
High Waist to Hip ratio			
Other Countries	46.7	34.0	2.21 (2.06 to 2.38)
South Asia	44.0	29.6	2.44 (2.05 to 2.91)
Psychosocial factors			
Other Countries	84.2	82.0	1.83 (1.58 to 2.13)
South Asia	86.0	82.6	2.62 (1.76 to 3.90)
Moderate or High Intensity Exercise			
Other Countries	15.8	21.6	0.70 (0.65 to 0.76)
South Asia	4.6	6.1	0.72 (0.53 to 0.97)
Alcohol Consumption >Once/week			
Other Countries	25.7	26.9	0.79 (0.74 to 0.85)
South Asia	13.3	10.7	1.06 (0.85 to 1.30)
Consumption of Fruits and vegetables			
Other Countries	38.3	45.2	0.70 (0.65 to 0.76)
South Asia	20.0	26.5	0.65 (0.53 to 0.81)

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1. Given the risk of diabetes amongst South Asians, strategies to prevent diabetes should be a high priority.
2. The recognition that socio-cultural factors play an important role in the management of chronic conditions has created a focus on incorporating these needs in healthcare packages.

Diabetes prevention

A detailed discussion on the prevention of diabetes in South Asians is beyond the scope of this review. However, given the risk of diabetes among South Asians, strategies to prevent it should be a high priority. It is clear from the diabetes prevention studies that lifestyle issues can effectively delay the onset of diabetes. In both the Diabetes Prevention Program and Finnish Diabetes Prevention Study (Knowler et al, 2002; Tuomilehto et al, 2001) a combined program of diet and exercise was shown to achieve a relative risk reduction of 58% in people with impaired glucose tolerance. In another similar study conducted in South India, lifestyle measures were again shown to be highly effective in reducing the incidence of diabetes (Ramachandran et al, 2006). It is also worth mentioning that lifestyle issues were more effective than pharmacological interventions in these studies. Individuals at risk must therefore be encouraged to adopt healthy lifestyles and given the high risk of developing diabetes such interventions must start relatively early in South Asians.

UKADS: A novel strategy

The recognition that socio-cultural factors play an important role in the management of chronic conditions has created a focus on incorporating these needs in health care packages. Results from earlier studies involving approaches such as community link workers have been encouraging, but such strategies have not been evaluated in larger studies. The United Kingdom Asian Diabetes Study (UKADS; O'Hare et al, 2004) is a community-based intervention study in South Asian people with type 2 diabetes. The study hypothesis is that a 'structured culturally sensitive care package tailored to the needs of the South Asian community will improve cardiovascular risk factors and ultimately morbidity and mortality in a cost effective manner'. In a pilot study involving six inner city practices in Birmingham and Coventry patients of South Asian ethnicity were randomised to enhanced or conventional care (O'Hare et al, 2004). The enhanced care group received additional practice nurse time supported by link workers and input from the diabetes specialist nurse. All practices worked to strict treatment protocols. The control group did not receive any additional support but were encouraged to adhere to the same treatment protocols. After one year there were significant improvements in the enhanced care group in blood pressure and total cholesterol levels (*Table 3*). There were no significant differences in HbA_{1c} between the groups.

To determine if the results of the pilot study can be reproduced in a bigger population, a much larger cluster randomised study involving 21 general practices in Birmingham and Coventry was commenced in 2004. Fifteen-hundred South Asians and 500 Caucasians with type 2 diabetes have been recruited for the study. The study has completed 2 years and the results of the intervention will be reported in the near future. Apart from the impact of the intervention on the cardiovascular risk, it will also provide a detailed economic analysis to determine if such an initiative is cost-effective.

Table 3. Changes in risk factors after one year follow up. Effect of one year culturally sensitive intervention on major risk factors in South Asians with type 2 diabetes. Adapted from: O' Hare et al, 2004.

	Mean difference intervention	Mean difference control	Difference between groups	95% CI	*P* value
Systolic BP (mmHg)	-6.69	-2.11	-4.58	-8.84 to -0.32	0.035
Diastolic BP (mmHg)	-3.14	+0.28	-3.14	-5.66 to -1.16	0.003
Total cholesterol (mmol/l)	-0.51	-0.12	-0.38	-0.65 to 0.12	0.005
HbA_{1c} (%)	-0.23	-0.20	-0.03	-0.36 to 0.30	0.866

Conclusions

Epidemiological studies have highlighted that the risk of diabetes and cardiovascular disease is not uniform across all ethnic groups. Certain ethnic groups such as South Asians are particularly at greater risk and even within this population, there appears to be considerable heterogeneity. The challenge for health professionals is to identify those at greatest risk and aggressively treat them.

There is considerable evidence to suggest that a major proportion of cardiovascular risk can be attributed to known risk factors such as obesity, hypertension, dyslipidemia and smoking. This is true regardless of ethnicity. Despite this, a significant proportion of South Asians fail to receive optimal care. One likely reason for this is that the treatment targets and risk engines based on studies in Caucasians grossly underestimate risk in South Asians. Current treatment targets are probably too high for South Asians and fail to address the risk profile commonly observed in this ethnic group. There is therefore an argument to use lower treatment targets in South Asians, but such an approach would need to be validated in prospective studies. In the authors' opinion, if current risk engines are used in the South Asian population then the health professional needs to add 50 % to the value obtained to get a more accurate picture of risk.

A bigger challenge for primary care is to develop effective preventative strategies with emphasis on lifestyle changes. Effecting behavioural changes, however, can take a long time and given the high risk of diabetes, such interventions must begin much earlier in South Asians. Identifying barriers to an active lifestyle and developing new approaches that encourage more exercise and dietary changes are necessary to achieve successful outcomes.

Significant proportions of South Asians live in deprived areas and have poor access to healthcare (Simmons et al, 1989). Cultural practices and linguistic difficulties may further interfere with education and often lead to poor adherence. Recognising these needs is vital for success of healthcare initiatives and novel approaches that integrate these needs must therefore be developed. ■

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