

# DYSLIPIDAEMIA IN SOUTH AFRICA

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## 1. INTRODUCTION

Dyslipidaemia remains a major cardiovascular risk factor in the South African population. It affects some groups more than others, but is also affecting those previously at lesser risk who are now caught up in the changes brought about by development, the association with a westernised lifestyle, and the HIV epidemic. South Africa is already weighed down by a quadruple burden of disease, including the pre-transitional diseases associated with poverty and underdevelopment, the emerging "Western" chronic diseases of lifestyle, injuries, both intentional and unintentional, and HIV/AIDS.<sup>1</sup> A dramatic increase in obesity and diabetes, appropriately referred to as diabetesity,<sup>2</sup> has been predicted globally for the next decade to the extent that it is referred to as a pandemic.<sup>3</sup> Dramatic increases in diabetesity have been noted in westernised countries and have given rise to concern.<sup>4</sup> To regard this epidemic of diabetesity as only a disorder of affluence is a profound misconception; the projected figures for sub-Saharan Africa tell another story<sup>5,6</sup> – the burden that diabetesity will place on developing countries, including South Africa, is even greater than that expected in first world countries.<sup>3</sup>

Diabetesity is associated with, and partly the result of, insulin resistance, and forms part of the insulin resistance syndrome.<sup>7</sup> Associated with this rise in diabetesity there is an increase in all those cases of the insulin resistance syndrome who have not yet developed dysglycaemia yet are regarded as prediabetics.<sup>8</sup> This insulin resistance syndrome brings with it a particular and characteristic form of dyslipidaemia that is partially qualitative rather than quantitative in nature.<sup>9</sup> The Adult Treatment Panel (ATPIII) of the National Cholesterol Education Program (NCEP) acknowledges the importance of this syndrome as a cardiovascular risk factor and incorporates two components of the associated dyslipidaemia into its diagnostic criteria (i.e., the ones most likely to have the greatest clinical utility).<sup>10</sup> There are some indications that the projected epidemic of the insulin resistance syndrome is already well on its way in South Africa.<sup>6,11,12</sup> Accordingly, this review will focus mainly on the lipid abnormalities of the insulin resistance syndrome and which are likely to be the commonest form of dyslipidaemia to be seen in the country in the future, if not already present.

## 2. THE SOUTH AFRICAN LIPID GUIDELINES

The history and development of lipidology in South Africa was eloquently reviewed in the previous compilation of Chronic Diseases of Lifestyle by the Medical Research Council.<sup>13</sup> The authors identified the need for a new and updated set of guidelines for the management and treatment of dyslipidaemia. The publication of clinical guidelines for the diagnosis, management and prevention of the common forms of dyslipidaemia in South Africa appeared not long thereafter.<sup>14</sup> These guidelines defined the management of hypercholesterolaemia identified during screening and was illustrated by way of an algorithm. An individual's risk of cardiovascular disease was assessed by applying a scoring system that utilises the person's age, gender, total cholesterol (TC) level, high-density lipoprotein cholesterol (HDLC) level, the presence, or absence of hypertension and diabetes, and smoking status. This methodology was derived from the Framingham study.<sup>15</sup> The guidelines did not allow a family history to be factored in, but were otherwise widely accepted and disseminated for use. Nonetheless, the detection and management of dyslipidaemia, and especially in patients at high risk of cardiovascular disease, were found to be suboptimal in general practice.<sup>16</sup> The guidelines are still often not appropriately applied, resulting in inappropriate pharmacological therapy. The practice of treating hypercholesterolaemia with tablets alone and with little or no advice or encouragement regarding lifestyle modification is widespread.<sup>17</sup>

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At the time these guidelines were deliberated, a general lack of awareness existed of the dyslipidaemia of the insulin resistance syndrome and its impact on the future management of dyslipidaemia. Despite the already predicted pandemic of diabetes,<sup>18</sup> it was not sufficiently appreciated that there would be such a rise in the prevalence of a dyslipidaemia other than hypercholesterolaemia. Although the data had already been published, the concept of type 2 diabetes as a coronary equivalent had not yet been propounded.<sup>19</sup> Cholesterol modifying treatment, in many aspects, has entered a new era; the cut-off points for the levels of TC to be targeted for statin therapy have decreased, the goals of therapy are ever lower, the pleiotropic effects of statins are increasingly appreciated, and the efficacy and cost of statins have improved. Clearly, in this altered environment there is a need for a revision of the guidelines for the management of dyslipidaemia in South Africa.

### 3. INTERACTION OF CARDIOVASCULAR RISK FACTORS

A cholesterol-centric, or even a lipid-centric, view of cardiovascular risk, and a management strategy aimed solely at the modification of lipids, have no role to play in the management of individuals at high risk for cardiovascular events. The amount of time, either educational or with patients, which is devoted to smoking-cessation or lifestyle modification is inordinately less than the time spent on risk factors where there is a vested interest of the pharmaceutical industry. A system where a patient's hypertension is treated in one clinic, the lipids managed in another, the diabetes in another venue, the ischaemic heart disease (IHD) or other vascular diseases in yet another clinic, while the smoking cessation and lifestyle modification are managed by yet other people, cannot be ideal or cost-effective. Rather, a holistic approach to the management of the patient with cardiovascular risk factors needs to be promoted.

Cardiovascular risk factors are particularly prevalent in the South African population and are set to increase because of increasing urbanisation.<sup>20</sup> There is no lack of these risk factors in the black population, the prevalences of which are linked to increasing urbanisation.<sup>21-30</sup> What atherosclerotic vascular disease there is in the black population manifests itself by a high incidence of stroke.<sup>24</sup> Even within this group of black patients with stroke the incidence of IHD may be as high as their white counterparts.<sup>25</sup> It is consistently reported that the caseload of IHD is on the increase in the black population of South Africa and that more of these persons are seen suffering from myocardial infarctions, particularly in urban hospitals catering for the black population.

### 4. LIPID ABNORMALITIES

The prevalence of lipid abnormalities in South Africa has not been determined in a random population sample through national surveys. However, available data were collected from smaller regional surveys of randomly selected groups. The settings in which these studies (9.1-9.10) were conducted and the number of participants are shown in Table 9.1.<sup>31-40</sup> The distribution of the lipid parameters in the different population groups is shown in Table 9.2 for men and women in the age groups 25-64 years.

Table 9.1. Ten randomised community-based studies of participants (aged 25-64 years) with lipid values in South Africa between 1982 and 1996

Population group	Study site	Year	Men (N)	Women (N)	Total (N)
African rural	QwaQwa (Free State) <sup>31*</sup>	1990/1	279	574	853
	Dikgale (Limpopo) <sup>32†</sup>	1997/8	237	957	1494
African urban	Cape Town (Western Cape) <sup>33</sup>	1990	292	373	665
	Mangaung (Free State) <sup>31*</sup>	1990/1	290	468	758
	Durban (KwaZulu-Natal) <sup>34</sup>	1986	125	107	232
Coloured	Cape Town (Western Cape) <sup>35</sup>	1982	384	395	779
	Mamre (Western Cape) <sup>36</sup>	1996	276	370	646
Indian	Durban (KwaZulu-Natal) <sup>37*</sup>	1984/6	300	301	601
	Durban (KwaZulu-Natal) <sup>38*</sup>	1987	173	181	354
White	Robertson, Swellendam, Riversdal (Western Cape) <sup>39**</sup>	1983	2722	-	-
	Riversdal, Caledon, Bredasdorp <sup>40††</sup>	1993	163	164	327

\* Oldest age category = 55-69 years

† Data of Dikgale study (1997/8) extracted from data from reference (32), youngest age group, 30-34 years

\*\* Data of the CORIS study (1983) extracted from data from reference (39)

†† Age group 35-44 years

Table 9.2. Lipid profile in South African studies between 1982 and 1996

Population group and study	MEN					WOMEN				
	25-34 Years	35-44 Years	45-54 Years	55-64 Years	55-64 Years	25-34 Years	35-44 Years	45-54 Years	55-64 Years	55-64 Years
Mean total serum cholesterol (SD) in mmol/l (TC)										
African rural	4.2 (1.1)	4.9 (1.2)	4.6 (1.0)	4.6 (1.5)	4.6 (1.3)	4.4 (1.0)	4.6 (1.0)	4.8 (1.1)	5.4 (1.1)	5.4 (1.3)
African urban	4.2 (0.8)	4.2 (1.5)	4.2 (1.0)	4.7 (0.7)	4.7 (1.0)	4.1 (0.9)	4.4 (1.0)	4.7 (1.0)	5.1 (1.0)	5.1 (0.7)
Coloured	4.7 (0.9)	4.9 (1.1)	5.1 (1.3)	5.1 (1.1)	5.1 (1.1)	4.4 (0.8)	4.9 (1.0)	5.5 (1.3)	5.4 (0.9)	5.4 (0.9)
Indian	4.5 (1.0)	4.8 (1.2)	4.9 (1.4)	4.9 (1.4)	4.9 (1.4)	4.6 (1.0)	4.8 (1.1)	4.8 (1.1)	4.8 (1.1)	4.8 (1.1)
White	5.6 (1.1)	5.9 (1.2)	6.1 (1.5)	6.1 (1.1)	6.1 (1.1)	5.3 (1.0)	5.8 (1.1)	6.3 (1.3)	6.6 (1.2)	6.6 (1.2)
Robertson, Riversdal, Swellendam <sup>39</sup>	5.2 (1.2)	5.7 (1.3)	5.6 (1.1)	5.5 (1.2)	5.5 (1.2)	4.7 (0.8)	5.3 (1.0)	6.0 (1.1)	6.5 (1.3)	6.5 (1.3)
Riversdal, Caledon, Bredasdorp <sup>40</sup>	5.5 (1.1)	6.1 (1.4)	6.3 (1.2)	5.6 (1.1)	5.6 (1.1)	5.1 (1.0)	5.4 (1.1)	5.9 (1.2)	6.1 (1.2)	6.1 (1.3)
	5.6 (1.1)	5.9 (1.2)	6.3 (1.4)	6.2 (1.1)	6.2 (1.1)	5.4 (1.2)	5.7 (1.2)	6.1 (1.2)	7.2 (1.4)	7.2 (1.4)
	5.7	6.2	6.4	6.3	6.3					
	6.0	6.0				5.6				
Mean HDL cholesterol levels (SD) in mmol/l (HDLc)										
African rural	1.2 (0.4)	1.3 (0.5)	1.2 (0.4)	1.3 (0.6)	1.3 (0.6)	1.2 (0.4)	1.2 (0.4)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)
African urban	1.2 (0.3)	1.2 (0.2)	1.2 (0.2)	1.2 (0.3)	1.2 (0.3)	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	1.2 (0.2)	1.2 (0.3)
Coloured	1.4 (0.4)	1.4 (0.5)	1.3 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.4)	1.4 (0.3)	1.5 (0.3)	1.5 (0.3)
Indian	1.4 (0.3)	1.3 (0.5)	1.4 (0.6)	1.4 (0.5)	1.4 (0.5)	1.3 (0.4)	1.4 (0.5)	1.3 (0.4)	1.4 (0.4)	1.4 (0.5)
White	1.3 (0.4)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)	1.3 (0.3)	1.2 (0.4)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)
	1.4 (0.3)	1.4 (0.6)	1.4 (0.4)	1.4 (0.5)	1.4 (0.5)	1.5 (0.4)	1.6 (0.5)	1.5 (0.5)	1.6 (0.5)	1.6 (0.5)
	1.3 (0.4)	1.5 (0.6)	1.3 (0.6)	1.2 (0.4)	1.2 (0.4)	1.3 (0.3)	1.3 (0.5)	1.4 (0.4)	1.3 (0.3)	1.3 (0.3)
	1.1 (0.3)	1.2 (0.4)	1.3 (0.6)	1.1 (0.3)	1.1 (0.3)	1.2 (0.3)	1.3 (0.7)	1.2 (0.4)	1.2 (0.4)	1.2 (0.3)
	1.1 (0.3)	1.4 (0.7)	1.2 (0.4)	1.3 (0.5)	1.3 (0.5)	1.3 (0.6)	1.5 (0.5)	1.6 (0.8)	1.3 (0.4)	1.3 (0.4)

		Mean HDL / total cholesterol ratio (%) (SD) (HDL/C/T/C)															
African rural	QwaQwa	26	(10)	27	(10)	28	(10)	31	(10)	28	(10)	27	(10)	25	(10)	23	(10)
African urban	Dikgale	31	(10)	29	(7)	27	(7)	27	(8)	31	(8)	29	(8)	28	(8)	26	(9)
	Cape Town	37	(11)	34	(11)	32	(11)	31	(10)	35	(10)	34	(10)	31	(8)	30	(60)
	Mangaung	30	(10)	28	(10)	29	(10)	29	(10)	20	(10)	29	(10)	26	(10)	27	(10)
	Durban	31	(10)	26	(60)	26	(60)	26	(60)	30	(10)	26	(11)	26	(9)	26	(9)
Coloured	Cape Town	26		25	25	25	24	24	24	30	28	28	25	25	24	24	
	Mamre	27		26	24	24	23	23	27	27	25	25	24	24	21	21	
Indian	Durban	21		20	20	20	21	21	24	24	23	23	22	22	20	20	
White	Durban	21		26	20	20	21	21	25	25	26	26	28	28	20	20	
		Mean triglyceride levels (SD) in mmol/l (non-fasting) (TG)															
African rural	QwaQwa (F)	1.3	(0.9)	1.7	(1.4)	1.5	(1.0)	1.5	(1.0)	0.9	(0.4)	1.1	(0.6)	1.4	(0.7)	1.5	(0.8)
African urban	Dikgale (F)	1.0	(0.7)	1.3	(0.9)	1.4	(1.0)	1.5	(0.9)	0.9	(0.4)	1.0	(0.6)	1.2	(0.6)	1.3	(0.7)
	Cape Town (NF)	1.3	(1.2)	1.6	(2.9)	2.0	(1.2)	2.2	(1.6)	1.0	(0.5)	1.2	(0.7)	1.5	(0.9)	1.9	(1.2)
	Mangaung (F)	1.3	(0.9)	1.5	(1.3)	1.8	(1.9)	1.4	(0.7)	0.8	(1.4)	1.1	(0.6)	1.5	(1.5)	1.5	(0.6)
	Durban (NF)	1.0	(0.4)	1.7	(1.6)	1.6	(1.1)	1.6	(1.1)	0.9	(0.4)	1.2	(0.8)	1.2	(0.9)	1.2	(0.9)
Coloured	Cape Town (NF)	1.3	(0.8)	1.8	(1.1)	2.2	(2.1)	2.8	(2.6)	2.5	(1.8)	1.4	(0.5)	1.6	(0.9)	2.2	(1.2)
	Mamre (F)	1.3	(1.0)	1.4	(1.0)	1.6	(1.0)	1.2	(0.6)	0.8	(0.4)	1.0	(0.4)	1.2	(0.6)	1.3	(0.6)
Indian	Durban (NF)	1.6	(1.1)	2.0	(1.6)	2.0	(1.2)	1.7	(0.8)	1.2	(0.6)	1.5	(0.8)	1.9	(1.2)	1.6	(0.8)
White	Durban (NF)	1.7	(1.5)	1.7	(1.4)	1.9	(1.3)	1.8	(0.8)	1.3	(1.1)	1.3	(0.9)	1.3	(0.5)	2.1	(1.0)
		Mean LDL cholesterol level (SD) in mmol/l (Friedewald equation) (LDLC)															
African rural	QwaQwa	2.9	(1.1)	2.9	(1.0)	2.7	(1.0)	2.4	(0.8)	2.8	(1.0)	2.9	(1.0)	3.0	(1.1)	3.5	(1.2)
African urban	Dikgale	2.5	(1.0)	2.5	(0.7)	2.7	(0.9)	2.8	(1.0)	2.6	(0.9)	2.8	(1.0)	2.9	(1.0)	3.1	(1.1)
	Cape Town	2.1	(0.7)	2.1	(0.7)	2.1	(0.9)	2.5	(0.8)	2.2	(0.8)	2.4	(0.9)	2.6	(0.8)	2.8	(0.6)
	Mangaung	2.8	(0.9)	2.9	(1.1)	2.9	(1.3)	3.0	(0.9)	2.7	(0.7)	3.1	(1.0)	3.4	(1.3)	3.5	(0.9)
Coloured	Cape Town	3.3	(1.0)	3.5	(1.1)	3.5	(1.1)	3.7	(1.1)	3.1	(0.9)	3.5	(1.0)	3.8	(1.1)	4.0	(1.1)
	Mamre	3.3	(1.2)	3.6	(1.1)	3.6	(1.1)	3.8	(1.1)	3.1	(0.8)	3.5	(1.0)	4.1	(1.1)	4.6	(1.1)

• Friedewald equation (triglyceride levels >4.5 mmol/l excluded)  
NF + F: Non-fasting and fasting blood samples used for triglyceride analyses

In general the serum TC values in the African population group were lower than the levels found in the other three population groups, and differences were larger in the older participants than in the younger ones. Typically, the TC values increased with age, though this phenomenon was far less marked in African population groups than in the other population groups.

The HDLC levels are also shown in Table 9.2. There were very few differences in the HDLC levels reported in the nine studies and consequently the ratio of HDLC to TC was generally found to be higher in the African population group than in the other three groups. This suggests that the African population group with its lower TC levels is experiencing additional protection against atherosclerosis-related diseases by virtue of its relatively higher proportion of protective HDLC.

Nine studies also reported the blood triglyceride (TG) levels of the different groups. Some studies analysed fasting blood samples while others used non-fasting samples. TG levels are the only lipid fraction that is influenced by fasting. This is seen in the significantly larger standard deviations of the distributions of TG levels in the studies where participants were non-fasting. Only six of the studies reported on the low-density lipoprotein cholesterol (LDLC) levels calculated with the Friedewald equation.<sup>41</sup> These six studies were all conducted in either the African or the coloured population group. As would be expected, the LDLC levels of the African population group were significantly lower than in the coloured group, again pointing to the relatively lower level of risk in the African group compared to other groups.

Table 9.3. Prevalence (%) of hypercholesterolaemia in South Africa in people 30 years and older. total cholesterol >5 mmol/l

	Years	African	Coloured	Indian	White
Men	20-44	13.9	80.8	84.9	83.9
	45-59	22.0	84.5	92.3	93.8
	60 +	33.3	79.6	78.4	96.0
	30 +	19.7	81.7	86.5	90.0
	Total number (≥30)	589 584	591 758	209 266	1 240 006
Women	20-44	10.4	66.9	65.1	75.0
	45-59	40.4	94.8	87.8	95.3
	60 +	53.9	97.9	90.3	99.4
	30 +	29.2	79.9	77.4	88.4
	Total number (≥30)	963 500	657 360	204 117	1 311 614
All Persons	20-44	12.1	73.6	74.9	79.5
	45-59	31.6	90.0	89.9	94.6
	60 +	44.7	90.4	85.2	97.9
	30 +	24.7	80.7	81.7	89.2
	Total number	1 553 084	1 249 117	413 384	2 551 620

Total number South Africans 30 years and older with hypercholesterolaemia = 5 767 205

Table 9.3 shows the prevalence of hypercholesterolaemia in the age groups 30 years and older using a cut-off point of 5 mmol/l. The prevalence rates were age-standardised against the actual population of the different groups recorded in the Census 2001 to obtain a national estimate for each population group and the entire population aged 30 years and older.<sup>42</sup> The marked differences between the prevalence rates among the African population and the other three groups are striking. However, it is an unexpected finding that about a quarter of all African people that were studied had a TC level of 5 mmol/l or higher, a similar prevalence rate as found for hypertension in this ethnic group. This suggests that health services should consider screening African people aged 30 years or older for hypercholesterolaemia on examination. The data suggest that at least 1.5 million African people aged 30 years or older are hypercholesterolaemic. Furthermore, the older women were found to have hypercholesterolaemia far more frequently than older men. This could probably be associated with the high obesity rates recorded in older African women. For the other groups, men tend to have hypercholesterolaemia at least as frequently as women, with younger women having lower rates than those of men and older women having much higher prevalence rates. By extrapolating the prevalence to all South Africans aged 30 years or older, these findings indicate that more than 5.5 million people carry a risk for a chronic disease of lifestyle by virtue of their TC level.

Familial hypercholesterolaemia (FH), by virtue of founder gene effects, is very common in the Afrikaner population. In fact, the overall prevalence was estimated to be 1:72 compared to 1:500 worldwide.<sup>43</sup> However, this disease has also been noted in other ethnic groups, including those of Jewish origin as well as in Indians.<sup>44-48</sup> Although less common, FH also occurs in the black population<sup>49</sup> and a relatively more frequent polymorphism has been noted in the promoter region of the LDL-receptor gene.<sup>50</sup> The characterisation of the commonly occurring mutations has led to the development of a procedure for mutational screening of FH which clinicians can easily request.<sup>51-53</sup>

A strong family history of IHD is common in patients with acute coronary syndrome, ranging from 30% to 54%, and yet who do not have FH, suggesting an inherited basis for other risk factors for IHD in South African populations.

Familial hypercholesterolaemia and other forms of high TC can usually be effectively managed by statins. Their favourable effects on cardiovascular morbidity and mortality, as demonstrated in other countries, are bound to also occur in South Africa. Unfortunately, unless a particular patient's hypercholesterolaemia is responsive to lifestyle modification, the statin therapy should probably be given lifelong to maintain the cardiovascular benefit, and this has profound financial implications for the individual as well as health funders.

## 5. THE DYSLIPIDAEMIA OF INSULIN RESISTANCE

This pattern of dyslipidaemia is distinguished from hypercholesterolaemia because an increased LDLC level is not present; it is characterised by increased TG and a decreased HDLC level. This is often additionally characterised by postprandial lipaemia, extremely atherogenic, small, dense LDL lipoprotein particles and increased levels of ApoB (HyperApoB), and is associated with endothelial dysfunction, including a hypercoagulability resulting from, among others, increased Plasminogen Activator Inhibitor type 1 (PAI-1) levels and hyperfibrinogenaemia. This dyslipidaemia is recognisable as that occurring in type 2 diabetes but it is important to stress that it occurs in the presence of insulin resistance long before the onset of dysglycaemia. Indeed, this characteristic dyslipidaemia comprises part of the five diagnostic criteria proposed by the ATP III of the NCEP for the insulin resistance syndrome: a) central obesity as measured by a waist circumference exceeding 102 cm in males and 88 cm in females, but there is evidence that an increased waist:hip ratio of more than 1 in males and greater than 0.8 in females may more accurately predict cardiovascular disease;<sup>54</sup> b) TG levels greater than 1.7 mmol/l; c) an HDLC level less than 1 mmol/l in males and less than 1.3 mmol/l in females; d) a blood pressure greater than 130/80 mmHg; and e) a fasting plasma glucose greater than 6.1 mmol/l. Of note is that diabetes need not be present to make the diagnosis of the common and ever-increasing syndrome. This pattern of dyslipidaemia clusters in certain ethnic groups susceptible to the development of insulin resistance<sup>55,56</sup> and may serve as a surrogate marker of the insulin sensitivity of a population.

Looking at the distribution of these dyslipidaemic parameters in the South African population can be instructive. This high TG/low HDLC pattern of dyslipidaemia is common in the South African Indian population<sup>37,57,58</sup> and also in Indians who suffer from IHD.<sup>20,59-61</sup> This comes as no surprise as this ethnic group has been demonstrated to have a very insulin resistant profile in which pre-diabetes and type 2 diabetes are common.<sup>12,22,62-66</sup> Again, it comes as no surprise that atherosclerotic vascular disease, and in particular IHD, also have a high frequency in this population.

Although the black population in Durban clearly was found to have lower TG levels than the Indian population<sup>57,67</sup> there is reason to believe that these differences may narrow with time as there are areas in South Africa where the black peoples are developing profiles associated with an increase in insulin resistance. Urbanisation has been associated with an increase in TG levels in black subjects,<sup>23</sup> and other epidemiological studies have demonstrated significantly raised triglyceride levels in blacks.<sup>23,26,33</sup> Whether these lipid profiles are indeed markers of insulin resistance remains to be determined. In the Western Cape, the relatively common occurrence of type 2 diabetes and its risk factors have been remarked on.<sup>68</sup> In an area predominantly inhabited by black subjects who have a high prevalence of hypertension, there were very strong associations with features of the metabolic syndrome and its other co-morbid conditions.<sup>69</sup> There is also a clear relationship between urbanisation in this population and the increase in cardiovascular risk factors.<sup>70</sup> There are firm data to confirm that urbanisation has an adverse effect on cardiovascular risk factors, including the lipid profiles,<sup>23,24</sup> and it has been suggested that urbanisation sets the stage for an epidemic of atherosclerotic vascular disease.<sup>28</sup>

The coloured population of the Western Cape has been shown to have a high prevalence of cardiovascular risk factors, particularly dyslipidaemia.<sup>71-73</sup> The data indicate that the presence of hypertriglyceridaemia is particularly common<sup>71</sup> as is hypertension and other co-morbid conditions of the metabolic syndrome. Diabetes and hypertension were also common causes of mortality – both co-morbid conditions of the insulin resistance syndrome. A recent study showed a high prevalence of central obesity and an associated clustering of cardiovascular risk factors, very

reminiscent of the insulin resistance syndrome.<sup>74</sup> Impressions gained from admissions at secondary hospitals in the Western Cape Province are that the insulin resistance is common in those admitted with an acute coronary syndrome.

## 6. INADEQUATE TREATMENT OF HYPERLIPIDAEMIA

A survey of 200 private practices across the country described the detection and management of hypercholesterolaemia in about 13 000 patients. Their mean TC level was 6 mmol/l and 14% of them had IHD. However, their treatment status was generally poor with only 28% having a TC level below 5 mmol/l. This demonstrates that large numbers of these patients who could benefit most and whose lives could be saved by cholesterol-lowering therapy were not receiving it.<sup>16</sup> The most effective treatment for hypercholesterolaemia is by the use of HMG-CoA reductase inhibitors, commonly referred to as statins. It seems astonishing that until 2004 in the Western Cape Province, statins were not freely available for managing dyslipidaemia, and patient's access in this huge geographical area was limited to lipid clinics at two academic centres where the waiting times exceeded one year. The reason for this has been attributed to financial constraints, despite abundant evidence to demonstrate the cost-effectiveness of statin therapy. A manager of a prominent academic health-care institution is purported to have stated that pharmacological lipid-modifying treatment would not be supported because dyslipidaemia was not a disease of the masses, whereas the statistics clearly show otherwise.

## 7. THE CHANGING PATTERN OF DYSLIPIDAEMIA

The various avenues of evidence suggest that there is an increasing trend towards an insulin-resistant phenotype in the different South African ethnic groups. Therefore, it has become apparent that lipidology can no longer be viewed in isolation, and the importance of screening individuals at high cardiovascular risk should be stressed repeatedly. At present, it is frequently found that many patients with acute coronary syndrome are discharged from hospital before having had a lipogramme done.

The various avenues of evidence suggest that there is an increasing trend towards an insulin resistant phenotype in the different South African ethnic groups. Therefore, it has become apparent that lipidology can no longer be viewed in isolation, and the importance of screening individuals at high cardiovascular risk should be stressed repeatedly. At present, it is frequently found that many patients with acute coronary syndrome are discharged from hospital before having had a lipogramme done. The high prevalence of dysglycaemia in patients with acute coronary syndrome suggests that it would be a highly cost-effective measure to perform a fasting glucose or a modified glucose tolerance test before discharge.<sup>20,75</sup> This is particularly relevant where the management of these patients is recommended,<sup>76</sup> and before the onset of type 2 diabetes at which stage the presence of IHD is already established.<sup>19</sup> The importance of this early, and hopefully preventative, management is all the more relevant because the atherogenic dyslipidaemia is already present long before dysglycaemia develops. Those managing dyslipidaemia should have a sound knowledge of insulin resistance and the consequent dysglycaemia.

A greater emphasis will have to be placed on the important role of lifestyle modification in the management of this syndrome. However, there are some data to indicate that lifestyle modification can be instituted with a beneficial effect even in South Africa,<sup>77</sup> but the large number of patients that are lost to follow-up in such a programme is a challenge that needs addressing.

Statins are now universally available, even in the public sector, and have been prescribed in the national Essential Drug List. They are extremely effective in the management of primary hypercholesterolaemia. They are the first choice drugs in patients with the high TG/low HDLC syndrome and who have a mild to moderately increased TG level; this is despite the fact that the effect of statins on TG and HDLC levels are minimal at best. The advent of a large portion of the population who will present with an insulin-resistant phenotype may in future dictate that other choices should be considered for the management of their dyslipidaemia, such as the Peroxisome Proliferator Activated Receptor (PPAR)-alpha agonists, the fibrates, or the more recent PPAR-gamma agonists. These both effectively decrease TG levels and increase HDLC levels, and, additionally, to a greater or lesser degree, improve insulin sensitivity. Unfortunately, the policies adopted by many health-care funders in both the public and private sectors still preclude the effective management of the dyslipidaemia of the insulin resistance syndrome. Implicit in the holistic management of the insulin resistance syndrome, before the onset of dysglycaemia, is the primary prevention of type 2 diabetes.<sup>78</sup>

## 8. THE COST OF LIPID-MODIFYING MANAGEMENT

There is no doubt that lipid-modifying therapy is expensive and, contrary to popular belief, the aggressive institution of lifestyle modification to achieve the results of published material is also expensive and may not be cost-effective.<sup>4</sup> Undoubtedly, the misuse and inappropriate use of lipid-modifying drugs have wasted much money and have engendered a resistance in those who decide how health-care funds are distributed. There is enough literature to support the ultimate cost-effectiveness of the use of statins in first-world countries. However, can this automatically be assumed for developing countries where studies to demonstrate similar benefits are lacking, and are all the formulae for cost-benefit ratios appropriate for South Africa?

## 9. DYSLIPIDAEMIA AND THE HIV EPIDEMIC

South Africa is in the middle of an HIV epidemic which is predicted to increase.<sup>79</sup> The experience internationally with highly active anti-retroviral treatment (HAART) has shown that these drugs, and especially the protease inhibitors, may result in a metabolic syndrome qualitatively similar to that seen in diabetes.<sup>80-82</sup> These patients develop insulin resistance which is frequently severe enough to cause lipodystrophy,<sup>83</sup> which in turn is manifested by a central distribution of adiposity, but at other times by lipo-atrophy – an apparent paradox also seen in other causes of insulin resistance. The dyslipidaemia also manifests as a high TG/low HDLC syndrome, and severe cases can present as a chylomicronaemia syndrome.<sup>84</sup> The insulin resistance associated with HIV is reminiscent of the metabolic syndrome of diabetes in other ways: these patients show evidence of endothelial dysfunction and even increased PAI-1 levels.<sup>85</sup> Therefore, it is not surprising that this syndrome should be associated with an increased cardiovascular risk,<sup>86</sup> and mediated by mechanisms very similar to those postulated in diabetes. However, not all HIV-infected patients treated with HAART develop this insulin resistance syndrome, and the presence of a pre-existing genetic predisposition needs to be investigated. The treatment of this syndrome<sup>87</sup> incorporates many of the principles of the management of diabetes and studies have shown that they respond well to metformin<sup>88</sup> and very well to PPAR agonists.<sup>89</sup> The dyslipidaemia responds well to fibrates, but statins (except pravastatin), because of their metabolism by the hepatic cytochrome system, have the potential to result in unfavourable interactions with HAART,<sup>90</sup> although other researchers have reported that statins can be safely used together with HAART.<sup>91,92</sup> As HAART has now become more readily available and used, we can expect to see many more patients with this peculiar insulin resistance syndrome.

## 10. CONCLUSIONS

Dyslipidaemia is, quantitatively and qualitatively, an important cardiovascular risk factor in all population groups of South Africa. The advent of the predicted global pandemic of diabetes will profoundly affect persons of all social strata. The burden imposed by the insulin resistance of diabetes will be compounded by that seen with the use of HAART and this will affect the pattern of dyslipidaemia.

Lipidology should not be seen as a discipline that is reserved for an exclusive few with a detailed knowledge of obscure monogenetic disorders. Rather, because of the large number of diverse common disorders associated with dyslipidaemia, it behoofs all health-care workers to have a modicum of knowledge of lipidology, and special interest groups and societies devoted to dyslipidaemia should identify this as their primary objective.

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