CHAPTER 6: RESULTS AND DISCUSSION

THE CHARACTERISTICS OF INSULIN RESISTANCE IN THE AFRICANS OF THE NORTHWEST PROVINCE

6.1 Introduction

Results in Chapter 5 showed that several metabolic and lifestyle variables correlated significantly with insulin sensitivity in this study population. One should, however, bear in mind that the subjects studied were apparently healthy and were not using medication. Epidemiological evidence suggests that the development of arterial damage or conditions for cardiovascular complications by the clustering of mild abnormalities probably start long before the diagnoses of DM or CHD (Fontbone and Eschwège, 1991). Harris *et al.* (1997) pointed out that there is an urgent need to develop cultural appropriate intervention programmes long before the long-term complications of a chronic disease of lifestyle have devastating effects on a population. Therefore, it will be appropriate to investigate trends in insulin resistance development in this population. This information should be helpful in the development of preventative health programmes for the Northwest province.

The trends between insulin sensitivity and the risk factors for the development of the chronic diseases of lifestyle such as NIDDM, CHD, obesity and other metabolic disturbances were therefore investigated. To investigate these trends, the quartile distribution of the insulin sensitivity index was calculated and differences in risk factors between these quartiles are reported. Due to the physiological fact that gender differences play a role in the occurrence and development of many metabolic processes, insulin sensitivity quartiles were calculated for men and women separately (Table 6.1). The results are therefore given for each gender separately per quartile of insulin sensitivity.

According to Colagiuri and Brand Miller (1997) there is no uniform definition of insulin resistance. It is therefore difficult to define and describe normal/abnormal insulin resistance. Accordingly, there is a lack of a suitable standardised quantitative method for assessing insulin resistance in epidemiological studies. Therefore, no official normal ranges for insulin sensitivity

versus insulin resistance exists, probably due to the differences in methodology as described in Chapter 2.

Table 6.1 Quartiles of the insulin sensitivity index

Gender	Insulin sensitivity Quartiles Donahue *et al.*, 1988 *	Quartile range	SD	N
Men	1 Low sensitivity	<=113	30.3	33
	2	>113 <=149.5	11.4	33
	3	>149.5 <=191.5	12	34
	4 High sensitivity	>191.5	37.1	33
Women	1 Low sensitivity	<=87.7	18.5	44
	2	>87.7 <= 117.5	8.8	44
	3	>117.5 <=158.95	12.2	44
	4 High sensitivity	>158.95	61.04	44

* **10 000 ÷ [fasting glucose(mmol/L) X fasting insulin (μU/ml)]**

However, if it is accepted that the normal ranges for fasting serum glucose are between 3 mmol/L and 7 mmol/L (WHO, 1997) and for insulin between 10 μU/L and 25 μU/L (Immuno Biological Laboratories, 1995), it can be assumed that the insulin sensitivity index will typically range between 57,1 and 333.3 [using the Donahue (1988) formula]. The expected insulin quartiles will then be <=65.1; >65.1 and <= 135; >135 and <= 291; >291. Thus, the quartiles calculated for this population (Table 5.1) are within biological accepted ranges. However, the value for the low insulin sensitivity quartile of the men seems to be higher in this population (<=113 *verus* <=65 as expected) and the values for high insulin sensitivity in both genders (men > 191.5 and women >159.95) seem to be less than expected (>291). For the purpose of this study it is assumed that subjects within the upper quartile (4) were those with high insulin sensitivity and those in the lower quartile (1) were insulin resistant.

6.2 Results

6.2.1 General variables of the subjects per insulin sensitivity quartile (IS quartile)

The age of the men did not increase with decreased insulin sensitivity (Table 6.2a). A consistent decrease in body mass was observed from the lowest insulin sensitivity quartile (1) towards the highest insulin sensitivity quartile (4) in the men. Although not statistical significant, an increase in alcohol consumption for the men in IS quartile one to IS quartile four can be observed (Table 6.2a). The mean weight of the men in quartile

four was 3.0 - 3.6 kg lower than in the other quartiles, but this difference was not significant.

The women in IS quartile four was significant older than in IS qaurtile two and three, but not older than those in IS quartile one. Although the mean age of the women differs between the insulin sensitivity quartiles, it does not constantly increase with an increase in insulin resistance and therefore might confirm the literature (Kohrt, 2000).

The mean body mass of the women (Table 6.2b) in IS quartile four was highly significant lower than in IS quartile one (p= 0.003) and IS quartile two (p=0.008). This significance was maintained after adjustment for age.

Table 6.2a Personal variables for the men per quartile of insulin sensitivity (IS)

IS Quartile	Stats	Age (years)	Temp (^{0} C)	Mass (kg)	Stature (cm)	Alcohol (g/day)	Energy intake (KJ)
1	Mean	34.3	36.4	60.3	167.6	9.1	8494
n=33	95% CI	29.8 - 38.8	36.1 - 36.6	56.9 - 63.6	165.2 - 169.9	(-8.8) - 27.1	7725.4 - 10172.6
2	Mean	34.9	36.1	60.7	172	15.3	9423.9
n=33	95% CI	30.1 - 39.8	35.9 - 36.4	57.1 - 64.2	169.4 - 174.5	(-3.8) - 34.5	8200.2 - 10647.5
3	Mean	33.5	36.3	59.9	170.7	24.9	8543.9
N=34	95% CI	28.9 - 38.2	36.1 - 36.6	56.5 - 63.3	168.2 - 173.1	6.6 - 43.1	7320.3 - 9767.6
4	Mean	34.9	36.3	56.9	168.6	26.1	9268.9
n=33	95% CI	30.2 - 39.5	36 - 36.6	53.5 - 60.4	166.1 - 171	7.6 - 44.7	8063.9 - 10473.9

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

The mean energy consumption of the women was highly significant lower in IS quartile four than in IS quartile one (p=0.005), IS quartile two (p=0.009) and IS quartile three (p=0.024). These differences were maintained after adjustment for age.

Table 6.2b Personal variables for the women per quartile of insulin sensitivity (IS)

IS. Quartile.	Stats	Age (years)	Temp (°C)	Mass (kg)	Stature (cm)	Alcohol (g/day)	Energy intake (KJ)
1	Mean	35.7	36.3	73.3 [c]	158.1	1.6	9655.9 [e]
n=44	95% CI	31.7 - 39.8	36.1 - 36.5	67.9 - 78.7	156.1 - 160	(-1.3) - 4.5	8121.4 - 9990.4
2	Mean	33.7 [a]	36.3	72 [d]	157.8	3.8	8819.2 [f]
n=44	95% CI	29.7 - 37.7	36.1 - 36.5	66.6 - 77.4	155.9 - 159.6	0.9 - 6.7	7884.7 - 9753.7
3	Mean	33.5 [b]	36.4	68.5	157	1.8	8629.4 [g]
n=44	95% CI	29.5 - 37.6	36.2 - 36.6	63.1 - 73.9	155.1 - 158.9	(-1.1) - 4.7	7705.6 - 9553.2
4	Mean	40.7 [ab]	36.4	61.7 [cd]	156.9	4.4	7022.2 [efg]
n=44	95% CI	36.8 - 44.6	36.2 - 36.6	56.5 - 67	155.1 - 158.8	1.5 - 7.2	6098.4 - 7945.9

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

From Tables 6.3a and 6.3b, except for level of urbanisation, no clear pattern between the different insulin sensitivity quartiles can be seen regarding the lifestyles and behaviours of the men and women. It is, however, interesting to note that substantially more men (Table 6.3a) in IS quartile four were smokers (63.6%) and had a job (53.1%) than in IS quartile one (smokers: 42.4%; job: 30.3%). However, seven out of the ten men whose households earned more than R3 000 per month fell in IS quartile one and only one in IS quartile four.

Most of the men in insulin quartile four were rural (Table 6.3a). No men living on farms were found in IS quartile one. The number of men living on farms increased consistently towards the higher insulin sensitivity quartile (IS Q4). The percentage squatter men decreased consistently towards the high insulin sensitivity quartile (IS Q4). Nine percent of the women in insulin quartile one were rural (Table 6.3b). The number of rural women increased consistently towards IS quartile four. Sixty one percent (61.4%) of the women in IS quartile one were urban and upper urban dwellers, while only 22.7% were in IS quartile four. Almost the same tendency was seen for the squatter dwellers. These results suggest that more squatters and urban men and women might be insulin resistant, confirming the results reported in Chapter 5.

Table 6.3a **Lifestyle markers for the men** [as a percentage (%) of the investigated population per quartile of insulin sensitivity]

Lifestyle markers	Insulin sensitivity quartile 1 n=33	Insulin sensitivity quartile 2 n=33	Insulin sensitivity quartile 3 n=34	Insulin sensitivity quartile 4 n=33
Stratum 1= rural 2 = farm dwellers 3 = squatters 4 = urban and upper urban	1 = 12.1% 2 = 0 % 3 = 36.4% 4 = 51.5%	1 = 18.1% 2 = 9.4 % 3 = 28.1% 4 = 43.8%	1 = 6.1% 2 = 12.1% 3 = 27.3 % 4 = 54.5 %	1 = 30.3 % 2 = 18.2 % 3 = 24.2 % 4 = 27.3 %
Smokers	42.4 %	46.9 %	69.7 %	63.6%
HIV-status	12.1%	6.3%	15.2 %	21.2 %
Employed	30.3%	34.4%	45.5%	53.1%
Education level	0 =21.2% <st6 =12.1% st6-8 +/-trade =27.3% st9-10 +/-trade =24.2% st9-10 + > =15.2%	0 =34.4% <st6 =18.8% st6-8 +/-trade =18.8% st9-10+/-trade=21.9% st9-10 + > = 6.3%	0 =18.2% <st6 =30.3% st6-8 +/-trade =30.3% st9-10 +/-trade=21.2% st9-10 + > =0 %	0 =31.3% <st6 =12.5% st6-8 +/-trade =25.0% st9-10 /-trade=31.3% st9-10 + > = 0 %
Physical activity level	low = 9.1% medium = 27.3% high = 63.6%	low =28.1% medium =18.8% high =53.1%	low =15.2% medium =30.3% high =54.5%	low =25.0% medium =21.9% high =53.1%
Total household income	R0-100 =18.2% R101-500 =6.1% R501-1000 =30.3% R1001-2000 =15.2% R2001-3000 =9.1% R3000+ =21.2%	R0-100 =9.4% R101-500 =28.1% R501-1000 =21.9% R1001-2000 =21.9% R2001-3000 =12.5% R3000+ =6.3%	R0-100 =15.2% R101-500 =21.2% R501-1000 =33.3% R1001-2000 =30.3% R2001-3000 =0% R3000+ =0%	R0-100 =12.1% R101-500 =30.3% R501-1000 =27.3% R1001-2000 =21.2% R2001-3000 =6.1% R3000+ =3.0%

Table 6.3b **Lifestyle markers for the women** [as a percentage (%) of the investigated population per quartile of insulin sensitivity]

Lifestyle markers	Insulin sensitivity quartile 1 n=44	Insulin sensitivity quartile 2 n=44	Insulin sensitivity quartile 3 n=44	Insulin sensitivity quartile 4 n=44
Stratum 1= rural 2 = farm dwellers 3 = squatters 4 = urban and upper urban	1 = 9.1% 2 = 13.6% 3 = 15.9% 4 = 61.4%	1 = 18.6% 2 = 18.6% 3 = 27.9% 4 = 34.9%	1 = 27.3% 2 = 15.9% 3 = 13.62% 4 = 43.2%	1 = 29.5% 2 = 29.5% 3 = 18.2% 4 = 22.7%
Smokers	6.8%	9.3%	4.5%	15.9%
HIV-status	13.6%	16.3%	25%	33.3%
Employed	16.3%	16.3%	22.7%	52.3%
Education level	0 =11.4% <st6 =34.1% st6-8 +/-trade =34.1% st9-10 +/-trade =13.6% st9-10 + > =6.8%	0 =25.6% <st6 =30.2% st6-8 +/-trade =34.9% st9-10 +/-trade =9.3% st9-10 + > =0%	0 =13.6% <st6 =34.1% st6-8 +/-trade =29.5% st9-10 +/-trade=15.9% st9-10 + > =6.8%	0 =20.5% <st6 =50% st6-8 +/-trade =18.2% st9-10 +/-trade =6.8% st9-10 + > =4.5%
Physical activity level	low = 38.6% medium = 9.1% high = 52.3%	low =27.9% medium =30.2% high =41.9%	low =36.4% medium =36.4% high =27.3%	low =27.3% medium =38.6% high =34.1%
Total household income	R0-100 =13.6% R101-500 =22.7% R501-1000 =40.9% R1001-2000 =13.6% R2001-3000 =2.3% R3000+ =6.8%	R0-100 =16.3% R101-500 =27.9% R501-1000 =39.5% R1001-2000 =16.3% R2001-3000 =0% R3000+ =0%	R0-100 =13.6% R101-500 =27.3% R501-1000 =38.6% R1001-2000 =13.6% R2001-3000 =2.3% R3000+ =4.5%	R0-100 =25% R101-500 =34.1% R501-1000 =25% R1001-2000 =13.6% R2001-3000 =0% R3000+ =2.3%

In both genders the number of subjects who were HIV positive were higher in the two high insulin sensitivity quartiles (IS quartile 3 & 4) than in the low insulin sensitivity quartiles (IS quartile 1 & 2) (Tables 6.3.a and b).

It also seems as if more women in the medium physical activity level, on the Beacke activity scale (Kruger, 1999), gained benefit regarding their insulin sensitivity level than those having high or little physical activity. However, no significant associations were found in Chapter 5 between insulin sensitivity and physical activity levels.

These results as well as the associations found between insulin sensitivity and some lifestyle factors (Chapter 5) suggested that the data should be adjusted for age, alcohol consumption and dietary energy intake in order to investigate an independent role of insulin sensitivity in the development of chronic diseases of lifestyle in these subjects.

6.2.2 Insulin sensitivity and risk markers for NIDDM

The mean fasting serum glucose values for the men (Table 6.4a) in the fourth IS quartile (highest insulin sensitivity) was significantly lower (4.4 mmol/L) than in IS quartile one (5.3 mmol/L; p=0.000) and IS quartile two (4.8 mmol/L; p=0.027). After adjustment for age, alcohol and energy intake, the mean glucose level of men in IS quartile one was significantly higher than in all the other quartiles (Table 6.4b).

The mean fasting serum insulin level in IS quartile four (9.8 μU/ml) was also significantly lower than the mean fasting serum insulin value of the men in the lowest IS quartile (31.5 μU/ml; p=0.000) and significantly lower than in IS quartile two (16.1 μU/ml; p=0.037). After adjustment for age, alcohol and energy intake, the insulin levels of subjects in IS quartile one were significantly higher than all the other quartiles.

The normal ranges given for serum insulin levels by the Immuno Biological laboratories (insulin kit used), indicate that a level of 10 μU/ml is low abnormal. The mean fasting serum insulin level of the men in IS quartile four was 9.8 μU/ml. If one considers the low fasting glucose levels of the men accompanied by these low fasting insulin levels, none of them showed the presence of a lack of insulin. Therefore, these low insulin levels of the men in IS quartile four were considered as normal.

Table 6.4a Markers for NIDDM of the men per quartile of insulin sensitivity (IS)

IS Quartile	Stats	S-GlucT_0 (mmol/L)	S-GlucT_{120} (mmol/L)	S-insulin (μU/ml)	Insulin sensitivity (IS) index
1	Mean	5.3 [a]	5.1	31.5 [a]	78.4 [abcd]
n=33	95% CI	5.1 - 5.5	4.6 - 5.7	27 - 35.9	67.7 - 89.1
2	Mean	4.8 [b]	5.3	16.1 [b]	131.4 [abcd]
n=33	95% CI	4.6 - 5	4.8 - 5.9	11.9 - 20.3	121.4 - 141.5
3	Mean	4.6	5.03	12.6	172.7 [abcd]
n=34	95% CI	4.4 - 4.9	4.5 - 5.6	8.1 - 17.2	161.8 - 183.6
4	Mean	4.4 [ab]	5.04	9.8 [ab]	236.5 [abcd]
n=33	95% CI	4.2 - 4.7	4.5 - 5.6	5.5 - 14	226.3 - 246.7

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.4b Markers for NIDDM of the men per quartile of insulin sensitivity (IS) after adjustment for age, energy and alcohol intake

IS Quartile	Stats	S-GlucT_0 (mmol/L)	S-GlucT_{120} (mmol/L)	S-insulin (μU/ml)	Insulin sensitivity (IS) index
1	Mean	5.5 [abcd]	5.3	36.3 [abcd]	68.0 [abcd]
n=33	95% CI	5.3 - 5.8	4.6 - 6.0	31.2 -41.5	53.3 - 82.0
2	Mean	4.8 [abd]	5	18.5 [abd]	114.5 [abcd]
n=33	95% CI	4.6 - 5.1	4.4 - 5.6	13.6 - 23.3	101.0 - 128.0
3	Mean	4.7 [ac]	5.3	13.8 [ac]	152.8 [abcd]
n=34	95% CI	4.5 - 4.9	4.8 - 5.8	9.9 - 17.8	141.7 - 163.9
4	Mean	4.5 [abcd]	5	10.4 [abd]	222.8 [abcd]
n=33	95% CI	4.3 - 4.7	4.6 - 5.5	6.8 - 13.9	212.9 - 232.7

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

The mean fasting serum glucose value for the women (Table 6.5a) in the first IS quartile was significantly higher (5.4 mmol/L) than in IS quartile four (4.4 mmol/L; p=0.000). After adjustment for the reported lifestyle factors it was significant higher than in all the other quartiles (Table 6.5b). The mean fasting serum insulin level in IS quartile four (11.3 μU/ml) was also significantly lower than in IS quartile two (21.2 μU/ml; p=0.028) and IS quartile one (37.3 μU/ml; p=0.000). These significant differences were independently maintained after adjustments for all the reported lifestyle factors.

The mean two hour serum glucose value of the women in IS quartile one (6.5 mmol/L) was statistically significant higher than in IS quartile two (5.4 mmol/L; p=0.02) and insulin quartile four (5.9 mmol/L;p=0.036). After adjustment for the combination of lifestyle factors the value in IS quartile one was significantly higher than in IS quartile three (Table 6.5b).

Table 6.5a Markers for NIDDM of the women per quartile of insulin sensitivity (IS)

IS Quartile	Stats	S-GlucT_0 (mmol/L)	S-GlucT_{120} (mmol/L)	S-insulin (μU/ml)	Insulin sensitivity (IS) index
1	Mean	5.4 [a]	6.5 [d]	37.3 [b]	67.1 [abcd]
n=44	95% CI	5.1 - 5.6	5.9 - 7.2	31.3 - 43.3	57.6 - 76.7
2	Mean	4.7	5.4 [de]	21.2 [c]	101.5 [abcd]
n=44	95% CI	4.4 - 5	4.8 - 6.1	15.1 - 27.2	91.8 - 111.1
3	Mean	4.5	5.8	16.5	138.1 [abcd]
n=44	95% CI	4.2 - 4.7	5.1 - 6.5	10.3 - 22.7	128.2 - 147.9
4	Mean	4.4 [a]	5.9 [e]	11.3 [bc]	212.9 [abcd]
n=44	95% CI	4.1 - 4.7	5.2 - 6.6	5.1 - 17.6	202.9 - 222.9

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.5b Markers for NIDDM of the women per quartile of insulin sensitivity (IS) after adjustment for age, energy and alcohol intake

IS Quartile	Stats	S-GlucT_0 (mmol/L)	S-GlucT_{120} (mmol/L)	S-insulin (μU/ml)	Insulin sensitivity (IS) index
1	Mean	5.3 ^{abcd}	6.7 ^{a}	34.5 ^{abcd}	71.0 ^{abcd}
n=44	95% CI	5.1 - 5.6	5.9 - 7.1	28.8 - 40.2	62.7 - 79.3
2	Mean	4.6 ^{abcd}	5.7	20.2 ^{ab}	110.0 ^{abcd}
n=44	95% CI	4.4 - 4.9	5.1 - 6.3	14.3 - 26.1	101.3 - 118.6
3	Mean	4.5 ^{abcd}	5.6 ^{a}	14.9 ^{ac}	151.0 ^{abcd}
n=44	95% CI	4.2 - 4.8	4.9 - 6.3	8.3 - 21.5	141.4 - 160.7
4	Mean	4.2 ^{abcd}	5.8	11.2 ^{ad}	228.8 ^{abcd}
n=44	95% CI	3.9 - 4.6	5.0 - 6.7	3.4 - 19.0	217.4 - 240.2

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

6.2.3 Insulin sensitivity and risk markers for CHD

The LDL-C:HDL-C ratio of the men (Table 6.6a) in IS quartile one (2.5) was significantly higher than in IS quartile four (1.9; p=0.008). After adjustment for the lifestyle factors (Table 6.6b), the level in IS quartile four was significantly lower than in IS quartile two. This result corresponds with those reported in Chapter 5. The mean total cholesterol (TC= 4 mmol/L) level of the men in IS quartile one, was significantly higher than in IS quartile four (3.5 mmol/L; p=0.05). After adjustments the total cholesterol level in IS quartile four was significantly lower than in IS quartile two. In Chapter 5, no association between insulin sensitivity and TC was reported. An inverse relation was reported between serum triglycerides and insulin resistance in Chapter 5. Although an increase in serum triglycerides from the highest IS quartile to the lowest occurred, no significant differences between the IS quartiles were found. However, after adjustment for age, energy and alcohol intake, serun TG in IS quartile one was significantly higher than in IS quartile four (Table 6.6b).

Both the systolic and diastolic blood pressure of the men in IS quartile two were significantly higher than in the other IS quartiles after adjustment for the reported lifestyle factors (Table 6.6b).

Table 6.6a Markers for CHD of the men per quartile of insulin sensitivity (IS)

IS Quartile	Stats	SBP (mmHg)	DBP (mmHg)	S-TC (mmol/L)	S-HDL_C (mmol/L	S-LDL_C (mmol/L	S-TG (mmol/L)	LDL:HDL	PI-Hc (%)	PI-Fib (g/L)
1	Mean	126.3	77.8	4.0 [a]	1.11	2.5	1.2	2.5 [b]	44.2	3.1
N=33	95% CI	120.7 - 132	74.2 - 81.3	3.7 - 4.4	1 - 1.2	2.2 - 2.8	0.9 - 1.4	2.1 - 2.8	42.5 - 45.8	2.7 - 3.5
2	Mean	130.5	78.1	3.9	1.14	2.4	1.1	2.3	45.3	2.8
N=33	95% CI	124.9 - 136.2	74.6 - 81.7	3.6 - 4.3	1 - 1.3	2.1 - 2.7	0.9 - 1.3	1.9 - 2.6	43.7 - 46.9	2.4 - 3.2
3	Mean	125.1	77.3	3.8	1.16	2.4	1.1	2.2	45.9	3
n=34	95% CI	119 - 131.1	73.5 - 81.1	3.5 - 4.2	1 - 1.3	2 - 2.7	0.9 - 1.3	1.8 - 2.6	44.1 - 47.6	2.6 - 3.4
4	Mean	125	75.4	3.5 [a]	1.15	2.1	0.9	1.9 [b]	44.2	2.8
N=33	95% CI	119.1 - 130.8	71.8 - 79.1	3.2 - 3.9	1 - 1.3	1.8 - 2.4	0.6 - 1.1	1.5 - 2.3	42.5 - 45.9	2.4 - 3.2

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.6b Markers for CHD of the men per quartile of insulin sensitivity (IS) after adjusted for age, energy and alcohol intake

IS Quartile	Stats	SBP (mmHg)	DBP (mmHg)	S-TC (mmol/L)	S-HDL_C (mmol/L	S-LDL_C (mmol/L	S-TG (mmol/L)	LDL:HDL	PI-Hc (%)	PI-Fib (g/L)
1	Mean	125.5 [a]	67.6 [a]	3.9	1.07	2.4	1.3 [a]	2.4	44.2	3
N=33	95% CI	119.2 - 131.8	72.8 - 80.4	3.6 - 4.3	0.92 - 1.2	2.1 - 2.8	1.1 - 1.6	1.9 - 2.8	42.2 - 46.1	2.6 - 3.5
2	Mean	134.9 [abc]	81.7 [abc]	4.1 [a]	1.17	2.6	0.99	2.5 [a]	45.3	3
N=33	95% CI	128.9 - 140.8	78.1 - 85.3	3.8 - 4.5	1.04 - 1.31	2.3 - 2.9	0.8 - 1.2	2.1 - 2.9	43.5 - 47.1	2.6 - 3.4
3	Mean	125.8 [b]	77.0 [b]	3.7	1.16	2.2	1.1	2.1	45.2	2.8
n=34	95% CI	120.5 - 131.0	73.9 - 80.2	3.4 - 4.1	1.03 - 1.28	1.9 - 2.5	0.9 - 1.3	1.8 - 2.5	43.5 - 46.8	2.4 - 3.2
4	Mean	123.0 [c]	74.5 [c]	3.7 [a]	1.14	2.2	0.95 [a]	2 [a]	44.8	2.9
N=33	95% CI	118.1 - 127.8	71.6 - 77.5	3.4 - 3.9	1.03 - 1.26	2.0 - 2.5	0.8 - 1.1	1.7 - 2.3	43.3 - 46.3	2.6 - 3.3

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.7a Markers for CHD of the women per quartile of insulin sensitivity (IS)

IS Quartile	Stats	SBP (mmHg)	DBP (mmHg)	S-TC (mmol/L)	S-HDL_C (mmol/L)	S-LDL_C (mmol/L)	S-TG (mmol/L)	LDL:HDL	PI-Hc (%)	PI-Fib (g/L)
1	Mean	130.2	81.8[e]	4.2	1.07 [b]	2.7	1.1	2.8	40.9	3.5
n=44	95% CI	124.6 - 135.7	78.4 - 85.2	3.8 - 4.5	1 - 1.2	2.4 - 3.1	0.9 - 1.2	2.4 - 3.2	39.7 - 42.2	3.1 - 3.9
2	Mean	128.3	79.8	4.4	1.07 [c]	3	1.1	2.9	41.1	3.8
n=44	95% CI	122.5 - 134.1	76.3 - 83.4	4.1 - 4.8	1 - 1.2	2.7 - 3.4	1 - 1.3	2.5 - 3.3	39.8 - 42.3	3.4 - 4.3
3	Mean	125.7	76.9	4.1	1.12	2.5	0.9	2.4	41.7 [d]	3.5
n=44	95% CI	119.9 - 131.5	73.4 - 80.4	3.7 - 4.4	1 - 1.2	2.2 - 2.9	0.7 - 1.1	2 - 2.8	40.5 - 43	3 - 3.9
4	Mean	124.1	76.5[e]	4.3	1.23 [bc]	2.6	1	2.4	39.7 [d]	3.2
n=44	95% CI	118.4 - 129.8	73 - 79.9	3.9 - 4.6	1.1 - 1.3	2.3 - 3	0.8 - 1.2	2 - 2.8	38.4 - 41	2.7 - 3.6

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.7b Markers for CHD of the women per quartile of insulin sensitivity (IS) after adjusted for age, energy and alcohol intake

IS Quartile	Stats	SBP (mmHg)	DBP (mmHg)	S-TC (mmol/L)	S-HDL_C (mmol/L)	S-LDL_C (mmol/L)	S-TG (mmol/L)	LDL:HDL	PI-Hc (%)	PI-Fib (g/L)
1	Mean	132.0 ^{acd}	82.4 ^{acd}	4.3 ^{a}	1.08 ^{a}	2.8 ^{b}	1.2 ^{a}	2.8 ^{a}	41.2	3.5
n=44	95% CI	127.3 - 136.8	79.4 - 85.3	4.0 - 4.5	0.99 - 1.17	2.5 - 3.1	1.0 - 1.3	2.5 - 3.2	40.1 - 42.4	3.1 - 3.9
2	Mean	129.1 ^{bd}	80.8 ^{bd}	4.5 ^{b}	1.05 ^{b}	3.1 ^{a}	1.1	3.1 ^{bcd}	41.6 ^{a}	3.8
n=44	95% CI	124.2 - 134.1	77.6 - 83.9	4.2 - 4.8	0.96 - 1.1	2.8 - 3.4	0.9 - 1.2	2.7 - 3.4	40.4 - 42.8	3.4 - 4.2
3	Mean	125.5 ^{c}	76.2 ^{ac}	4.3 ^{c}	1.3 ^{ab}	2.6 ^{a}	1	2.3 ^{abc}	40.7	3.4
n=44	95% CI	119.9 - 131.0	72.7 - 79.7	3.9 - 4.6	1.14 - 1.35	2.3 - 2.9	0.8 - 1.1	1.9 - 2.7	39.4 - 42.1	2.9 - 3.8
4	Mean	117.6 ^{abd}	73.0 ^{abd}	3.7 ^{abc}	1.2	2.2 ^{ab}	0.8 ^{a}	2.1 ^{abd}	39.3 ^{a}	3.2
n=44	95% CI	111.4 - 123.7	69.1 - 76.9	3.4 - 4.1	1.04 - 1.26	1.8 - 2.6	0.6 - 1.0	1.7 - 2.6	37.8 - 40.8	2.7 - 3.7

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

The mean diastolic blood pressure of the women in IS quartile four (76.5 mmHg) was significantly lower than in IS quartile one (81.8 mmHg; $p=0.033$). When adjusted for the lifestyle factors, it was also lower than in all the other IS quartiles. Although the mean systolic blood pressure of the women increased steadily from the highest IS quartile towards the lowest IS quartile, large inter-subject variations were responsible for the absence of significant differences. However, after adjustment for the reported lifestyle factors, these increases in diastolic blood pressure towards the lowest IS quartile differed significantly from each other (Table 6.7b). These results are in accordance to the relationships between insulin sensitivity and diastolic as well as systolic blood pressure of the women reported in Chapter 5.

The mean heamatocrit of the women in IS quartile four (39.7%) was significantly lower than in IS quartile three (41.7%; $p=0.026$). After adjustment for the reported lifestyle factors, the value in IS quartile four was significantly lower than in IS quartile two (Table 6.7b).

The mean serum HDL-cholesterol of the women in IS quartile four (1.23 mmol/L) was significantly higher than in IS quartile one (1.07 mmol/L; $p=0.024$) and IS quartile two (1.07 mmol/L; $p= 0.032$). These significant differences were not maintained when adjusted for the combination of lifestyle factors. With adjustment the HDL-C level in IS quartile three was significantly higher than in IS quartile one and two (Table 6.7b).

After adjustments for the reported lifestyle factors, the women in IS quartile four had significantly lower levels of serum TC, LDL-C and LDL-C:HDL-C ratio than those in IS quartile one, two and three as well as significantly lower levels of TG than in IS qaurtile one (Table 6.7b).

6.2.4 Insulin sensitivity and markers for obesity

The mean triceps skinfold thickness of the men (Table 6.8a) in IS quartile four (6.9 mm) was significantly smaller than in IS quartile three (9.2 mm; p=0.037), IS quartile two (9.2 mm; p=0.033) and in IS quartile one (9.5 mm; p=0.017). After adjustment for the reported lifestyle factors IS quartile four was significantly smaller than IS quartile two and three (Table 6.8b). The abdominal skinfold thickness of the men in IS quartile four (11.4 mm) was significantly smaller than in IS quartile one (17.9 mm; p=0.003). After adjustment it was significantly smaller than in all the other quartiles (Table 6.8b). In Chapter 5 an inverse relationship was found between insulin sensitivity and the triceps skinfold thickness of the men.

After adjustment for the reported lifestyle factors, the BMI and the minimum waist circumference of the men in IS quartile two were significantly higher than in IS quartile three and four. The percentage body fat calculated from girths was also significantly higher in IS quartile two than in IS quartile four (Table 6.8b).

The mean BMI of the women (Table 6.9a) in IS quartile four (25.2 kg/m^2) was significantly smaller than in IS quartile one (28.7 kg/m^2; p=0.018). When adjusted for the combination of lifestyle factors, the mean BMI of the women in IS quartile four was significantly smaller than in IS quartile two (Table 6.9b). An inverse correlation between insulin sensitivity and BMI of the women was found in Chapter 5.

Table 6.8a Markers for obesity of the men per quartile of insulin sensitivity (IS)

IS Quartile	Stats	BMI (kg/m²)	Triceps (mm)	Abdomen (mm)	Waist-Min (cm)	Hip-Max (cm)	W/H ratio	Body Fat (%)
1	Mean	21.5	9.5 [a]	17.9 [d]	74.4	87.5	0.8	21.7
n=33	95% CI	20.4 - 22.5	8 - 11	14.9 - 20.8	72 - 76.8	85.4 - 89.6	0.8 - 0.9	20 - 23.3
2	Mean	20.1	9.2 [b]	15.4	72.3	87.3	0.8	20.6
n=33	95% CI	19 - 21.1	7.7 - 10.8	12.4 - 18.4	69.8 - 74.7	85.1 - 89.4	0.81 - 0.85	18.9 - 22.2
3	Mean	20.9	9.2 c	15.1	73.5	87.7	0.8	20.6
n=34	95% CI	19.8 - 21.9	7.6 - 10.7	12.2 - 18.1	71.1 - 75.9	85.5 - 89.8	0.82 - 0.86	19 - 22.2
4	Mean	20.3	6.9 [abc]	11.4 [d]	71.8	85.1	0.8	19.6
n=33	95% CI	19.2 - 21.3	5.3 - 8.4	8.4 - 14.4	69.4 - 74.3	82.9 - 87.2	0.8 - 0.9	18 - 21.3

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.8b Markers for obesity of the men per quartile of insulin sensitivity (IS) after adjusted for age, energy and alcohol intake

IS Quartile	Stats	BMI (kg/m²)	Triceps (mm)	Abdomen (mm)	Waist-Min (cm)	Hip-Max (cm)	W/H ratio	Body Fat (%)
1	Mean	20.9	8.8	17.5 [e]	73.8	87	0.85	21.1
n=33	95% CI	19.6 - 22.1	7.1 - 10.6	14.2 - 20.8	71.2 - 76.4	84.5 - 89.5	0.83 - 0.87	19.3 - 22.9
2	Mean	21.7 [ab]	10.6 [c]	17.8 [f]	75 [h]	89.6 [km]	0.84	22.2 [o]
n=33	95% CI	20.6 - 22.9	8.9 - 12.2	14.8 - 20.9	72.6 - 77.4	87.3 - 91.9	0.82 - 0.85	20.6 - 23.9
3	Mean	20.2 [a]	9.4 [d]	16.7 [g]	72.4	86.4 [m]	0.84	20.4
n=34	95% CI	19.2 - 21.2	8 - 10.8	14 - 19.3	70.3 - 74.5	84.4 - 88.4	0.82 - 0.85	18.9 - 21.8
4	Mean	20.2 [b]	6.6 [cd]	10.4 [efg]	71.5 [h]	85.1 [k]	0.84	19.5 [o]
n=33	95% CI	19.3 - 21.2	5.3 - 7.9	8 - 12.9	69.6 - 73.5	83.3 - 87	0.83 - 0.85	18.1 - 20.8

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.9a also reveals that the mean minimum waist circumference of the women in IS quartile four (76 cm) was significantly smaller than in IS quartile three (77.1 cm; p=0.024), IS quartile two (81.6 cm; p=0.022) and in IS quartile one (81.1 cm; p=0.021). After adjustment for the combination of lifestyle factors, these significant differences disappeared.

When adjusted for the reported lifestyle factors, the mean maximum hip circumference of the women in the highest IS quartile differed significantly from IS quartile three and IS quartile two (Table 6.9b). Similarly the abdominal and triceps skinfold thicknesses of the women in IS quartile four were significantly smaller than in IS quartile one and two.

Table 6.9a Markers for obesity of the women per quartile (Q) of insulin sensitivity (IS)

IS Quartile	Stats	BMI (kg/m²)	# Triceps (mm)	# Abdomen (mm)	Waist-Min (cm)	Hip-Max (cm)	W/H ratio	Body Fat (%)
1	Mean	28.7 [a]	20.3	28	81.1 [b]	104.3	0.8	50.4
n=44	95% CI	26.6 - 30.7	17.3 - 23.4	23 - 33	77.1 - 85.1	100.3 - 108.2	0.76 - 0.8	47.3 - 53.5
2	Mean	28.7	21.9	26.5	81.6 [c]	104.3	0.8	51.5 [f]
n=44	95% CI	26.6 - 30.8	18.8 - 25.1	21.4 - 31.7	77.5 - 85.6	100.3 - 108.3	0.76 - 0.8	48.4 - 54.7
3	Mean	27	20.9	24.5	77.1 [d]	104.1	0.7 [e]	50.2
n=44	95% CI	25 - 29.1	17.9 - 23.8	19.6 - 29.3	73.1 - 81	100.1 - 108	0.7 - 0.8	47.1 - 53.3
4	Mean	25.1 [a]	17.4	24.4	76 [bcd]	97.7	0.8 [e]	46.4 [f]
n=44	95% CI	23 - 27.2	14.6 - 20.2	19.8 - 29.1	72 - 80	93.7 - 101.6	0.76 - 0.8	43.2 - 49.5

The number of women with measured skin fold thicknesses (triceps and abdominal) were only 115: IS Q1=27; IS Q2=27; IS Q3=29; IS Q4=32). The skinfold callipers used were too small to measure skinfold thicknesses in these obese women

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.9b Markers for obesity of the women per quartile of insulin sensitivity (IS) after adjusted for age, energy and alcohol intake

IS Quartile	Stats	BMI (kg/m²)	# Triceps (mm)	# Abdomen (mm)	Waist-Min (cm)	Hip-Max (cm)	W/H ratio	Body Fat (%)
1	Mean	24.1	21 [a]	28.4 [e]	72.4	96.1	0.75	43.7
n=44	95% CI	22.6 - 25.6	18 - 24.1	23.5 - 33.2	69.5 - 75.3	92.6 - 99.6	0.73 - 0.77	41.1 - 46.4
2	Mean	24.3 [a]	22.1 [b]	28.1 [d]	72.4	97.1 [g]	0.75	45.1
n=44	95% CI	22.9 - 25.7	19.4 - 24.9	23.6 - 32.5	69.7 - 75	93.9 - 100.3	0.73 - 0.77	42.7 - 47.5
3	Mean	23.9	20.6	25.4	71.3	97.8 [f]	0.73	45.3
n=44	95% CI	22.3 - 25.4	17.5 - 23.6	20.4 - 30.3	68.4 - 74.2	94.3 - 101.4	0.71 - 0.75	42.6 - 48
4	Mean	21.9 [a]	15.5 [ab]	20.1 [de]	68.4	91.4 [fg]	0.75	41.3
n=44	95% CI	20.2 - 23.6	12 - 18.9	14.5 - 25.6	65.1 - 71.7	87.4 - 95.3	0.73 - 0.77	38.3 - 44.3

The number of women with measured skin fold thicknesses (triceps and abdominal) were only 115: IS Q1=27; IS Q2=27; IS Q3=29; IS Q4=32). The skinfold callipers used were too small to measure skinfold thicknesses in these obese women

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

The mean percentage body fat calculated from girths of the women in IS quartile four (46.4%) was significantly smaller than in IS quartile two (51.5%; $p=0.023$). After adjustment for the reported lifestyle factors this significance disappeared.

6.2.5 Insulin sensitivity and markers of other metabolic disorders

No significant differences before and after adjustments for the reported lifestyle factors for serum excretion products (Table 6.10) of the men between the IS quartiles were found in this study population.

Table 6.10 Serum excretion products of the men per quartile of insulin sensitivity (IS)

IS Quartile	Stats	S-Urea (mmol/L)	S-uric acid (mmol/L)	S-Creat (μmol/L)	S-T_Bili (μmol/L)
1	Mean	3.8	0.4	95.5	4.9
n=33	95% CI	3.3 - 4.3	0.3 - 0.5	90.8 - 100.1	3.9 - 5.9
2	Mean	3.6	0.38	90.5	4.8
n=33	95% CI	3.1 - 4.1	0.3 - 0.5	85.6 - 95.5	3.8 - 5.9
3	Mean	3.7	0.3	93.7	4
n=34	95% CI	3.2 - 4.2	0.2 - 0.4	89 - 98.5	3 - 5
4	Mean	3.3	0.29	91.5	4.7
n=33	95% CI	2.8 - 3.8	0.2 - 0.4	86.7 - 96.2	3.7 - 5.7

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

The mean serum urea of the women (Tables 6.11a and b) in IS quartile four (3.0 mmol/L) was significantly lower than in IS quartile one (3.7 mmol/L; $p=0.007$). After adjustment for the reported lifestyle factors, this difference was maintained.

Table 6.11a Serum excretion products of the women per quartile of insulin sensitivity

IS Quartile	Stats	S-Urea (mmol/L)	S-uric acid (mmol/L)	S-Creat (μmol/L)	S-T_Bili (μmol/L)
1	Mean	3.7 [a]	0.26	83.4	4.1
n=44	95% CI	3.3 - 4	0.2 - 0.3	79.9 - 87	3.2 - 4.9
2	Mean	3.4	0.26	81.4	4.4
n=44	95% CI	3.1 - 3.7	0.2 - 0.3	77.7 - 85.1	3.5 - 5.3
3	Mean	3.3	0.26	78.5	4.7
n=44	95% CI	2.9 - 3.6	0.2 - 0.3	74.5 - 82	3.9 - 5.6
4	Mean	3.0 [a]	0.24	78.5	4.7
n=44	95% CI	2.7 - 3.3	0.2 - 0.3	75 - 82	3.9 - 5.6

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.11b Serum excretion products of the women per quartile of insulin sensitivity after adjusted for age, energy and alcohol intake

IS Quartile	Stats	S-Urea (mmol/L)	S-uric acid (mmol/L)	S-Creat (μmol/L)	S-T_Bili (μmol/L)
1	Mean	3.6 [a]	0.26 [ab]	83.9	4.1
n=44	95% CI	3.3 - 3.9	0.25 - 0.28	80.6 - 87.2	3.3 - 4.9
2	Mean	3.3 [b]	0.27	79.6	4.5
n=44	95% CI	3 - 3.6	0.25 - 0.29	76.2 - 83	3.6 - 5.3
3	Mean	3.4	0.25 [b]	78.8	5.1
n=44	95% CI	3.1 - 3.8	0.23 - 0.27	75 - 82.5	4.2 - 6
4	Mean	2.8 [ab]	0.23 [a]	78.1	4.5
n=44	95% CI	2.5 - 3.2	0.21 - 0.25	73.9 - 82.2	3.5 - 5.5

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

When adjusted for the reported lifestyle factors, the mean serum uric acid levels of the women in IS quartile four were significantly lower than in IS quartile two and in IS quartile one (table 6.11b). Similarly, the serum creatinine levels of the women in IS quartile four

and three were significantly lower than in IS quartile one.

The measured variables which reflect the iron status of the study population are given in Tables 6.12a and b for the men and in Table 6.13 for the women.

Table 6.12a Iron status of the men per quartile of insulin sensitivity (IS)

Ins. Quartile	Stats	S- Fe (μmol/L)	S- TIBC (μmol/L)	S-Fe saturat. (%)	S- Ferritin μg/L
1	Mean	19.7 [a]	62.7	32 [b]	217.4
n=33	95% CI	17.1 - 22.3	58.2 - 67.2	27.8 - 36.1	98.1 - 336.6
2	Mean	18.8	66.1	29.1	203
n=33	95% CI	16.2 - 21.4	61.5 - 70.7	24.8 - 33.3	81.8 - 324.1
3	Mean	14.6 [a]	61.6	23.6 [b]	211.7
n=34	95% CI	12 - 17.2	57.1 - 66.1	19.5 - 27.8	92.4 - 330.9
4	Mean	17	64.7	26.9	123.1
n=33	95% CI	14.4 - 19.6	60.1 - 69.2	22.8 - 31.1	3.8 - 242.3

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

Table 6.12b Iron status of the men per quartile of insulin sensitivity (IS)

Ins. Quartile	Stats	S- Fe (μmol/L)	S- TIBC (μmol/L)	S-Fe saturat. (%)	S- Ferritin μg/L
1	Mean	19.6	60.5	32.7	273.1
n=33	95% CI	16.4 - 22.8	55.4 - 65.7	27.6 - 37.8	135.9 - 410.2
2	Mean	18.6	64.7	29.1	170.5
n=33	95% CI	15.6 - 21.6	60 - 69.5	24.4 - 33.8	44.1 - 296.9
3	Mean	17.3	65.7	26.9	192.2
n=34	95% CI	14.8 - 19.9	61.6 - 69.8	22.9 - 31	82.8 - 301.5
4	Mean	16	63.2	25.6	156.2
n=33	95% CI	13.6 - 18.4	59.4 - 67	21.9 - 29.4	55.3 - 257.1

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

The mean serum iron of the men in IS quartile three (14.6μmol/L) was significantly lower than in IS quartile one (19.7 μmol/L; p=0.007). After adjustment for the reported lifestyle factors this significance disappeared. A correlation between serum iron and insulin sensitivity was also reported for the men in Chapter 5.

The mean serum percentage iron saturation of the men in IS quartile three (23.6%) was significantly lower than in IS quartile one (32%; p=0.006). After adjustment for the reported lifestyle factors, the serum percentage iron saturation of the men in IS quartile four was significantly lower than in IS quartile one (Table 6.12b).

No significant differences in the iron status of the women before or after adjustment for the reported lifestyle factors between the IS quartiles were found (Table 6.13).

Tabel 6.13 Iron status of the women per quartile of insulin sensitivity (IS)

Ins. Quartile	Stats	S- Fe (μmol/L)	S- TIBC (μmol/L)	S- Fe Satur. (%)	S- Ferritin μg/L
1	Mean	15.6	67.2	24.5	53.2
n=44	95% CI	13.2 - 18	62.5 - 71.9	20.5 - 28.4	36.1 - 70.3
2	Mean	15.1	68.2	23.3	49.2
n=44	95% CI	12.7 - 17.6	63.4 - 72.9	19.3 - 27.3	31.9 - 66.5
3	Mean	15.8	69.6	23.4	43.4
n=44	95% CI	13.4 - 18.2	64.9 - 74.3	19.5 - 27.4	26.3 - 60.5
4	Mean	13.8	66.4	22.2	58.8
n=44	95% CI	11.4 - 16.2	61.7 - 71	18.3 - 26.1	41.7 - 75.9

CI = confidence intervals ; Means with the same symbol differ significantly ($p<0.05$)

6.3 Discussion

Most of the measured markers of the mentioned chronic diseases of lifestyle were within low to normal ranges. These results confirm the "apparently healthy status" of the participating subjects. The study however, reflected "subtle shifts" in some of the measured markers for chronic diseases, which can be related to insulin resistance. To clarify the position of insulin resistance in this population, the trends that the risk factors followed from low to high insulin sensitivity quartiles (chapter 6) and the associations between the risk factors and insulin sensitivity (Chapter 5) will be discussed.

6.3.1 Insulin sensitivity and personal variables of the subjects

The stature of both genders did not vary significantly between different IS quartiles. Adult height may reflect possible stunting in childhood. The absence of a relationship between adult height and insulin sensitivity might be in contrast with the hypothesis of Barker (Hales and Barker, 1992) that early foetal and childhood malnutrition predispose to risk of chronic diseases in adulthood. However, no other markers of foetal or childhood stunting were measured, and a conclusion based on this data is not possible. It seems as if insulin sensitivity did not decline with age although an inverse relation with insulin sensitivity and age in the women was reported in Chapter 5.

6.3.2 Insulin sensitivity and markers of NIDDM

In both genders the mean fasting glucose and insulin levels were the lowest in the highest IS quartile (4) and increased significantly towards the lowest IS quartile (1). This tendency

was maintained after adjustment for age, energy and alcohol intake.

An important observation from Tables 6.4a and b and 6.5a and b is that in both men and women, the high insulin sensitivity groups (IS Q4) had lower fasting glucose as well as low fasting insulin levels. A high IS index was therefore not the result of higher insulin secretions that lowered glucose levels, but rather low glucose levels were maintained with low insulin levels. However, the women "needed" more insulin to maintain similar glucose levels than the men. After adjustment for age, energy and alcohol intake the insulin "needs" of both genders were similar. The first IS quartile (or insulin resistant quartile) clearly showed that higher insulin levels were needed by both men and women to maintain "normal" glucose levels, although these levels were on average 1 mmol/L higher than those in the highest IS quartile (IS Q4).

These results suggested that insulin resistance might be the underlying factor in the development of NIDDM in both genders.

Obesity in the women might play a role in the development of insulin resistance and/or hyperglycaemia as obesity is directly and indirectly related to the lifestyle factors (energy and alcohol intake). This corresponds with results reported on black Americans (Banerji and Lebovitz, 1992). Results on the prevalence and identification of risk factors for NIDDM in urban Africans in Cape Town, suggested urbanisation as a significant independent and obesity as a dependent risk factor (Levit *et al.*, 1993). The development of DM in the men may also be influenced by an iron overload as reflected in percentage serum iron saturation, also described by Seftel *et al.* (1961).

6.3.3 Insulin sensitivity and markers of CHD

The women in the second lowest IS quartile (two) had significantly higher mean serum levels for total cholesterol, LDL-cholesterol, percentage heamatocrit and LDL-C:HDL-C-ratio than the women in IS quartile four after adjustment for age, energy and alcohol intake. This may be an indication that the women in IS quartile one had more confounding factors regarding the measured markers for CHD, which influenced the outcome of insulin resistance in this quartile. Except for an inverse association between insulin sensitivity and LDL-C:HDL-C-ratio, no other associations were reported in Chapter 5.

In both genders there were worsening results in the measured markers for CHD with an increase in insulin resistance, influenced by lifestyle. This might be an alarming sign because CHD/IHD is still regarded as a rare condition in black South Africans (Walker *et al.*, 1990). These results suggest a potential increase in the prevalence of CHD in black South Africans with a shift to a Western type of a lifestyle during urbanisation. These results are consistent with those of Mollentze *et al.* (1995), although these researchers did not investigate insulin resistance.

6.3.4 Insulin sensitivity and markers of obesity

The occurrence of obesity in the men was rare (Table 6.8a). Their BMI ranged between 20.1 kg/m^2 and 21.5 kg/m^2 between the four IS quartiles. However, in Chapter 5 significant relationships between insulin sensitivity and markers for obesity were reported. Significant differences, independent of age, energy and alcohol intake in mean body mass, triceps and abdominal skinfold thicknesses between the high insulin sensitivity quartile (IS Q4) and the lower insulin sensitivity quartile (IS Q2), were also observed in Chapter 6. These results give an indication of the relevance of obesity in the development of insulin resistance in these men, dependent on a lifestyle related to urbanisation.

Obesity was predominant in the women. The smallest mean BMI (IS Q4) was 25.1 kg/m^2 but after adjustment for the reported lifestyle factors the estimated mean was 21.9 kg/m^2. Relationships between insulin sensitivity and body mass, BMI, energy intake and maximum hip circumference were reported in Chapter 5. In Chapter 6 significant differences independent of age, energy and alcohol intake between the highest insulin sensitivity quartile towards the lowest IS quartile were reported in BMI, triceps and abdominal skinfold thicknesses and maximum hip circumference. A consequent decline, from the higher insulin resistant quartiles (IS Q1 and 2) to the higher insulin sensitivity quartiles (IS Q 3 and 4), in most of the obesity markers measured were detected in these women. These results indicate that age, energy and alcohol intake explained a large part of the high BMI found in the women. However, BMI remained an independent risk factor in the development of insulin resistance in these women.

6.3.5 Insulin sensitivity and markers of other metabolic disorders

An inverse relationship between insulin sensitivity and serum uric acid in the men was reported in Chapter 5. No significant differences between the IS quartiles in the levels of serum uric acid of these men were found. However, a very subtle constant decrease from IS quartile one towards IS quartile four was found. In the women the serum uric acid level in IS quartile four was significantly lower than in IS quartile one and followed a consistent decline from IS quartile one towards IS quartile four. These results may be an indication that increased serum uric acid is part of the metabolic syndrome as discussed in Chapter 5.

The serum urea levels of the women were significantly lower in IS quartile four than in IS quartile one and followed a steady increasing pattern towards IS quartile one. The women in IS quartile one also had a significantly higher systolic blood pressure than in IS quartile four. The systolic and diastolic blood pressures of the women consistently increased from IS quartile four to IS quartile one. These results may support the possibility of urea being partly responsible for higher levels in blood pressure in African women, as hypothesised in Chapter 5.

6.4 Conclusion

From the above results it can be concluded that insulin resistance is already present in this population, albeit in an "early stage." The measured markers for the development of some chronic diseases of lifestyle were within low to normal ranges except for the unadjusted BMI's of the women. However, definite worsening trends in these markers towards an insulin resistant condition were detected.

It is still not clear whether the metabolic syndrome *per se* occurs in the study population. In Chapter 7 the clustering of risk factors for chronic diseases of a Western lifestyle will be addressed.