Acanthosis nigricans, hyperinsulinaemia and risk factors for cardiovascular disease

A. Bener,[1] G.G. Lestringant,[2] B.L. Nyomba,[3] P. Frossard [4] and H. Saadi [3]

الشواك الأسود وفرط إنسولين الدم وعوامل اختطار الأمراض القلبية الوعائية

عبد الباري بنر وجيلز ج. لسترنجانت وبولانجو ل. نيومبا وفيليب فروسارد وحسين فضل السعدي

خلاصة: في هذه الدراسة بحثنا الترابط بين الشواك الأسود وفرط إنسولين الدم وعوامل الاختطار الأخرى للأمراض القلبية الوعائية في مرضى من الإمارات العربية المتحدة. فقد تم تسجيل الطول والوزن وضغط الدم في وضع الجلوس وذلك في 122 مريضاً بالشواك الأسود. كما أخذت منهم عينات دم لقياس مستويات الكولسترول والبروتين الشحمي الرفيع الكثافة وثلاثي الغليسريد وحمض اليوريك، وذلك في حالة الصيام. وفضلاً عن ذلك أجري اختبار تحمُّل الغلوكوز الفموي، وأخذت عينات دم لقياس مستويات الإنسولين والغلوكوز. وتُبيِّن نتائجنا أن المصابين بالشواك الأسود كان لديهم معدل انتشار مرتفع لعدم تحمُّل الغلوكوز الفموي وفرط إنسولين الدم. وفضلاً عن ذلك فإن المرضى ذوي سكر الدم السوي مع فرط إنسولين الدم كانت لديهم مجموعة من عوامل اختطار الأمراض القلبية الوعائية.

ABSTRACT We examined the association between acanthosis nigricans, hyperinsulinaemia and other risk factors for cardiovascular disease in patients from the United Arab Emirates. Height, weight and sitting blood pressure were recorded in 122 patients with acanthosis nigricans, and blood samples were obtained for measuring fasting cholesterol, high-density lipoprotein cholesterol, triglyceride and uric acid levels. In addition, a glucose tolerance test was performed and blood was sampled for insulin and glucose. Our results indicate that the patients with acanthosis nigricans had a high prevalence of abnormal glucose tolerance and hyperinsulinaemia. In addition, euglycaemic patients with hyperinsulinaemia had a cluster of risk factors for cardiovascular disease.

Acanthosis nigricans, l'hyperinsulinémie et les facteurs de risque de maladies cardiovasculaires

RESUME Dans notre étude, nous avons examiné l'association entre l'acanthosis nigricans, l'hyperinsulinémie et d'autres facteurs de risque de maladies cardiovasculaires chez des patients aux Emirats arabes unis. La taille, le poids et la tension artérielle en position assise ont été enregistrés chez 122 patients atteints d'acanthosis nigricans, et des prélèvements sanguins ont été obtenus pour mesurer les niveaux de cholestérol à jeun, de cholestérol des lipoprotéines lourdes, de triglycérides et d'acide urique. De plus, une épreuve d'hyperglycémie provoquée par voie orale a été réalisée et un prélèvement sanguin a été effectué pour l'insuline et le glucose. Nos résultats indiquent que les patients atteints d'acanthosis nigricans avaient une forte prévalence de tolérance anormale au glucose et d'hyperinsulinémie. De plus, les patients dont la glycémie était normale et qui avaient une hyperinsulinémie avaient un ensemble de facteurs de risque de maladies cardiovasculaires.

[1]Department of Community Medicine; [3]Department of Internal Medicine; [4]Department of Pathology, Faculty of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates.
[2]Department of Dermatology, Tawam Hospital, Al-Ain, United Arab Emirates.
Received: 28/02/99; accepted: 08/09/99

Introduction

Prior studies have supported the association between acanthosis nigricans (AN), hyperinsulinaemia and type 2 diabetes mellitus (DM) [*1–3*]. In addition, a significant correlation has been established between hyperinsulinaemia, hyperuricaemia and a variety of risk factors for cardiovascular disease (CVD), such as hypertension, dyslipidaemia, DM and obesity [*4–8*]. In this study, we examined the association between AN, hyperinsulinaemia and other risk factors for CVD in patients from the United Arab Emirates (UAE).

Patients and methods

This cross-sectional study was conducted between 1994 and 1997. The study population was UAE nationals who were diagnosed with AN by one of the authors at the time they were attending the dermatology clinic at Tawam Hospital, a tertiary health care centre in Al-Ain, UAE. A total of 122 patients (30 males and 92 females, ages 16–65 years) participated in the study. All the patients were self-referred for various skin problems, and none was known to have DM. AN was identified on the nape of the neck and other body sites. The degree of AN severity was not recorded.

The following data were collected at the time of the diagnosis of AN. Height and weight were recorded and obesity was defined as a body mass index (BMI) of ≥ 30 kg/m^2. Blood pressure was measured with a mercury sphygmomanometer while the patients were sitting. Systolic and diastolic pressures were determined at the time of the appearance and disappearance of Korotkoff sounds respectively. Venous blood samples for uric acid, triglycerides, total cholesterol and high-density lipoprotein (HDL) cholesterol were collected after an overnight fast. A standard (75 g) oral glucose tolerance test (OGTT) was performed according to World Health Organization (WHO) recommendations, and blood was sampled at 0, 30, 60 and 120 minutes for the determination of serum insulin and glucose levels [*9*].

Samples of insulin were centrifuged and the serum was stored at –20 °C until assay. Serum insulin levels were determined by a solid-phase ^{125}I radioimmunoassay kit [Diagnostic Products, United States of America (USA)]. This assay indicated a fasting 2-SD insulin range of 0–180 pmol/L for healthy patients. The intra- and inter-assay coefficients of variation were 5% and 10% respectively. Serum glucose was determined by the glucose dehydrogenase method (Dimension Clinical Chemistry System, Dade International Incorporated, USA). Total cholesterol and triglycerides were measured using enzymatic techniques on a Technicon Analyzer (Technicon In-struments). Measurement of HDL cholesterol was performed using the same technique following heparin manganese precipitation of very-low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) cholesterol. The level of LDL cholesterol was calculated using the Friedewald formula [*10*]. Uric acid levels were determined using a commercial kit (Dimension Clinical Chemistry System, Dade International Incorporated, USA).

Data were coded and analysed using *SPSS*. Data are expressed as mean and standard deviation unless otherwise stated. The Student *t*-test was used to ascertain the significance of differences between mean values of two continuous variables. A chi-squared analysis was performed to test for differences in proportions of categorical variables between two or more groups. An ANOVA test was used for comparison of

several group means and to determine the presence of significant differences between group means of continuous variables. A multiple regression model was fitted to adjust for potential confounding variables. $P < 0.05$ was considered significant.

Results

A total of 122 patients (30 males and 92 females) with AN were enrolled in the study. The physical and metabolic characteristics of the patients by sex are shown in Table 1. Overall, the patients were normotensive, but the men had significantly higher systolic blood pressure than the women. As expected, the women had higher HDL cholesterol levels. Most of the patients were overweight but fewer than half had a BMI of ≥ 30 kg/m^2.

The patients were divided into three groups based on the results of the OGTT. Although this test was not repeated to confirm the results, we labelled 18 patients as having DM based on a 2-hour OGTT serum glucose of ≥ 11.1 mmol/L (11 patients), or a fasting serum glucose value of ≥ 7 mmol/L (7 patients). Twenty-six (26) were labelled as having impaired glucose tolerance (IGT) based on a 2-hour OGTT serum glucose value of 7.8–11.0 mmol/L, or a fasting serum glucose value of 6.1–6.99 mmol/L. Patients with normal fasting and 2-hour OGTT glucose were labelled as euglycaemic. The physical and metabolic characteristics of the patients grouped by glucose

Table 1 **Baseline physical and metabolic characteristics of all the patients grouped by sex**

Variable	Men	Women
Number of patients (%)	30 (24.6)	92 (75.4)
Age ± *s* (years)	30.2 ± 12.5	28.9 ± 1 1.2
Body mass index ± *s* (kg/m^2)	29.2 ± 11.4	30.6 ± 6.3
Body mass index ≥ 30 kg/m^2 (%)	43.3	48.3
Blood pressure ± *s* (mmHg)		
Systolic	132.5 ± 16.3[a]	126.0 ± 15.2
Diastolic	80.1 ± 7.5	81.7 ± 9.2
Fasting serum glucose ± *s* (mmol/L)	5.7 ± 0.91	5.8 ± 1.4
Insulin ± *s* (pmol/L)	193.0 ± 10.2	164.0 ± 13.4
Total cholesterol ± *s* (mmol/L)	4.7 ± 0.8	5.1 ± 1.1
HDL cholesterol ± *s* (mmol/L)	0.9 ± 0.2	1.2 ± 0.3[b]
LDL cholesterol ± *s* (mmol/L)	3.0 ± 0.2	3.3 ± 0.2
Triglycerides ± *s* (mmol/L)	1.1 ± 0.4	1.2 ± 0.8
Uric acid ± *s* (mmol/L)	0.35 ± 0.06	0.32 ± 0.26

[a] *P < 0.05*
[b] *P < 0.01*
s = *standard deviation*
HDL = high-density lipoprotein
LDL = low-density lipoprotein

tolerance are shown in Table 2. Diabetic patients were significantly older in age ($P < 0.01$), had significantly higher systolic blood pressure ($P < 0.05$), and a significantly lower fasting insulin level ($P < 0.01$) than euglycaemic and IGT patients.

Of the 78 euglycaemic patients, 16 had missing insulin results. The remaining 62 patients were included in subsequent analyses (Tables 3–5). Thirty-two (32) (51.6%) patients had hyperinsulinaemia (defined as fasting serum insulin level > 180 pmol/L).

Table 3 shows the baseline character-istics of euglycaemic patients (with and without hyperinsulinaemia) as well as their mean serum insulin and glucose levels before and after OGTT. Hyperinsulinaemic patients had mean fasting and post-OGTT insulin levels that were twice those of patients with normal insulin levels. In addition, BMI and fasting glucose level were significantly higher in hyperinsulinaemic patients ($P < 0.05$).

Table 4 shows blood pressure, fasting serum uric acid, and lipid and lipoprotein values in the euglycaemic patients with and without hyperinsulinaemia. Uric acid and triglyceride levels were significantly higher in the hyperinsulinaemic group ($P < 0.05$). Total cholesterol and HDL cholesterol levels, however, were not significantly different between the two groups. Systolic and

Table 2 Baseline physical and metabolic characteristics of all the patients by glucose tolerance

Variable	Euglycaemic ($n = 78$)	Impaired glucose tolerance ($n = 26$)	Diabetes mellitus ($n = 18$)
Males (%)	22 (28.2)	4 (15.4)	4 (22.2)
Females (%)	56 (71.8)	22 (84.6)	14 (77.8)
Age ± *s* (years)	26.1 ± 10.1	29.9 ± 5.9	41.8 ± 9.7[a]
Body mass index ± *s* (kg/m²)	29.4 ± 5.9	31.9 ± 5.6	30.8 ± 6.5
Family history of diabetes mellitus (%)	58 (74.4)	16 (61.5)	11 (61.1)
Blood pressure ± *s* (mmHg)			
Systolic	123.4 ± 14.5	132.6 ± 15.2	141.1 ± 11.8[a]
Diastolic	80.5 ± 8.4	80.3 ± 10.0	86.2 ± 7.6
Fasting serum glucose ± *s* (mmol /L)	5.2 ± 0.5	5.9 ± 0.5[b]	8.1 ± 0.9[a]
Insulin ± *s* (pmol/L)	163.8 ± 17.4	208.4 ± 20.4	146.0 ± 16.9[a]
Cholesterol ± *s* (mmol/L)	4.6 ± 1.1	5.3 ± 1.2	5.0 ± 1.0
HDL cholesterol ± *s* (mmol/L)	1.5 ± 0.29	1.4 ± 0.4	1.4 ± 0.8
LDL cholesterol ± *s* (mmol/L)	3.3 ± 0.2	3.7 ± 0.4	3.9 ± 0.5
Triglycerides ± *s* (mmol/L)	1.2 ± 0.7	1.4 ± 0.7	1.5 ± 0.8
Uric acid ± *s* (mmol/L)	0.33 ± 0.28	0.34 ± 0.06	0.29 ± 0.08

[a] *P < 0.01 compared to euglycaemic and impaired glucose tolerance groups*
[b] *P < 0.01 compared to euglycaemic and diabetes mellitus groups*
s = *standard deviation*
HDL = high-density lipoprotein
LDL = low-density lipoprotein

diastolic blood pressure was also significantly higher in the hyperinsulinaemic group ($P < 0.01$).

Multiple regression analysis was used to examine further the relationship between hyperinsulinaemia and the variations in the

Table 3 Baseline characteristics and serum glucose and insulin levels before and after oral glucose tolerance test in the euglycaemic patients

Variable	Patients with hyperinsulinaemia ($n = 32$)	Patients with normal insulin levels ($n = 30$)
Women (%)	20 (60.6)	24 (80.0)
Age ± *s* (years)	30.0 ± 10.7	26.5 ± 8.1
Body mass index ± *s* (kg/m²)	32.4 ± 1.0[a]	28.1 ± 1.0
Glucose level ± *s* (mmol/L)		
Fasting	5.4 ± 0.5[a]	5.2 ± 0.4
After 1 hour	8.0 ± 2.0	7.6 ± 1.3
After 2 hours	6.0 ± 1.1	5.6 ± 1.2
Insulin level ± *s* (pmol/L)		
Fasting	229.9 ± 72.8[b]	95.5 ± 29.3
After 1 hour	1332.0 ± 866.4[b]	782 ± 382
After 2 hours	1014.6 ± 618[b]	466 ± 222

[a] *P < 0.05*
[b] *P < 0.01*
s = *standard deviation*

Table 4 Blood pressure, serum uric acid, lipid and lipoprotein levels in the euglycaemic patients

Variable	Patients with hyperinsulinaemia ($n = 32$)	Patients with normal insulin levels ($n = 30$)
Cholesterol (mmol/L)	4.6 ± 1.3	4.4 ± 1.0
High-density lipoprotein cholesterol (mmol/L)	1.1 ± 0.3	1.2 ± 0.3
Triglycerides (mmol/L)	1.4 ± 0.7[a]	1.0 ± 0.5
Uric acid (mmol/L)	0.32 ± 0.07[a]	0.25 ± 0.07
Blood pressure (mmHg)		
Systolic	129.8 ± 15.8[a]	118 ± 13.9
Diastolic	82.4 ± 7.4[a]	77.6 ± 10.4

[a] *P < 0.01*
Values are expressed as mean ± standard deviation

dependent variables uric acid, triglycerides, lipid and lipoprotein levels and blood pressure. Other independent variables, such as age ≥ 30 years, sex, fasting glucose and obesity (BMI ≥ 30 kg/m^2), were also evaluated.

The results of these analyses are shown in Table 5. Hyperinsulinaemia remained significantly associated with systolic blood pressure ($t = 2.319$, $P < 0.05$), diastolic blood pressure ($t = 2.047$, $P < 0.05$) and uric acid (t

Table 5 **Multiple regression analysis for fasting insulin, lipids, uric acid levels, blood pressure and other relevant variables in the euglycaemic patients**

Dependent variable	Independent variables	Regression coefficient	Standard error of regression coefficient	*t*-test value	*P*-value
Systolic blood pressure	Age ≥ 30 years	0.227	3.879	0.058	NS
	Sex	−10.313	4.194	−2.459	< 0.05
	Body mass index ≥ 30 kg/m^2	4.090	4.067	1.006	NS
	Hyperinsulinaemia	9.931	4.282	2.319	< 0.05
	Fasting glucose	−4.322	4.591	−0.941	NS
Diastolic blood pressure	Age ≥ 30 years	0.568	2.469	0.423	NS
	Sex	1.130	2.669	0.230	NS
	Body mass index ≥ 30 kg/m^2	−0.555	2.588	−0.215	NS
	Hyperinsulinaemia	5.578	2.726	2.047	< 0.05
	Fasting glucose	1.272	2.922	0.435	NS
Cholesterol	Age ≥ 30 years	0.493	0.328	1.502	NS
	Sex	0.189	0.355	0.534	NS
	Body mass index ≥ 30 kg/m^2	−0.273	0.344	−0.794	NS
	Hyperinsulinaemia	0.059	0.362	0.163	NS
	Fasting glucose	0.403	0.388	1.037	NS
High-density cholesterol	Age ≥ 30 years	0.038	0.079	0.488	NS
	Sex	0.250	0.085	2.948	< 0.01
	Body mass index ≥ 30 kg/m^2	−0.009	0.082	−0.110	NS
	Hyperinsulinaemia	−0.062	0.087	−0.726	NS
	Fasting glucose	0.032	0.093	0.351	NS
Triglycerides	Age ≥ 30 years	0.248	0.120	2.063	< 0.05
	Sex	−0.203	0.130	−1.565	NS
	Body mass index ≥ 30 kg/m^2	0.036	0.126	0.291	NS
	Hyperinsulinaemia	0.217	0.132	1.642	NS
	Fasting glucose	0.054	0.142	0.381	NS
Uric acid	Age ≥ 30 years	−0.046	0.017	−2.709	< 0.01
	Sex	−0.066	0.018	−3.627	< 0.01
	Body mass index ≥ 30 kg/m^2	0.009	0.019	0.493	NS
	Hyperinsulinaemia	0.058	0.020	2.983	< 0.01
	Fasting glucose	−0.014	0.020	−0.702	NS

NS = not significant

– 2.983, $P < 0.01$), independent of age, sex, obesity and fasting glucose. However, the association between hyperinsulinaemia and triglyceride levels became statistically insignificant ($t = 1.642$, $P = 0.107$). The relationship between insulin, cholesterol and HDL cholesterol did not change when the other variables were considered. The analysis also showed that males had higher systolic blood pressure, lower HDL cholesterol and higher uric acid levels. In addition, patients who were ≥ 30 years had higher triglyceride and lower uric acid levels.

Discussion

We studied patients from the UAE, a population in which insulin resistance and DM are particularly prevalent [*11–13*]. In addition, all the patients had AN, a hyperplastic skin lesion that is known to be associated with DM and a variety of insulin-resistance states [*1–3*]. Indeed, more than one-third of these patients had abnormal OGTT and nearly half of the remaining patients had hyperinsulinaemia. Unfortunately, we did not study a control group and did not repeat the OGTT. Thus, the relative risk of hyperinsulinaemia, undiagnosed DM or IGT in patients with AN cannot be accurately determined from this study. The reported prevalence of abnormal OGTT and hyperinsulinaemia in the UAE, however, is substantially lower than our findings, which suggests that AN plays an important role [*12,14*].

There is considerable evidence linking hyperinsulinaemia to hyperuricaemia, and multiple risk factors for CVD such as hypertension, dyslipidaemia, DM and obesity [*4–8*]. In addition, hyperinsulinaemia, without fasting hyperglycaemia, has been shown to be a significant risk factor for the development of CVD [*15–17*]. Insulin also has a direct regulatory effect on triglyceride and HDL cholesterol levels, and has a possible role in blood pressure regulation [*18*].

Similar to other cross-sectional studies, we found that patients with hyperinsulinaemia and normal glucose tolerance had higher blood pressure, uric acid and triglyceride levels than those with normal insulin levels [*19–23*]. Although in some of these studies the strength of the correlation was substantially diminished once obesity was accounted for, the correlation was independent of BMI in our study [*22,23*]. When age and sex were entered as independent variables, however, the correlation between hyperinsulinaemia and triglyceride level became statistically insignificant. Total cholesterol, LDL cholesterol and HDL cholesterol levels were not significantly different between the patients with hyperinsulinaemia and those with normal insulin levels. Although total and LDL cholesterol levels are not closely related to hyperinsulinaemia, several studies have shown that inverse relationships exist between insulin and HDL cholesterol levels in patients with this condition and normal glucose tolerance, and in patients with IGT and DM [*24*]. In some studies, however, HDL cholesterol levels in women did not correlate with insulin sensitivity [*25*]. Thus, the lack of correlation between hyperinsulinaemia and HDL cholesterol levels in our study may be related to the relatively high proportion of female patients included.

Conclusions

Our results indicate that patients with AN have a high prevalence of abnormal OGTT and insulin resistance. In addition, these results are in agreement with previous conclusions that patients with hyperinsulinaemia and normal glucose tolerance, who are pre-

sumably insulin resistant, have a cluster of risk factors for CVD. The implications of these findings are important as CVD and DM are emerging as major causes of morbidity and mortality in the UAE [*11,26*].

Acknowledgement

We are indebted to Dr Anthony Townsend for critical review of our manuscript.

References

1. Stuart CA et al. Acanthosis nigricans as a risk factor for non-insulin dependent diabetes mellitus. *Clinical pediatrics*, 1998, 37(2):73–9.
2. Stuart CA et al. Acanthosis nigricans among Native Americans: an indicator of high diabetes risk. *American journal of public health*, 1994, 84(11):1839–42.
3. Kahn CR et al. The syndromes of insulin resistance and acanthosis nigricans. Insulin-receptor disorders in man. *New England journal of medicine*, 1976, 294(14):739–45.
4. Stout RW. Insulin and atheroma: 20-year perspective. *Diabetes care*, 1990, 13(6):631–54.
5. DeFronzo RA. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidaemia and atherosclerosis. *Netherlands journal of medicine*, 1997, 50(5):191–7.
6. Opara JU, Levine JH. The deadly quartet—the insulin resistance syndrome. *Southern medical journal*, 1997, 90(12):1162–8.
7. Zavaroni I et al. Risk factors for coronary artery disease in healthy persons with hyperinsulinemia and normal glucose tolerance. *New England journal of medicine*, 1989, 320(11):702–6.
8. Vuorinen-Markkola H, Yki-Jarvinen H. Hyperuricaemia and insulin resistance. *Journal of clinical endocrinology and metabolism*, 1994, 78(1):25–9.
9. *Diabetes mellitus*. Geneva, World Health Organization, 1985 (WHO Technical Report Series, No. 727).
10. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry*, 1972, 18(6):499–502.
11. El-Mugamer IT et al. Diabetes, obesity and hypertension in urban and rural people of Bedouin origin in the United Arab Emirates. *Journal of tropical medicine and hygiene*, 1995, 98(6):407–15.
12. Pugh RN et al. Arabian peninsula men tend to insulin resistance and cardiovascular risk seen in South Asians. *Tropical medicine and international health*, 1998, 3(2):89–94.
13. King H, Rewers M. Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adults. *Diabetes care*, 1993, 16(1):157–77.
14. Townsend T. Undetected diabetes in Al-Ain primary health care clinic attenders. *International journal of diabetes*, 1996, 4:129–36.
15. Haffner SM et al. Hyperinsulinemia in a population at high risk for non-insulin-dependent diabetes mellitus. *New England journal of medicine*, 1986, 315(4): 220–4.
16. Welborn TA, Wearne K. Coronary heart disease incidence and cardiovascular mortality in Busselton with reference to

glucose and insulin concentrations. *Diabetes care*, 1979, 2(2):154–60.

17. Pyorala K et al. Plasma insulin as coronary heart disease risk factor: relationship to other risk factors and predictive value during 9½-year follow-up of the Helsinki Policeman Study population. *Acta medica scandinavica supplementum*, 1985, 701:38–52.

18. Mitchell BD et al. The relation between serum insulin levels and 8-year change in lipid, lipoprotein and blood pressure levels. *American journal of epidemiology*, 1992, 136(1):12–22.

19. Ferrannini E et al. Hyperinsulinaemia: the key feature of a cardiovascular and metabolic syndrome. *Diabetologia*, 1991, 34(6):416–22.

20. Lichtenstein MJ et al. Sex hormones, insulin, lipids, and prevalent ischemic heart disease. *American journal of epidemiology*, 1987, 126(4):647–57.

21. Zavaroni I et al. Evidence for an independent relationship between plasma insulin and concentration of high density lipoprotein cholesterol and triglyceride. *Atherosclerosis*, 1985, 55(3):259–66.

22. Bonora E et al. Relationship of uric acid concentration to cardiovascular risk factors in young men. Role of obesity and central fat distribution. The Verona Young Men Atherosclerosis Risk Factor Study. *International journal of obesity and related metabolic disorders*, 1996, 20(11):975–80.

23. Cambien F et al. Body mass, blood pressure, glucose and lipids. Does plasma insulin explain their relationships? *Arteriosclerosis*, 1987, 7(2):197–202.

24. Stout RW. Insulin resistance, hyperinsulinaemia, dyslipidaemia and CVD. In: Moller DE, ed. *Insulin resistance*. London, John Wiley and Sons Limited, 1993:355–84.

25. Chaiken RL et al. Do blacks with NIDDM have an insulin-resistance syndrome? *Diabetes*, 1993, 42(3):444–9.

26. Omar A et al. Diabetes mellitus in Al-Ain: the impact on hospital services. *Emirates medical journal*, 1985, 3:119–22.