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Full Length Research paper

Correlation of serum free thyroxine with components of metabolic syndrome in euthyroid South Asian men and women

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Metabolic syndrome is a combination of risk factors for cardiovascular disease, whose prevalence is rising rapidly. Recently, a few studies have suggested that serum thyroxine, even in the reference range, may be associated with components of metabolic syndrome. However, this issue remains to be settled and has not been explored in the Pakistani population. So, we aimed to determine serum free thyroxine level and its relationship, if any, with components of metabolic syndrome in a euthyroid local population. This analytical, cross-sectional study included 130 euthyroid subjects (age range of 45 to 55 years). The subjects had their history taken and underwent clinical examination, after which, fasting blood was analysed for free thyroxine and thyroid stimulating hormone (chemiluminescence), along with glucose, triglycerides and high density lipoprotein cholesterol (using enzymatic methods). Free thyroxine showed a positive correlation with systolic and diastolic blood pressure in all subjects and with serum glucose in males, which was statistically significant (p = 0.022, p = 0.005 and p = 0.032, respectively). However, the correlation of serum free thyroxine with waist circumference, serum triglycerides and high-density lipoprotein cholesterol in males and with all components of metabolic syndrome in females was not significant. These results indicate that high-normal free thyroxine may be associated with raised blood pressure in all subjects and with raised glucose in males. Larger studies need to be done in Pakistani population to confirm our findings.

Key words: Free thyroxine, metabolic syndrome, correlation, euthyroid.

INTRODUCTION

Metabolic syndrome (MS) (Dysmetabolic syndrome X, ICD10CM, 2012) is a combination of risk factors for cardiovascular disease (CVD). Its diagnosis is indicated by the presence of at least three of the following five components: abdominal obesity, raised glucose, raised blood pressure (BP), raised triglycerides (TG) and low high-density lipoprotein cholesterol (HDL-C) (Grundy et al., 2005). MS has become epidemic in most countries (Grundy, 2008). Prevalence of MS in the Greek population is 17.9% according to the National Cholesterol Education Program definition (Pitsavos, 2008). It is becoming one of the major public health problems in developing countries (Mohan and Deepa, 2006). A study on a group of urban Pakistanis found a prevalence of 34.8% (Alvi et al., 2011). The prevalence of MS in Iran is reported to be 41.6% according to the latest criteria (Delavari et al., 2009). The increasing MS prevalence is associated with excess consumption of calories and sedentary habits (Saidie, 2005; Bonow and Eckel, 2003). Asian populations are particularly susceptible to developing MS (Hossain et al., 2007). Insulin resistance is a common underlying causative mechanism (McLaughlin et al., 2003). Studies have indicated that MS and its components are linked to higher risk of CVD (Galassi et al., 2006).

Thyroid hormones have significant effects on energy balance, BP, metabolism of carbohydrates and lipids,

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which are also deranged in MS (Ayturk et al., 2009). Interestingly, recent studies have pointed to the fact that there may be some relationship between thyroid hormones and components of MS even in euthyroid individuals (Kim et al., 2009). Serum free thyroxine (T4) level in the normal range is inversely related to abdominal obesity and directly related to elevated BP, elevated fasting glucose and HDL-C levels; this relationship between serum free T4 and components of MS varies with age and gender (Kim et al., 2009; Roos et al., 2007). MS and insulin resistance is related to low free T4 in subjects with normal thyroid function and free T4 also has a significant negative association with total cholesterol and TG (Lin et al., 2005; Fernandez-Real et al., 2006).

The above limited evidence indicates that free T4 in the reference range may be associated with components of MS. However, little data is available on this association, particularly in South Asia. We proposed to elucidate the relationship of serum free T4 with components of metabolic syndrome (raised glucose, BP, TG, abdominal obesity and low HDL-C) in euthyroid South Asians of Pakistan.

MATERIALS AND METHODS

This analytical, cross sectional was conducted at the Department of Physiology, University of Health Sciences, Lahore, Pakistan. It comprised 130 euthyroid subjects (age range of 45 - 55 years), whose sampling was done by the non-probability, purposive technique. Subjects with history of thyroid disease, thyroid surgery, use of thyroid drugs and steroids were excluded from the study.

Definition of MS

Any three of the following five criteria (Grundy et al., 2005) indicated the presence of MS in our subjects: elevated BP (≥130 mm Hg systolic and ≥85 mm Hg diastolic) or drug treatment for elevated BP, central obesity (waist circumference ≥90 cm in men and ≥80 cm in women), elevated serum TG (≥150 mg/dl), low serum HDL-C (<40 mg/dl in men and <50 mg/dl in women) and elevated fasting blood glucose (≥100 mg/dl) or drug treatment for elevated blood glucose.

Reference ranges for thyroid function tests

According Ortho Clinical Diagnostics (2012), the reference range was given as: Serum TSH, 0.465-4.68 mIU/L and serum free T4: 10-28.2 pmol/L.

Data and sample collection

Each subject underwent a detailed history and clinical examination. BP was measured from the right arm of the subject in the sitting position after a rest of 5 min. Three BP readings were taken, the mean of which was recorded. Waist circumference was measured at a level of the top of the iliac crest in a horizontal plane, at the end of normal expiration (Grundy et al., 2005). In brief, 5 ml of venous blood was obtained in the morning following an overnight fast of 8 to 12 h and collected in vacutainer tubes. The serum was separated by centrifugation at 3000 revolutions per minute for 10 to 15 min, aliquoted and stored at a temperature of -80℃ until analysis.

Blood analysis

Glucose level was measured on the day of sample collection by the glucose oxidase method using kits by AMP Diagnostics (AMP Medizintechnik GmbH, Graz, Austria) in Microlab 300 (Merck) semi-automated analyzer. Serum TG was measured by an enzymatic-colorimetric technique using kits by AMP Diagnostics (AMP Medizintechnik GmbH, Graz, Austria) in Metrolab 2300 automated analyzer (Ortho Clinical Diagnostics, 2012; Burtis et al., 2006).

Serum HDL-C was measured by a direct enzymatic method (immunoinhibition technique) using kits by AMP Diagnostics (AMP Medizintechnik GmbH, Graz, Austria) in Metrolab 2300 automated analyzer. Serum TSH and free T4 levels were measured immunodiagnostically using kits (REF 148 7249 and 172 8872, respectively) by Ortho-Clinical Diagnostics, Johnson and Johnson, High Wycombe, United Kingdom, VITROS EciQ analyzer.

Ethical considerations

The study was conducted as per the Helsinki declaration of human rights (The World Medical Association homepage, 2012) and was approved by the ethical review committee of the University of Health Sciences, Lahore, Pakistan. Written informed consent was given by each subject for participation in the study.

Statistical analysis

The collected data was entered and analysed using Statistical Package for the Social Sciences (SPSS) version 16 software. Qualitative variables were expressed as percentage (%). Shapiro-Wilk test showed that our quantitative variables were not normally distributed except for serum free T4. So, the non-normally distributed quantitative variables were expressed as median (interquartile range: IQR) and the normally distributed quantitative variable was expressed as mean ± standard error of the mean (SEM). Spearman rank correlation was applied to observe correlations. A p value of <0.05 was considered as statistically significant.

RESULTS

As shown in Table 1, the median (IQR) age of the subjects (N = 130) was 48.00 (46.00 - 51.25) years. The gender distribution of the study subjects included 42.30% males and 57.70% females (Table 1). Moreover, the median (IQR) waist circumference of the subjects was 97 (90 - 103) cm. The median (IQR) systolic BP, diastolic BP and serum glucose were 130 (120 - 140) mm Hg, 80 (80 - 90) mm Hg and 113.50 (82.75-157.25) mg/dl, respectively. As also indicated in Table 1, the median (IQR) serum TG and HDL-C status of the subjects was 156.30 (105.08-230.25) mg/dl and 42.97 (38.14-48.43) mg/dl, respectively. Overall, 77% of all the subjects had MS (Table 1). The median (IQR) serum TSH of our subjects was 1.76 (1.13-2.21) mIU/L, while the mean ± SEM serum free T4 was 15.10 ± 0.18 pmol/L, as listed in Table 1.

Table 1. Baseline characteristics of the subjects.

Characteristics		Values (N =130)
Age (years)		48.00 (46.00 - 51.25)
Gender	Male (%)	42.30
	Female (%)	57.70
Waist Circumference (cm)		97 (90 - 103)
Systolic BP (mm Hg)		130 (120 - 140)
Diastolic BP (mm Hg)		80 (80 - 90)
Serum Glucose (mg/dl)		113.50 (82.75 - 157.25)
Serum TG (mg/dl)		156.30 (105.08 - 230.25)
Serum HDL-C (mg/dl)		42.97 (38.14 - 48.43)
MS (%)		77
Serum TSH (mIU/L)		1.76 (1.13 - 2.21)
Serum free T4 (pmol/l)		15.10 ± 0.18

Data are given as percentage (%), median (IQR) or mean ± SEM.

Table 2. Correlation between serum free T4 and components of MS in all subjects.

Components of MS	Serum free T4	
	Correlation coefficient	p value†
Waist Circumference	0.005	0.957
Systolic BP	0.200	0.022*
Diastolic BP	0.243	0.005**
Serum Glucose	0.172	0.05
Serum TG	- 0.132	0.134
Serum HDL-C	0.122	0.165

†Determined by Spearman rank correlation. *Significant at 0.05 level. **Significant at 0.01 level.

Spearman rank correlation analysis in all subjects showed that serum free T4 had statistically significant positive correlation with systolic BP (correlation coefficient = 0.200, p = 0.022) and diastolic BP (correlation coefficient = 0.243, p = 0.005) in all subjects (N = 130) (Table 2). However, the correlation of serum free T4 with waist circumference, serum glucose, serum TG and serum HDL-C in all subjects was statistically insignificant (correlation coefficient = 0.005, p = 0.957; correlation coefficient = 0.172, p = 0.05; correlation coefficient = -0.132, p = 0.134; correlation coefficient = 0.122, p = 0.165 respectively). Correlation analysis in males (N = 55) showed that serum free T4 had a significantly positive relationship with systolic BP, diastolic BP and serum glucose (correlation coefficient = 0.302, p = 0.023; correlation coefficient = 0.330, p = 0.013 and correlation coefficient = 0.287, p = 0.032, respectively) (Table 3). Serum free T4 had statistically insignificant correlation with waist circumference, serum TG and serum HDL-C (correlation coefficient = 0.060, p = 0.659; correlation coefficient = -0.087, p = 0.526 and correlation coefficient = 0.133, p = 0.328 respectively) (Table 3).

Additionally, Spearman rank correlation analysis in females (N = 75) showed serum free T4 to have no significant relationship with waist circumference (correlation coefficient = - 0.032, p = 0.784), systolic BP (correlation coefficient = 0.138, p = 0.242), diastolic BP (correlation coefficient = 0.201, p = 0.086), serum glucose (correlation coefficient = 0.086, p = 0.464), serum TG (correlation coefficient = -0.172, p = 0.144) and serum HDL-C (correlation coefficient = 0.087, p = 0.461) (Table 4).

DISCUSSION

There is paucity of data on the relationship between thyroxine and components of MS, particularly in the South Asian population. Thyroid hormones have marked effects on metabolism (carbohydrate and lipid), energy balance and BP which are also deranged in MS (Ayturk et al., 2009). A few recent studies have pointed to the fact that these effects of thyroid hormones may even be present in the normal range of thyroid function (Kim et al., 2009; Roos et al., 2007). The present study was conducted in order to determine the correlation between serum free T4 and components of MS in euthyroid South

Table 3. Correlation between serum free T4 and components of MS in males.

Components of MS	Serum free T4	
	Correlation Coefficient	p value†
Waist Circumference	0.060	0.659
Systolic BP	0.302	0.023*
Diastolic BP	0.330	0.013*
Serum Glucose	0.287	0.032*
Serum TG	- 0.087	0.526
Serum HDL-C	0.133	0.328

†Determined by Spearman rank correlation. *Significant at 0.05 level.

Table 4. Correlation between serum free T4 and components of MS in females.

Components of MS	Serum free T4	
	Correlation Coefficient	p value†
Waist Circumference	- 0.032	0.784
Systolic BP	0.138	0.242
Diastolic BP	0.201	0.086
Serum Glucose	0.086	0.464
Serum TG	- 0.172	0.144
Serum HDL-C	0.087	0.461

†Determined by Spearman rank correlation.

Asians of Pakistan.

In this study, serum free T4 showed a low but statistically significant direct correlation with systolic BP and diastolic BP, in all the subjects. This can be explained by the positive inotropic effect of thyroid hormones along with their ability to increase sympathetic system activity and angiotensinogen levels (Kim et al., 2009). Also, thyroid hormones cause peripheral vasodilation, decreasing peripheral vascular resistance, and in turn lead to stimulation of the renin-angiotensin-aldosterone system and consequent retention of sodium (Fommei and Iervasi, 2002). Some studies (Kim et al., 2009; Roos et al., 2007; Taneichi et al., 2011) have shown similar results, but studies by Lin et al. (2005) and Garduno-Garcia et al. (2010) are not in agreement. In the present study, serum free T4 correlated positively with serum glucose in males. A previous study has shown a similar finding in both males and females (Kim et al., 2009). Suggested mechanisms include decreased insulin secretion by pancreas and increased gluconeogenesis associated with increasing thyroxine levels (Kim et al., 2009). However, the study by Garduno-Garcia et al. (2010) done in a Hispanic population, showed a negative correlation between serum free T4 and glucose.

Another possible reason for the relationship between serum free T4 and components of MS could be indirect, through a common underlying factor, which may have led to simultaneous changes in free T4 and in components of MS. This factor could be genetic or environmental (Kim et al., 2009; Fernandez-Real et al., 2006). Serum free T4 correlated positively with BP in all subjects, and with serum glucose in males but not in females. So the relationships between serum free T4 and components of MS are different according to gender. This has been seen in a previous study in a Chinese population (Kim et al., 2009). Moreover, in our study, waist circumference, serum TG and HDL-C did not correlate with serum free T4 in males and in females. A study by Roos et al. (2007) in a Caucasian population showed a negative relationship of free T4 with waist circumference, TG and a positive association with HDL-C. Another study done in a Chinese population showed negative association of waist circumference with free T4 (in females and in males above 50 years of age), TG (in males below 50 years of age) and a positive relationship with serum HDL-C (Kim et al., 2009). The discordant results in our study may be due to the small sample size and the subjects being of South Asian origin. A larger study in the local population may clarify the relationships further.

Our study has limitations. It is cross-sectional in design, so a causal relationship between high-normal free thyroxine and components of MS cannot be ascertained. The sample size is small. Direct measures of insulin resistance were not undertaken in this study. However, MS is a well known clinical expression of insulin resistance, which we studied. In addition, we did not measure, blood triiodothyronine levels; the active form of thyroid hormone in target tissues. It has been suggested

that triiodothyronine acts with insulin to modulate glucose and lipid homeostasis (Kim et al., 2000). The correlation between serum free T4 and BP in all subjects was statistically significant but low. This may also be due to the fact that the subjects were South Asian and the sample size was small.

In summary, our study has shown that high-normal thyroid function (free T4) is positively correlated with raised BP and with raised serum glucose levels in males. So, there may be increased risk of hypertension in subjects with high-normal thyroid function. Males with high-normal thyroid function may be at risk of developing raised blood glucose. Future large studies are required in the South Asian population to confirm and validate our findings.

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Full Length Research paper

The prevalence and management of hypertension in a population of adults with type 2 diabetes in the Adamawa Region (Cameroon): A retrospective analysis

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This study aimed to assess the prevalence, treatment and control of hypertension in adult Cameroonian population in Adamawa with type 2 diabetes. Medical files of patients under follow-up at the hypertension and diabetes Unit of the Ngaoundéré Regional Hospital (Adamawa Region, Cameroon) were evaluated over one year period from January 2008 to January 2009. Medical follow-up consisted of a regular monthly clinical evaluation, with measurements of anthropometric parameters and monitoring of blood pressure and fasting blood sugar. A total of 317 diabetics were surveyed in this study. The overall prevalence of hypertension was 60.3%. The prevalence of hypertension was higher for the female population (61.1%) as compared to male (58.6%). Overall, 36.7% patients (n=70) were treated for hypertension; only 5.7% of the treated patients had their blood pressure controlled. The commonly prescribed drugs were: alpha methyldopa (26%), association reserpine and chlortalidone (25%), diuretics (22%), angiotensin-converting enzyme (ACE)-inhibitors (10%), and calcium channel blockers (8%). Our study indicates a low control rate of hypertension in Cameroonian diabetic patients in our setting and underlines the need for improving their blood pressure management with effective prevention of cardiovascular risk.

Keys words: Hypertension, type 2 diabetes, prevalence, drugs, control.

INTRODUCTION

Hypertension is the major share burden of cardiovascular disease in the world (Lawes et al., 2006). Available epidemiological data on hypertension in Cameroon indicate that its prevalence varies between 12 and 22% for subjects above 25 years (Mbanya et al., 1998; Kearney et al., 2004). At the same time, high blood pressure often occurs in association with diabetes for which, it is an extremely common comorbidity. Hypertension in diabetes is due to several pathophysiological mechanisms which include increased volume expansion, altered sodium homeostasis, increased peripheral vascular resistance, hyperinsulinemia and lipid abnormalities, which have been associated with increased risk of cardiovascular disease (Sowers, 2003; Coccheri, 2007).

The presence of hypertension in individuals with diabetes increases the mortality 4-5 folds, largely through coronary artery disease and stroke (Sahay and Sahay, 2003). It is now well documented that the association between hypertension and diabetes increases the risk of cardiovascular disease that causes about 85% of deaths in diabetic patients (Arrauz-Pacheco et al., 2002). Therefore, acknowledgement of the prevalence of hypertension and blood pressure control in diabetic patients is important for health policy and public health strategy. In Cameroon, studies specifically addressing the prevalence, treatment and control of high blood

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Table 1. Prevalence of hypertension in diabetic patients according to age (N = 317).

Age (years)	Men		Women		All		P value
	N = 162		N = 155		N = 317		
	n	(%)	n	(%)	n	(%)	
20-29	2	(22.2)	2	(18.2)	4	(20.0)	0.83
30-39	10	(55.6)	10	(40.0)	20	(46.5)	0.33
40-49	18	(45.0)	23	(57.5)	41	(51.3)	0.27
≥50	65	(68.4)	60	(76.9)	125	(72.3)	0.21
Total	95	(58.6)	96	(61.9)	191	(60.3)	0.55

pressure in diabetic patients have taken little attention in northern areas of the country. This research was undertaken to assess the prevalence, management and control of hypertension in a population of adult Cameroonian diabetics in the Adamawa region (northern Cameroon).

MATERIALS AND METHODS

The study was conducted at the hypertension and diabetes Unit of the Ngaoundéré Regional Hospital (Adamawa, Cameroon). The target population consisted of patients registered for the first time or old cases on monitoring. During the study period (January 2008 - January 2009), clinical examinations were carried out and laboratory parameters were measured for all the patients; these included: sex, age, fasting blood sugar, blood pressure, weight and height. When necessary, further investigations were performed.

Fasting blood sugar was measured in the morning after an overnight fast. One Touch Profile 1 blood glucose meter (LifeScan, Germany) calibrated for blood glucose measurements was used. Blood pressure (BP) was measured, according to World Health Organization (WHO) guidelines (Chobanian et al., 2003), on calm subjects in a sitting position. Three measurements were taken with 3 min intervals between consecutive measurements. An automatic sphygmomanometer brand OMRON HEM-705 Automatic CP was used to measure the blood pressure. Average systolic blood pressure (SBP) and diastolic blood pressure (DBP) were determined from the second and third measurements. In addition, all subjects were asked whether they were taking any medications for the treatment of hypertension or diabetes. The clinical data were collected and kept in the individual patient file and were also summarized in a collective register. This register served as the source of data for the present study. This study received approval from the administrative authorities of the hospital.

Hypertension was defined as SBP ≥ 140 mm Hg or DBP ≥ 90mm Hg or self reported use of antihypertensive medication, with adaptation of the recent WHO definitions (Chobanian et al., 2003). Controlled hypertension was defined as blood pressure < 140/90 mmHg. Patients of both sexes and responding to the diagnostic criteria of diabetes mellitus as defined by the American Diabetic Association (ADA) (American Diabetes Association, 2007) were included in the study. Patients less than 20 years old, patients with gestational hypertension, or hypertensive patients without diabetes and patient with type 1 diabetes were excluded.

Statistical analysis

Statistical analysis was performed using SPSS 12 version 12.01. Data were expressed as percentages, proportions and mean of standard deviation. A Student t test was used to discriminate between the means. Significance level was considered at $p<0.05$ for all analysis.

RESULTS

In total, 317 patients with diabetes were included in the study (162 men and 155 women). Among these patients, 191 were diagnosed with hypertension, giving an overall prevalence of hypertension of 60.3%. The prevalence of hypertension increased steadily with age and was higher in female (61.9%) when compared to male (58.6%) regardless of age. The prevalence of hypertension in diabetic patients according to age is presented in Table 1. Diabetic hypertensive patients (n = 191) had a mean age of 53.7 ± 1.8 years old and were predominantly female (p = 0.28). Mean body mass index was 26.2 ± 0.8 kg/m^2 and was statistically higher in women than in men (p = 0.02). The mean fasting blood sugar was 2.3 ± 0.02 g / l for the whole population. The average SBP and DBP were respectively 160.9 ± 4.3 and 94.5 ± 2.3 mmHg. There was no significant statistical difference between men and women with regard to level of blood pressure.

Among patients with hypertension and diabetes, 37.2% had systolic hypertension, while 14.7% had diastolic hypertension, and 48.2% both systolic and diastolic hypertension. Moreover, 36.7% (n = 70) of patients were under treatment for hypertension, 39 women (40.6%) and 31 men (32.6%) among these patients, only 5.7% (n = 4) had a blood pressure level below 140/90 mmHg at their most recent clinical evaluation. General characteristics of diabetic hypertensive patients are presented in Table 2.

The patients treated were subjected to dietary measures, and antihypertensive drug. The distribution of the most frequently prescribed drugs was: Alpha methyldopa (26%), association reserpine and chlortalidone (25%), thiazide diuretics (22%), angiotensin-converting-enzyme inhibitors (ACE inhibitors) (10%), and calcium channel blockers (8%).

DISCUSSION

Prevalence of hypertension

Epidemiological data on hypertension in diabetics vary

Table 2. General characteristics of diabetic hypertensive patients (N = 191).

Parameter	Men N = 95	Women N = 96	All N = 191	P value
	Mean or n (%)	Mean or n (%)	Mean or n (%)	
Mean age (years)	54.7 ± 2.6	52.7 ± 2.5	53.7 ± 1.8	0.28
Fasting blood sugar (g/L)	2.3 ± 0.2	2.4 ± 0.3	2.3 ± 0.2	0.68
Age groups (years)				
20-29	2 (2.1)	2 (2.1)	4 (2.1)	1.00
30-39	10 (10.5)	10 (10.5)	20 (10.5)	1.00
40-49	18 (18.9)	23 (24.2)	41 (21.6)	0.38
≥50	65 (68.4)	60 (63.2)	125 (65.8)	0.45
Weight status				
BMI (kg/m²,mean±SD)	24.9 ± 1.0	27.5 ± 1.3	26.2 ± 0.8	0.002
BMI <25 kg/m^2	54 (57.5)	34 (37.0)	88 (47.3)	0.005
25 kg/m^2 ≤ BMI ≤ 29.9 kg/m^2	29 (30.9)	28 (30.4)	57 (30.7)	0.95
BMI≥30 kg/m^2	11 (11.7)	30 (32.6)	41 (22.0)	0.001
Blood pressure				
SBP mean (mmHg)	161.8 ± 6.2	159.9 ± 6.2	160.9 ± 4.3	0.66
DPB mean (mmHg)	95.2 ± 3.2	93.8 ± 3.4	94.5 ± 2,3	0.54
Treatment and control				
Treated subjects	31 (32.6)	39 (40.6)	70 (36.7)	0.10
Control among treated	1 (3.2)	3 (7.7)	4 (5.7)	0.43
Type of hypertension				
Isolated systolic	33 (34.7)	38 (39.6)	71 (37.2)	0.49
Diastolic	11 (11.6)	17 (17.7)	28 (14.7)	0.23
Systolic and diastolic	51 (53.7)	41 (42.7)	92 (48.2)	0.13

throughout the world in type and distribution, especially between the developed and the developing countries. In our study, the average age of diabetic hypertensive patients was 53.7 ± 1.8 years old, with a female to male ratio of 1.01. The female predominance reported in this work reflects African literature data (Mengesha, 2007; Damorou et al., 2008). The prevalence of hypertension in diabetic patients was 60.3%, which was close to the rates reported in Caucasian series (Geiss et al., 2002), but clearly higher than those previously described in other Sub-Saharan African countries (Dembele et al., 2000). This could be explained by methodological differences on the threshold used to define hypertension in diabetic patients. Since the threshold selected in this study was 140/90 mmHg, it can be assumed that the prevalence rate found is significantly underestimated taking into account the international recommendations fixing the optimal blood pressure level in the diabetic hypertensive at 130/80 mmHg (Ryden et al., 2007). As with other studies, the prevalence of hypertension increased with age, reaching its maximum in patients older than 50 years (Dembele et al., 2000; Mengesha, 2007).

Drug therapy

In our series, thiazide diuretics, reserpine-chlortalidone association, central antihypertensives, angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers were used in the treatment of diabetic hypertensive patients. Our work indicates that alpha methyldopa and reserpine-chlortalidone association are frequently used in our environment (51% of patients). Their low cost and the difficult socio-economic background may justify their widespread use. Paradoxically, ACE inhibitors have been used in 10% of patients giving them a modest place among the different classes of drugs used, despite their proven effectiveness in cardiovascular and renal prevention in diabetic patients (Yusuf et al., 2000; Maggioni, 2006; Cohn, 2007; Sharma and Weir, 2011); this is held in their high costs in our milieu. Probably for similar reasons, the treatment of hypertensive patients did not involve any angiotensin II receptors blockers whose renal protective effects have been demonstrated in patients with diabetes (Atkins et al., 2005; Murohara et al., 2012; Verdecchia et al., 2012).

The results of the present study suggest that therapeutic classes reputed for being effective on cardiovascular risk in diabetic patients are prescribed very little in our context on one hand, and on the other, the choice of treatment is still largely dependent on drug costs. Indeed, most therapeutic classes used in our series were also the least expensive.

Control of treated hypertension

Results from many large-scale clinical trials have demonstrated that a strict control of systolic and / or diastolic blood pressure can significantly decrease cardiovascular events and stroke in diabetic patients (Hansson et al., 1998; Ravid and Rachmani, 2005; Holman et al., 2008). This suggests that optimal control of blood pressure is a priority in the management of hypertensive patients with diabetes. In this study, 36.5% (n = 70) of patients were treated and among them, only 5.7% (n = 4) had a blood pressure below 140/90 mmHg at their last clinical evaluation. The data obtained in our work indicate a sub-optimal control of blood pressure and corroborate those reported in the literature relating on difficulties of adequate control of BP in Africa (Ben et al., 2011), Asia (Azarisman et al., 2010) and the West (Geiss et al., 2002; Mann et al., 2009).

The most commonly reported factors in the literature explaining the low rate of control include the lack of adherence due to the silent nature of hypertension, an inadequate understanding of the therapeutic usefulness of measures of lifestyle (Ho et al., 2008), the coexistence of other pathologies (Turner et al., 2008) and the cost of treatment (Ohene Buabeng et al., 2004). In our context, the propensity to use central antihypertensive could be an additional element that could explain the low control rate observed in our series. Indeed, the use of centrally acting antihypertensive molecules can sometimes cause side effects altering the quality of patient's life, and results in a change or discontinuation of treatment (Jones et al., 1995). This decreased compliance is associated with poor blood pressure control. In addition, cultural and social influences could have contributed to the low rate of control observed. In our environment, most patients hardly accept the chronic nature of hypertension and are reluctant to take a long-term antihypertensive treatment.

This study should be considered in light of some limitations. Particularly, it consisted of a monocenter study whose results need to be confirmed in a larger scale. Furthermore, it concerns semi urban population, and consequently does not prejudge the prevalence, treatment and control of hypertension in diabetics patients in the rural setting where access to care is still difficult. Other possible sources of bias include lack of out of office blood pressure measurements. Nevertheless, no study on this subject has been carried out with a group of such an important number of patients in the Adamawa region (Cameroon).

Conclusion

High blood pressure in diabetics is common in our environment and the management of blood pressure in diabetic patients is suboptimal. This dual finding reflects the need for better management of hypertension in our diabetic patients with the aim of an effective prevention of cardiovascular risk. Further studies will be oriented towards the search for specific factors associated with low blood pressure control in our diabetic population.

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Short Communication

Signet ring carcinoma of the esophagogastric junction in a Nigerian man

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Globally, the majority of cancers of the esophagogastric junction are adenocarcinomas. Of the four histological subtypes, the signet ring carcinomas are rare. There is a dearth of reports of this relatively rare histological finding from patients in sub-Saharan Africa. We present such a case in 69 year old Nigerian with advanced malignant disease.

Key word: Signet ring carcinoma, esophagogastric junction, endoscopy, Nigeria.

INTRODUCTION

Adenocarcinomas that cross the esophagogastric junction (EGJ) are called adenocarcinomas of the EGJ, regardless of where the bulk of the tumor lies (Sons et al., 1986). The World Health Organization (WHO) classification distinguishes four histological types: papillary, tubular, mucinous, and signet ring cell adenocarcinoma (Hamilton and Aaltonen, 2000).

The disease appears to have a low prevalence rate in sub-Saharan Africa generally and Nigeria specifically (Kachala, 2010; Abdulkareem et al., 2008). Although, exact data about EGJ tumors is not presently available, its rarity can be inferred from other published work that investigated incidence and prevalence patterns of all esophageal and gastric cancers. A worrying increase in the incidence and prevalence of adenocarcinoma of the esophagus has been noted in Western countries (Vizcaino et al., 2002).

The signet ring cell subset of adenocarcinomas is characterized by abundant intracellular mucin accumulation leading to compressed nucleus which is eccentrically located within the cell. It must be distinguished from the mucinous variety which possesses abundant extracellular mucin. For the lesion to qualify as signet ring cell carcinoma, the adenocarcinoma's predominant component (more than 50%) must be composed of isolated malignant cells containing this intracytoplasmic mucin. Primary signet ring cell carcinoma of the EGJ is infrequent (Hamilton and Aaltonen 2000).

This study presents the case of a 69 year old Nigerian with this rare histologic subtype and briefly discusses the clinical presentation and the prognostic implications of such a diagnosis.

CASE REPORT

A 69 year old male presented with a four month history of difficulty with swallowing and repeated vomiting. There was no history of blood and bile in the vomitus as it contained only recently ingested meals mixed with what he described as a slimy material. Dysphagia was associated with the feelings of food being "caught up in the chest", and frequently, he noted a feeling of fullness in his chest following meals which preceded the vomiting episodes. All symptoms had progressively increased in frequency leading to a considerable loss of weight over the course of the illness. There was no history of chronic heartburn nor regurgitation (these might have be suggestive of underlying reflux disease) and patient had never smoked in the past. No family history of gastrointestinal malignancy of any kind was reported in the patient.

His general examination findings were significant for cachexia with pallor and palmar erythema. The abdominal findings revealed a mobile mass palpable just below the xiphisternum. It was a freely mobile, firm and tender mass

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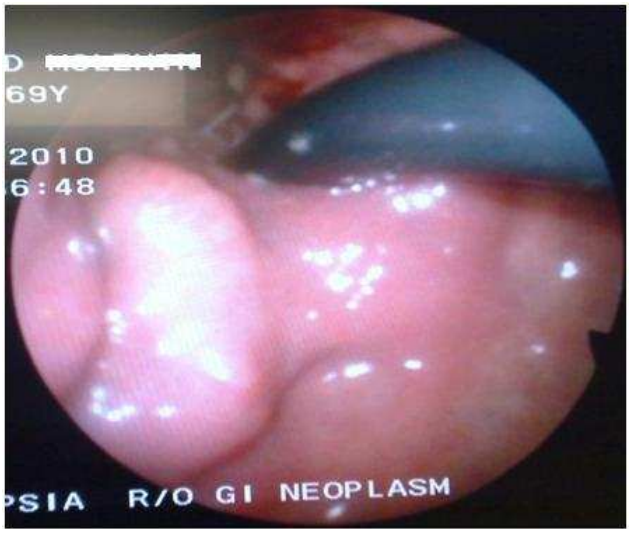

Figure 1. Esophagogastroduodenoscopy retroflexed view from within the stomach shows a large, irregular, ulcerated mass in the gastric cardia.

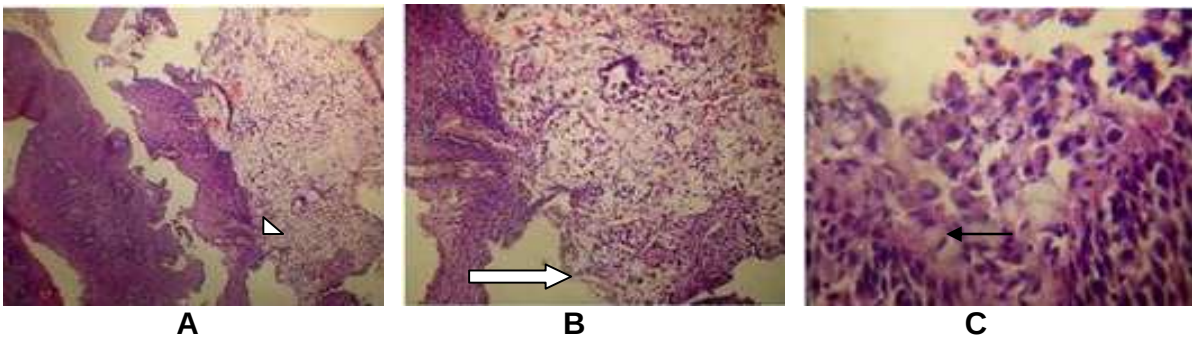

Figure 2. (A) Photomicrograph of signet ring carcinoma invading the stratified squamous epithelium of the esophagus. (white arrow) (hematoxylin and eosin stain; original magnification × 40). (B) Same section as A, but at higher magnification showing localized area of epithelial erosion (bold arrow) (hematoxylin and eosin stain; original magnification × 100). (C) Same section as A, but at higher magnifications showing signet ring cells having abundant mucin filled cytoplasm pushing the nuclei to the periphery (black arrow) (hematoxylin and eosin stain × 400).

tender mass whose upper dimensions could not be made out on palpation. The bedside test for succussion splash was negative.

The esophagogastroscopy revealed that the proximal portion of the esophagus was littered with food debris. At the lower end, there was a huge circumferential mass which had infiltrated the esophagogastric junction (EGJ) till near obliteration of the passage into the stomach. The distal portion of the esophagus was grossly dilated. There was a large, ulcerated, nodular mass in the gastric cardia which appeared to be in continuity with the esophageal mass, but its irregularity had very nearly completely distorted the architecture of the cardia (Figure 1).

Biopsy samples were taken from the esophageal and gastric ends of the mass and also at the level of the EGJ. The biopsy of the cardia showed an area of ulceration of the epithelial lining by tumor cells which consist of poorly differentiated adenocarcinoma with more than 75% being diffusely disposed signet ring cells. These cells have pleomorphic hyperchromatic nuclei and mucin-distended cytoplasm and eccentrically located nuclei within the cell. Adjacent suppurative inflammatory reaction was also noted. Similar tumorous cells were found in the samples from the esophagus and the EGJ. Additionally, the esophageal mucosa showed no evidence of Barrett's or dysplasia (Figure 2A to C).

Computed tomography study revealed infiltrative masses in the liver suggestive of distant metastasis from the tumor and was referred to the gastrointestinal surgeon for co-management with oncologists. The patient was reviewed and adjudged not to be fit for surgery. Hence, palliative measures were instituted. The surgeons

put in a percutaneous gastrojejunostomy tube for feeding which helped ameliorate the patient's symptoms and the oncologists commenced anticancer regime which included the drug, imatinib. But the patient succumbed soon afterwards.

DISCUSSION

The first documented case of esophageal signet ring carcinoma was in Japan by Takubo et al. (1987). The case being reported here seeks to document the presence of this infrequent histologic type of adenocarcinoma of the EGJ in sub-Saharan Africa. A recent large pathology series from Lagos, Nigeria, one of the most densely populated cities in sub-Saharan Africa (Abdulkareem et al., 2008) reported that not a single case of esophageal carcinoma with similar histology was found. It is to be noted that the bulk of malignant esophageal tumors in this environment have been reported to be of the squamous cell carcinoma variety as this accounts for over 90% of cases (Pindiga et al., 1997). The age of the patient and clinical features are typical for the presentation of esophageal cancers in this part of the world (Pindiga et al., 1997).

Previous workers have highlighted late presentation and delay in diagnosis as the key factors responsible for the abysmal prognosis of esophageal carcinomas in Nigeria (Pindiga et al., 1997). Another mitigating factor to prompt diagnosis of this disease in our environment is the unavailability and inaccessibility of endoscopy services in general (Onyekwere et al., 2008; Agbakwuru et al., 2006). The case further emphasizes the importance of these two factors as the patient's alarm features of repeated vomiting with marked weight loss warranted both earlier presentation and endoscopic assessment.

Additionally, the prognosis of signet ring carcinoma of any organ is, in general, poor. This dismal outcome is mainly accounted for by the diffusely infiltrating nature of the neoplasm, leading to widespread metastases before being clinically apparent (Chirieac et al., 2005). In many cases, as illustrated by the index report, at the time of diagnosis, there is evidence distant metastasis.

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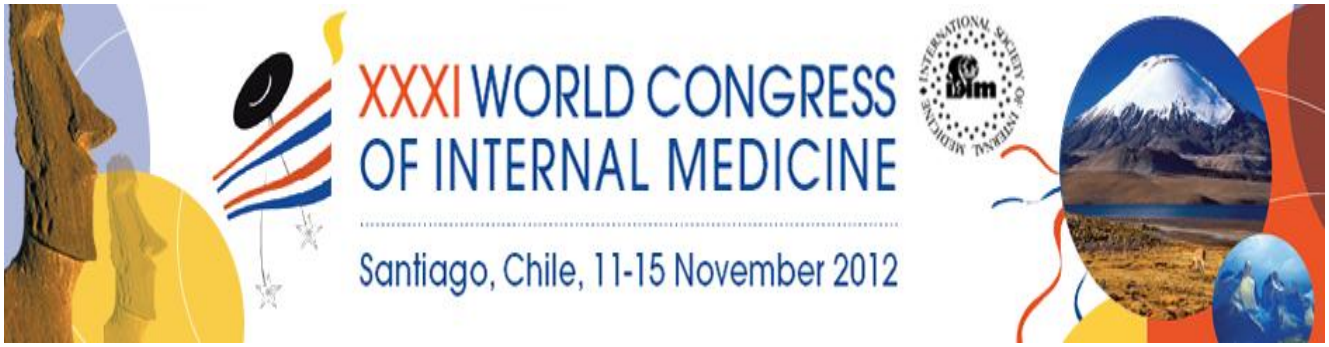

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