Hyperuricaemia and other cardiometabolic risks among type 2 diabetes patients

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Abstract Cardiovascular disease (CVD) is a leading cause of further morbidity and mortality in type 2 diabetes patients. This study aimed to find the serum lipid profile, serum uric acid levels, other CVD risk factors, and how these factors are affected by diabetes duration in adults with type 2 diabetes. The cross-sectional study, involving 100 subjects, was carried out at the Diabetes Centre, Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana. Adult type 2 diabetes patients, 20 years or older, were recruited for the study. The National Cholesterol Education Program (NCEP) Adult Panel III and American Diabetes Association (ADA) guidelines were used to find the metabolic status of the patients. Of the 100 patients, 74% and 62% had high systolic blood pressure and abdominal obesity, respectively. Also, high LDL-cholesterol and hypercholesterolaemia were found in 47% and 46% of the patients, respectively. Forty-six percent (46%) of the patients were hyperuricaemic. Cardiovascular disease risk increased with age from 20 to 79 years. The female diabetics had more adverse CVD risk profile than the male diabetics (high LDL, 55% vs. 23.1%; high total cholesterol, 54.1% vs. 23.1%; high triglycerides, 32.4% vs. 30.8%; low HDL, 25.7% vs. 3.8%). Fifty percent (50%) of females compared to 34.6% of males were hyperuricaemic. However, hypertension was more prevalent among males (systolic blood pressure, 76.9%; diastolic blood pressure, 38.5%) than among females (systolic blood pressure, 73%; diastolic blood pressure, 37.8%). In conclusion, the prevalence of hyperuricaemia and other cardiometabolic risks was high among type 2 diabetes patients.

Keywords: type 2 diabetes, obesity, hypertension, lipid profile, uric acid

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1. Introduction

Cardiovascular disease is a leading cause of death in type 2 diabetes patients.[1] The metabolic determinants of CVD include serum lipid profile, serum uric acid, blood glucose, blood pressure (BP), body mass index (BMI), and waist circumference (WC). Dyslipidaemia (i.e. high total cholesterol, high LDL-cholesterol, high triglycerides and low HDL-cholesterol) is a significant CVD risk factor.[2] It is common in type 2 diabetes patients causing both microvascular and macrovascular complications.[3,4] Insulin deficiency and resistance affect pathways and enzymes of lipid metabolism.[5] The most common abnormality is increased serum triglyceride levels, followed by decreased serum HDL-cholesterol levels and increased serum LDL-cholesterol levels.[6,7] Many of the patients are overweight, with some even overtly obese.[7] Total cholesterol:HDL-cholesterol ratio (TC:HDL-C) as well as LDL-cholesterol:HDL-cholesterol ratio is also an index of CVD, the former being a better indicator.[8] Hyperuricaemia has been related to CVD. Hyperuricaemia increased the prevalence of metabolic syndrome, and was associated with abdominal obesity, hypertriglyceridaemia, low HDL-cholesterol, and high BP among type 2 diabetics.[9-11]

High BP is a cardiovascular risk factor and this is more severe in patients with type 2 diabetes.[12] A combined increase in systolic blood pressure (SBP)

and decrease in diastolic blood pressure (DBP), however, is a higher CVD risk factor.[13] Body mass index, a measure of obesity, is the ratio of weight in kilogram to the square of height in metre. It is a common parameter measured in investigative studies involving patients with type 2 diabetes, hypertension, dyslipidaemia, and obesity. The higher the BMI, the greater the risk for these disorders.[14] Other anthropometric indices that have been used to study risks for metabolic diseases include WC[15] and waist-to-hip ratio.[16] Body mass index, when used in combination with WC, has proven to be a better indicator of cardiometabolic disorder and CVD.[17,18] In urban Ghana, type 2 diabetes which is associated with age and obesity affects at least, 6% of adults.[19] Overweight, which has been related to advancing age, female gender, urban environment, high income, and tertiary education affects about 23% of adults.[20] This study aimed to find the blood lipid profile, uric acid level and anthropometric indices of type 2 diabetes patients, and how diabetes duration affects these parameters.

2. Materials and Methods

Study design

This study was cross-sectional, involving 100 type 2 diabetes patients who visited the Diabetes Centre of the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana, as out-patients. These patients were with or without complications.

Inclusion and exclusion criteria

Only type 2 diabetes patients of 20 years or older at the Out-patient Department (OPD) were recruited in the study. They should have been registered at the Diabetic Centre, and their medical records should be available. Type 1 diabetes patients and gestational diabetes women were excluded from the study.

Anthropometric and BP measurements

The weights of the subjects were taken using an electronic scale, Seca Ltd., Germany and their heights measured with the stadiometer, Seca Ltd., Germany. The BMI for each subject was then calculated as weight in kilogram divided by height in metre squared, and this determined central obesity. Waist circumference, which determined abdominal obesity, was measured (in centimetre), with a tape measure. The measurement was taken, midway between the lower border of the rib cage and the iliac crest, in the mid axillary line, with patients standing and breathing normally.

Patients were allowed to rest for 20 minutes prior to measuring their BP. Blood pressure was measured by standard methods using a mercury sphygmomanometer and a stethoscope with the patient in a sitting position. Three measurements were made on all subjects at 5-minute intervals; the average of the measurements was used in the analysis. These measurements were made by trained personnel to ensure accuracy.

Biochemical measurements

About 5 ml of venous blood samples were collected (by a phlebotomist) in the morning from subjects who had fasted for at least 8 hours. Two millilitre (2 ml) of each sample was kept in fluoride tube and the remaining in serum tube. Laboratory tests were conducted on blood samples of subjects to find serum lipid profile (total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides), fasting blood glucose (FBG), and uric acid.

Fasting blood glucose was estimated by Trinder's method, an end point/ fixed time assay, with a kit from Fortress Diagnostics, UK. The total cholesterol was determined by the cholesterol oxidase-peroxidase (CHO-POD) method, with kits from Medsource Ozone Biomedicals, Pvt. Ltd., India. Triglycerides were determined by the glycerol-3-phosphate oxidase-peroxidase (GPO-POD) method, with kits from Fortress Diagnostics, UK and HDL-cholesterol was determined by the precipitation end-point method with reagents from Fortress Diagnostics, UK. LDL-cholesterol concentration was calculated by Friedewald's formula.[21] Serum uric acid levels were determined by uricase-peroxidase (Uricase-POD), end point assay method,[22] with reagents from Medsource Ozone Biomedicals, Pvt. Ltd, Haryana, India. The Kenza BioChemis Try, BIOLABO Diagnostics, France, a semi-automated spectrophotometer, was used to measure all the parameters. The TC:HDL-C ratio, referred to as coronary risk, was calculated.

Definition of diabetes

Diabetes was defined, based on WHO diagnosis of diabetes, as FBG $\geq$ 6.1 mmol/L,[23] and/or persons who had been previously diagnosed by a medical doctor or were on diabetes medication. Diabetes duration was defined as the number of years a subject had been with diabetes since diagnosis.

Definition of hyperuricaemia and other cardiometabolic risk factors

High blood uric acid levels were defined as serum uric acid concentration > 360 μmol/L for females, and > 420 μmol/L for males.[24] The undesirable lipid profile (high total cholesterol, high LDL-cholesterol, high triglycerides, and low HDL-cholesterol) is as follows: total cholesterol ≥ 5.2 mmol/L, LDL-cholesterol ≥ 3.0 mmol/L, triglycerides ≥ 1.71 mmol/L, and HDL-cholesterol < 1.03 mmol/L for males; < 1.3 mmol/L for females. A subject was considered to have dyslipidaemia if at least one of the above criteria is attained.[25,26] Overweight and obesity were defined according to BMI (overweight, 25.0–29.9 kg/m^2; obesity, ≥ 30.0 kg/m^2) and WC (overweight men, 94.0-101.9 cm; overweight women, 80.0-87.9 cm; obese men, ≥ 102.0 cm; obese women, ≥ 88.0 cm).[6] A subject was considered hypertensive if the subject had SBP ≥ 130 mmHg and DBP ≥ 85 mmHg, or on anti-hypertensive drug.[25,26]

Statistical analysis

The data for this study was analysed using Statistical Package for Social Sciences (SPSS Inc., software version 20.0). Means and standard deviations for continuous variables were calculated and compared by one-way ANOVA. Comparisons of frequency counts and percentages for categorical variables between male and female diabetics were done using Student's t-test. *P* value < 0.05 was considered significant for comparisons between groups.

Ethical approval and informed consent

The study protocol was forwarded to the Committee on Human Research, Publications and Ethics of the School of Medical Sciences of Kwame Nkrumah University of Science and Technology, and Komfo Anokye Teaching Hospital, Kumasi, Ghana, which gave approval to the research. Informed written consent was obtained from all subjects in the study.

3. Results

Anthropometric, blood pressure, and biochemical indices

The anthropometric indices, lipid profile and uric acid of the subjects are shown in Table 1. The mean BMI of the female participants was significantly higher (*p*=0.002) than that of the male participants. The mean total cholesterol and mean LDL-cholesterol of females were also significantly higher (*p*=0.042 for total cholesterol; *p*=0.039 for LDL-cholesterol) than those of males. Though not significant, females had higher mean waist circumference, DBP, FBG, triglycerides, HDL-cholesterol, TC:HDL-C and uric acid, but lower mean SBP than males.

Table 1: Mean anthropometric indices, BP, lipid profile and uric acid by gender

Parameters	Male n = 26	Female n = 74	Total N = 100	*p*-value
BMI (kg/m^2)	24.39 ±4.08	28.37 ±5.88	27.34±5.73	0.002*
WC (cm)	92.7 ±12.8	97.5 ±14.8	96.2±14.4	0.145
SBP (mmHg)	137.3 ±17.8	134.46 ±18.6	135.2±18.35	0.499
DBP(mmHg)	78.9 ±10.7	80.2 ±12.1	79.9±11.7	0.614
FBG (mmol/L)	9.7 ±4.9	10.5 ±5.0	10.3±4.9	0.479
TC (mmol/L)	4.7 ±1.2	5.3 ±1.3	5.2±1.3	0.042*
TG (mmol/L)	1.5 ±0.9	1.6 ±0 .7	1.6±0.8	0.762
HDL-C (mmol/L)	1.4 ±0.4	1.5 ±0.4	1.5±0.4	0.597
LDL-C (mmol/L)	2.6 ±0.9	3.1 ±0.1	3.0±1.1	0.039*
TC:HDL-C	3.3 ±0.7	3.7 ±0.9	3.6±0.9	0.102
Uric acid (μmol/L)	381.8 ±164.2	408.7 ±166.1	401.8±165.0	0.533

Values are recorded as Mean ± Standard deviation; *indicates significant difference. Body mass index (BMI), waist circumference (WC), fasting blood glucose (FBG), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C).

The prevalence of cardiometabolic risks by gender

Table 2 shows the prevalence of dyslipidaemia, hyperuricaemia, hypertension, obesity and hyperglycaemia by gender. The percentage of subjects with raised body mass index, raised waist circumference, elevated FBG level, elevated triglyceride, elevated total cholesterol, elevated LDL-cholesterol, reduced HDL-cholesterol, and elevated uric acid were higher in females than in males. Conversely, hypertension was more prevalent among males than among females as the percentages of SBP as well as DBP of the patients were more elevated in

males than in the females. Interestingly, 80% of the participants had normal HDL-cholesterol (HDL-cholesterol > 1.03 mmol/L for males; and > 1.3 mmol/L for females).

Table 2: Prevalence of dyslipidaemia, hypertension, obesity, hyperglycaemia and hyperuricaemia by gender

Variable	Classification	Mean ± SD	Male n (%)	Female n (%)	*p*-value
BMI (kg/m^2)	< 18.5 Underweight	16.37 ±1.68	1(3.8)	2(2.7)	
	18.5-24.9 Normal	22.14 ±1.72	14(53.8)	21(28.4)	
	25.0-29.9 Overweight	27.65 ±1.41	8(30.8)	25(33.8)	
	≥ 30 Obese	34.40 ±3.41	3(11.5)	26(35.1)	0.025*
WC (cm)					
	< 94.0 Normal	84.3 ±7.9	15(57.7)	N/A	
Male	94.0-101.9 Overweight	96.8 ±2.5	5(19.2)	N/A	
	≥ 102 Obese	110.2 ±6.0	6(23.1)	N/A	
					0.000*
	< 80 Normal	71.4 ±8.8	N/A	7(9.5)	
Female	80.0-87.9 Overweight	83.8 ±1.8	N/A	11(14.9)	
	≥ 88 Obese	103.4 ±11.1	N/A	56(75.7)	
FBG (mmol/L)	< 6.1 Normal	5.3 ±0.8	9(34.6)	10(13.5)	
	≥ 6.1 High	11.4 ±4.8	17(65.4)	64(86.5)	0.038*
SBP (mmHg)	< 130 Normal	110.8 ±7.4	6(23.1)	20(27.0)	
	≥ 130 High	143.8 ±12.3	20(76.9)	54(73.0)	0.799
DBP (mmHg)	< 85 Normal	72.6 ±8.5	16(61.5)	46(62.2)	
	≥ 85 High	91.7 ±4.1	10(38.5)	28(37.8)	0.955
TC (mmol/L)	< 5.2 Normal	4.2 ±0.6	20(76.9)	34(45.9)	
	≥ 5.2 High	6.3 ±0.9	6(23.1)	40(54.1)	0.011*
TG (mmol/L)	< 1.7 Normal	1.1 ±0.3	18(69.2)	50(67.6)	
	≥ 1.7 High	2.5 ±0.7	8(30.8)	24(32.4)	1.000
HDL-C (mmol/L)					
Male	< 1.03 Normal	1.0 ±0.0	1(3.8)	N/A	
	≥ 1.03 High	1.5 ±0.4	25(96.2)	N/A	
					0.021*
Female	< 1.3 Normal	1.1 ±0.1	N/A	19(25.7)	
	≥ 1.3 High	1.6 ±0.3	N/A	55(74.3)	
LDL-C (mmol/L)	< 3.0 Normal	2.1 ±0.6	20(76.9)	33(44.6)	
	≥ 3.0 High	3.9 ±0.7	6(23.1)	41(55.4)	0.006*
Uric acid (μmol/L)	> 420 High males	535.3 ±81.1	9(34.6)	N/A	
	> 360 High females	510.8 ±103.9	N/A	37(50)	0.253

Values are recorded as Mean ± Standard deviation; *p*-value represents significance between male and female for low HDL-C, obese, and high categories of other parameters at $p<0.05$; *indicates significant difference. n is the number of males or females in a particular category, percentages are in parentheses. Body mass index (BMI), waist circumference (WC), fasting blood glucose (FBG), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C). Not applicable (N/A).

Table 3: Age distribution of some CVD risk factors

Components	Age groups (years)				
	20-39	40-59	60-79	≥ 80	Total
WC (≥102 cm for males; ≥88 cm for females)	2	24	35	1	62
FBG (≥ 6.1 mmol/L)	1	41	39	0	81
SBP (≥ 130 mmHg)	0	30	44	0	74

DBP (≥ 85 mmHg)	0	18	20	0	38
TC (≥ 5.2 mmol/L)	1	23	22	0	46
TG (≥1.7 mmol/L)	0	14	17	1	32
HDL-C (< 1.03 mmol/L for males; < 1.3 mmol/L for females)	1	8	11	0	20
LDL-C (≥ 3.0 mmol/L)	2	22	23	0	47
Uric acid (> 420 μmol/L for males; >360 μmol/L for females)	0	24	21	1	46

Waist circumference (WC), fasting blood glucose (FBG), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C).

The number of subjects with various CVD risk factors, according to NCEP criteria, was stratified by age groups. These are shown in Table 3. Generally, the 60-79 age group had the highest number of subjects for all factors, except FBG (highest in the ages between, 40-59). Apart from FBG which was obviously high, BP and WC were seen to be the risk factors with the highest frequencies. The lowest risk was recorded with low HDL-cholesterol. The highest number of subjects with hyperuricaemia was recorded within the 40-59 age group, followed by the 60-79 age group.

The relation of diabetes duration to anthropometric indices, FBG, BP, serum lipid profile, and uric acid

As shown in Table 4, WC was significantly different between the categories of diabetes duration. The WC increased with diabetes duration between 1 to 19 years. Mean BMI of subjects within 11-19 years of diabetes duration was significantly higher than that of those within 1-5 years of diabetes duration. Mean FBG for both 6-10 and ≥ 20 years of diabetes duration were significantly lower than for 1-5 years of diabetes duration. Generally, the differences between the diabetes duration categories for the other parameters measured did not show any particular pattern.

Table 4: Anthropometric indices, FBG, SBP, DBP, serum lipid profile and uric acid by diabetes duration

Parameter	< 1 year	1-5 years	6-10 years	11-19 years	≥ 20 years
n	**8**	**23**	**34**	**26**	**9**
BMI (kg/m^2)	27.55 ±3.44	25.20 ±4.92[a]	27.91 ±6.00	28.84 ±6.51[b]	26.12 ±4.93
WC (cm)	97.9 ±11.8[a]	86.5 ±14.6[b]	98.7 ±11.9[a]	101.1 ±15.2[a]	96.0 ±13.1
FBG (mmol/L)	9.6 ±5.7	12.4 ±6.4[b]	9.4 ±4.5[a]	10.5 ±3.9	8.2 ±2.6[a]
SBP (mmHg)	132.5 ±16.7	130.4 ±17.4	137.4 ±18.8	139.0 ±16.7	130.6 ±24.3
DBP (mmHg)	78.8 ±9.9	78.3 ±12.3	82.2 ±11.8	80.4 ±11.8	74.4 ±11.3
TC (mmol/L)	5.4 ±0.7	5.0 ±1.2	5.3 ±1.4	4.9 ±1.4	5.4 ±0.8
TG (mmol/L)	1.7 ±0.8	1.4 ±0.8	1.7 ±0.9	1.4 ±0.6	1.6 ±0.9
HDL-C (mmol/L)	1.5 ±0.3	1.5 ±0.3	1.5 ±0.4	1.4 ±0.4	1.5 ±0.2
LDL-C (mmol/L)	3.1 ±0.6	2.9 ±0.9	3.1 ±1.3	2.8 ±1.2	3.2 ±1.1
TC:HDL-C	3.6 ±0.8	3.3 ±0.5	3.8 ±1.1	3.5 ±0.8	3.7 ±0. 9
Uric acid (μmol/L)	373.0 ± 278.1	405.4 ± 129.0	428.8 ± 156.5	384.3 ± 152.3	366.3 ± 230.2

Values are recorded as Mean ± Standard deviation; n is the number of subjects within a duration category. Different superscripts ([a] and [b]) between categories indicate that the categories were significantly different ($p < 0.05$) for parameter. Body mass index (BMI), waist circumference (WC), fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), systolic blood pressure (SBP), diastolic blood pressure (DBP).

4. Discussion

Overweight was more prevalent among the females (33.8%) than among the males (30.8%) (Table 2). Seventy-eight percent (78%) of the diabetes patients had their WC beyond the normal range. The prevalence of obesity was also higher among the females (BMI, 35.1%; WC, 75.7%) than among the males (BMI, 11.5%; WC, 23.1%). This is similar to results obtained in earlier studies on prevalence of obesity.[4,27-29] From Table 4, WC as well as BMI was associated with diabetes duration; the longer the duration of the condition, the greater the WC and the BMI. This trend however, did not include < 1 year and > 19 years of diabetes duration. The patients who had been with the condition for 11-

19 years had the highest WC and BMI. A study by Gautier *et al*.[30] which focused on the association of WC with the incidence of type 2 diabetes, found that individuals with high WC had higher risk of type 2 diabetes. According to Bays *et al*.,[14] BMI also increases the risk of type 2 diabetes. Contrary to WC and BMI, mean FBG decreased with increasing diabetes duration as it was highest within 1-5 years of diabetes duration compared to 6-10 and ≥ 20 years of diabetes durations. Since management of type 2 diabetes does not delay after diagnosis, longer duration of management might have caused the lower FBG in the two groups.

Hyperlipidaemia was a common condition with type 2 diabetes patients in this study (Table 2). A study by Meigs *et al*.[31] supports this finding. High LDL-cholesterol was the commonest lipid profile abnormality in this study and the second, high total cholesterol. This contradicts an earlier study by Jha,[27] which found total cholesterol to be higher among patients than LDL-cholesterol levels. The prevalence of low HDL-cholesterol was higher among patients within 60-79 years, as compared to younger patients, a similar finding to that of Jha,[27] in which, low HDL-cholesterol was found to be more common in patients > 60 years than those <60 years of age. As shown in Table 3, CVD risk factors were commonest in type 2 diabetes patients within the ages of 60-79 years, followed by 40-59 years of age. This is similar to findings in studies by Hu *et al*.[32] and Ogbera,[33] in which the prevalence of CVD risk factors increased with age. However, Al-Mukhtar *et al*.[34] found cardiovascular risk factors to be significantly higher among young type 2 diabetes adults (< 60 years), compared to their older counterparts. High SBP (≥ 130 mmHg) and DBP (≥ 85 mmHg) were more prevalent among the males than among the females, with the former being more prevalent. The higher prevalence of SBP may explain why it has been suggested to be the target of antihypertensive treatment.[12,35] Most of the diabetics in the present study were on anti-hypertensive drugs. Hypertension frequently exists at time of diagnosis of type 2 diabetes and is associated with CVD risks.[36] Patients with hypertension are more likely to have hyperlipidaemia. There is some evidence that hyperlipidaemia itself may be a risk factor for hypertension and that lipid-lowering interventions may also lower BP. Type 2 diabetes and hypertension together pose a higher cardiovascular risk in patients with metabolic syndrome.[34,37] The results of Danquah *et al*.[4] in an earlier study conducted at the Diabetes Centre, KATH, are slightly different from the findings of this study. Danquah *et al*. reported mean SBP, mean DBP, mean total cholesterol and mean LDL-cholesterol higher than the findings of the present study. Also, mean BMI, mean triglyceride and mean HDL-cholesterol were lower than those reported in this study. Danquah *et al*.[4] thus, generally reported higher CVD risk profile. The difference may be due to improvement in lifestyles of patients at the Diabetes Centre over the period between these two studies. As shown in Table 1, the mean coronary risk (TC:HDL-C) was 3.6. This is within the normal ratio of less than 5.0, though higher than the optimum of 3.5. Further, only 6% of the diabetics had CVD risk ratio greater than 5.0.

Close to half (46%) of the study population had hyperuricaemia (Table 2), with the highest prevalence seen in patients within the age range of 40-59 years (Table 3). The majority of the hyperuricaemic patients were females, as reported in a study by Wang *et al*.[38]

In the present study, women had more adverse cardiovascular risk profile than the men. Such findings had been reported in earlier studies.[4,39-42] Results of other studies have shown obesity to be associated with increased CVD risks.[15,43] In a cross-sectional study of postmenopausal women, Hernandez-Ono *et al*.[44] found visceral fat, a determinant of obesity, to be directly linked with dyslipidaemia and high FBG. The high prevalence of obesity might have contributed to the high prevalence of the other CVD risk factors in the present study.

The study, however, had limitations. The sample size was small and was not uniform in terms of gender, as women predominated.

5. Conclusion

The prevalence of hyperuricaemia and other cardiometabolic risks was high among type 2 diabetes patients. The female diabetics had more adverse CVD risk profile than the male diabetics. Waist circumference and BMI increased with increasing diabetes duration, but not after 20 years, whereas FBS decreased with increasing diabetes duration.

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