Factors Associated with Hyperuricaemia in a Tertiary Care Center in Ghana

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Abstract

Background

Hyperuricemia is known to be an independent risk factor for cardiovascular disease. The condition has been poorly researched in Sub-Saharan Africa and Ghana in particular.The aim of this study was to investigate the distribution of hyperuricaemia among metabolic conditions in a tertiary care center in Ghanaand the association of serum uric acid (SUA) with known demographic, anthropometric, and cardiovascular risk factors.

Methods

We designed a cross-sectional descriptive study comprising 372 subjects aged 20 years and above. Demographic and social data were obtained using a questionnaire. Anthropometric (height, weight, waist circumference) and blood pressure measurements were taken. Ten millilitres of venous blood samples were taken for SUA and other biochemistry investigations. Hyperuricaemia was defined as SUA ≥ 0.36 mmol/L in females and ≥ 0.42 mmol/L for males.

Results

One hundred and forty five men and 227 women participated in the study. The mean (SD) SUA level was 367.8 (110.2) µmol/L for men and 312.1 (108.8) µmol/L for women. The overall prevalence of hyperuricaemia *was 29.8% (Males 30.3% vs. Females 29.5%, p = 0.87) .Measures of obesity, hypertension and diabetes were significant predictors of uric acid levels in univariate analyses. In multivariate linear regression analysis, after adjusting for age and sex, uric acid level was still associated with BMI (r=4.92, p<0.001) and SBP (r=0.89, p<0.01).*

Conclusions

Obesity, diabetes mellitus and hypertension were all significant predictors of hyperuricaemia. These observations call for subsequent studies into the clinical importance of treating hyperuricaemia among patients with cardiovascular complications.

Background

There are reports that urate levels correlate with many recognized cardiovascular risk factors. In the past, the destructive and pro-inflammatory role of insoluble deposited urate crystals has attracted more clinical attention than hyperuricemia per se, but new evidence is accumulating that rising levels of soluble urate in body fluids may also lead to kidney disease, hypertension and cardiovascular disease[1].It is not immediately clear whether hyperuricemiaun complicated by gout or kidney stones is incidental or a clinically relevant finding. However, recent reports have given indication of a possible link between serum uric acid(SUA) and cardiovascular disease, as hyperuricemia was associated with increased mortality and my ocardial infarction in individuals with renal failure, even after adjustment for renal function and risk factors for metabolic syndrome[2, 3].

Several large epidemiologic studies published in the past have found that serum urate level predictsthe later development of hypertension [4-7]. The Normative Aging Study[7], showed that the serum urate level independently predicts the development of hypertension when using age-adjusted and multivariate models that include body mass, waist and hip indices, alcohol use, serum lipid levels, plasma glucose level, and smoking status. Animal studies have demonstrated that elevated SUA concentration increases blood pressure without affecting the morphology of the kidney[8], and that lowering uric acid can normalize blood pressure[9]. In addition to the association between SUA and hypertension, many authors have confirmed the correlation between SUA and development of type 2 diabetes [10]. There sults showed that every 59.5 μmol/L increase in SUA results in a 60% increase in risk for developin g diabetes [11].Large epidemiological studies have shown that SUA is often high in individuals with metabolic syndrome and that its prevalence increases according to SUA levels[12, 13]. Similar to many other developing countries, Ghana is facing a growing incidence of obesity and cardiovascular disturbances[14, 15]. However, there is scarce data regarding SUA in Ghana and so far, there is a dearth of population studies on the association between hyperuricemia and other cardiovascular factors. Studies that reflect the general Ghanaian population with diverse ethnic groups, food intake and physical activity habits are desirable. Therefore, we sought to investigate the distribution of hyperuricaemia in a tertiary healthcare setting and the association of SUA with known demographic, anthropometric, and cardiovascular risk factors.

Patients, Materials and Methods

Study Design and Study setting

From April 2008 to January 2009, 424 patients who reported to the Directorate of Medicine and the Polyclinic Directorate of Komfo Anokye Teaching Hospital (KATH) in Kumasi were recruited into this study. All study participants were of Ghanaian origin, and gave informed consent in line with institutional requirements: participants gave formal consent by signing or thumb-printing an informed consent form after the study was thoroughly explained to them in private.All participants received treatment as outpatients. Refusal to give consent, age less than 20 years, clinical history of liver cirrhosis and inability to stand for weight and height measurement were the exclusion criteria. After applying exclusion criteria, 372 participants remained to take part in the study.

Anthropometrics

All participants completed an interviewer-administered questionnaire and underwent a physical examination. Hip and waist circumferences were measured to the nearest 0.5cm using a standard plastic measuring tape. Height was measured to the nearest 0.5cm and weight was measured to the nearest 0.1 kg using a standardized combined manual scale and Asimed MB 201T Plusstadiometer(Aparatos Y Sistemas De Medida, S. A.)After participants had removed their footwear.Hip circumference was measured at the outermost points of the greater trochanters.

Blood Pressure

After participants had been sitting undisturbed for at least five minutes, blood pressure (BP) and pulse rate were measured with an automatic BP machine (OMRON M7 sphygmomanometer; Omron Matsusaka Co. Ltd, Matsusaka City, Mie-Ken, Japan) using the appropriate size of cuff.Three readings were taken 1 minute apart but the mean of the last two readings was used in the data analysis having discarded the first reading.

Biochemical Investigations

Patients received the appropriate medical treatment for the various conditions for which they had presented at the clinic but had to report the following day after an overnight fast for biochemical investigations. Ten ml of venous blood was drawn from the antecubital vein of each participant for these investigations which were undertaken using a BT3000 auto analyser (Biotechnica Instruments S.P.A. Rome, Italy).

Definitions

Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or use of antihypertensive medication[16, 17]. Overall Obesity was Body Mass Index (BMI) ≥ 30 kg/m[18, 19]. Central Obesity or High Waist Hip Ratio (WHR) was considered to be WHR > 0.9 for males and > 0.8 for females[19].Waist circumference was defined as the average of 2 measurements taken at the midpoint between the lowest rib and the iliac crest after inspiration and expiration [20]. High Waist Circumference (WC)was considered as WC ≥ 94cm in men or ≥80cm in women. Diabetes mellitus was defined as fasting venous blood glucose ≥ 6.1 mmol/L (equivalent to plasma glucose ≥7.0 mmol/L) and or 2h post prandial capillary whole blood ≥ 11.1 mmol/L or being on drug or diet therapy for DM[21]. Hyperuricaemia was defined as SUA ≥ 0.36 mmol/L in females and ≥ 0.42 mmol/L for males[22].

Ethical Approval

The study was approved by the Committee on Human Research, Publication and Ethics, Kwame Nkrumah University of Science and Technology, School of Medical Sciences (KNUST-SMS) and Komfo Anokye Teaching Hospital (KATH), Kumasi. Study participants were adequately informed of the purpose, nature, procedures, risks and hazards of the study. Strict emphasis was placed on anonymity, confidentiality and the freedom to decline to participate at any time without penalty.

Statistical Analysis

The data analysis was carried out using Stata version 8.0 statistical packages and Microsoft Excel 2007. The mean and standard deviation were calculated for continuous variables, and were compared using the Student t-test. Percentages were calculated for discrete variables and these were compared using Pearson Chi-square test. Univariate and multivariate analysis were carried out with uric acid as the outcome variable. P-values of less than 0.05 were considered statistically significant.

Results

Out of the 424 subjects recruited to participate in the study, 372 (145 males and 227 females) met all requisite criteria and were included in this study. The mean (SD) age of participants was 49.9 (13.8) years. There was no significant age difference between males and females. Table 1 shows the characteristics of the study population stratified by gender. The females had significantly higher mean BMI, WC and HC than the males. Mean weight, WHR, SBP, DBP and FBG were similar in the two sexes. The mean (SD) SUA level was 367.8 (110.2) μmol/L for men and 312.1 (108.8) μmol/L for women.

The clinical characteristics of study participants stratified by gender are shown in Table 2. Overall, the prevalence of hyperuricaemia was approximately 30%. The prevalence of exclusive diabetes mellitus and hypertension in the present study were 23.1% and 22.3% respectively. Thirty seven percent of the population were suffering from both diabetes and hypertension. Table 3 shows the characteristics of the study population stratified by uric acid status. Participants with hyperuricaemia had significantly higher mean age, weight, BMI, WHR, WC, HC, and blood pressure (both SBP and DBP).

The distribution of hyperuricaemia among study participants according to various clinical characteristics is shown in Table 4. The prevalence of high WHR and high WC were significantly higher in participants with hyperuricaemia. Even though the prevalence of BMI≥30 was higher in those with than those without hyperuricaemia, this was not statistically significant. In participants with neither DM nor HPT and those with only DM, the proportion with hyperuricaemia was significantly lower compared to those with normal uric acid levels. The proportions were similar in those with only HPT while in participants with both DM and HPT the proportion with hyperuricaemialevels were twice the proportion with normal levels. However when all the participants with DM were considered, the proportion with hyperuricaemia was significantly higher compared to those with normal uric acid levels and a similar result was obtained with all the HPT participants combined (Table 4).

The prevalence of hyperuricaemia in various age groups for males and females is shown in Figures1 and 2. Generally the prevalence rates rises with increasing age groups however the prevalence in the 50 - <60 years was higher than that of the ≥60 years age group in the females, while the prevalence for the 40 - <50 years was lower than the <40 years age group in the males. The association between the age group and hyperuricaemia was also not statistically significant in males (p=0.18), in females (p=0.28) and when the sexes were combined (p=0.06).Figure 3 shows the scatter plot SUA levels against age in men and women. In both sexes SUA levels rises with age. However on applying formal statistical test this relationship was not statistically significant in either sexes or when the data was combined (Male p=0.14, Female p=0.19, both p=0.09). The univariate linear regression analysis results with uric acid as the outcome variable is shown in Table 5. All the variables were significantly associated with uric acid except age and hip circumference which were not up to statistical significance. In multivariate linear regression analysis, after adjusting for age and sex, uric acid was still associated with BMI (r=4.92, p<0.001) and SBP (r=0.89, p<0.01).

Table 6 is the results of univariate logistic regression analysis with hyperuricaemia as the outcome variable. Apart from gender and BMI which were not significantly associated with hyperuricaemia, age, WHR, WC, DM and HPT were significantly associated with hyperuricaemia. When age and sex were adjusted for in multivariate logistic regression analysis, hyperuricaemia remained associated with high WHR (OR=2.15, p=0.02), DM (OR= 1.97, p<0.01) and HPT (OR=3.04, p<0.001).

Discussion

The prevalence of hyperuricemia we report in this group from the Ashanti Region of Ghana is high compared to another report from Sub-saharan Africa[23]and from other world regions[24-27]. This is variance may be attributable to differences in study populations. Significant relationships were observed between serum uric and cardio-metabolic risk factors in univariate analysis. This relationship was significantly strong for systolic hypertension and obesity as indicated by the waist-to-hip ratio (but not BMI) suggesting a close link between serum uric acid and central obesity.

The effect of gender on uric acid levels seen in the present study has been extensively reported[28, 29]. Here, mean serum uric acid level was higher in men than in women, and was remarkably increased in women aged over 50 years. Although mean serum uric acid was significantly higher in men, there are different reference intervals for interpreting uric acid levels in men and women. Consequently, although there seems to be a significant statistical difference, it is not a clinically significant one. Nevertheless, sex differences of serum uric acid levels and the subsequent piquing of uric acid in post-menopausal females have been reported previously and attributed to the influence of sexual hormones and other lifestyle habits such as alcohol consumption [30].

The present study observed significant correlations between serum uric acid and several cardiovascular disease risk factors, such as a higher BMI, waist-to-hip-ratio, and isolated systolic hypertension. Conen et al., [31] point out that a number of plausible theories have been advanced to explain the path physiological basis of these associations between serum uric acid and components of the metabolic syndrome such as insulin resistance [32], the use of diuretics [33]and impaired renal function accompanying hypertension [31, 34]. Hyperuricaemia secondary to peripheral insulin resistance suggests that the kidney may be the potential link between hyperinsulinaemia and the development of hyperuricemia and eventually hypertension [31]. Insulinresistant individuals adapt to their physiological challenge by secreting greater than normal quantities of the hormone in order to maintain an adequate glucose metabolism. The resulting hyper-insulin state compels the kidneys to decrease uric acid clearance, probably via insulin-induced urinary sodium retention [35]. Insulin resistance may increase blood pressure directly via enhanced proximal tubular sodium reabsorption [36], or indirectly by the sympatho-adrenal system [37]. The persistent association of serum uric acid and systolic blood pressure has led some to believe that uric acid may be a prognostic marker in elderly patients with isolated systolic hypertension[38, 39].

Obesity is no longer a problem of the developed world but an epidemic in developing nations as well[40]. The 22% prevalence of BMI≥30 found in this study compares with the finding of 21.2% in a cross-sectional study in south-western Nigeria [41]. Kadiri *et. al.*,found obesity in 21% and 28% of males and females respectively in a study of 146 middle-aged Nigerians [42].There have been previous reports on the association between obesity and hyperuricaemia in the sub-Region. A cross-sectional study of 300 healthy adults conducted in an urban city in northern Nigeria found that in univariate analysis, the odds of obesity were higher in women and in the presence of hypertension, and hyperuricaemia. In fact in multivariate analysis, hyperuricaemia remained a significant independent factor of obesity in this population as well (OR 2.906, 95% CI 1.444-5.847, p = 0.003)[43]. Leptin, an adipokine,is thought to be the underlying factor mediating the relationship between body mass index and hyperuricemia[44]. In fact higher adiposity and weight gain are strong risk factors for gout, whereas weight loss is protective [45-47]. Dyslipidemia may induce hyperuricemia through its negative effect on renal function[48].In a study of the relation of serum uric acid with cardiovascular risk factors in a developing country, Conen *et. al.*, [31] found that serum uric acid was strongly related to serum triglycerides in both men and women. It is worth noting that the correlation of triglycerides with uric acid has been found previously in several groups of patients[32, 49, 50] and gives further support to the relationship between elevated uric acid in the obese. It is believed that both hyperuricemia and hypertriglyceridemia reflects the life style of the obese patient, as part of the metabolic syndrome.

Based on the preponderance of recent epidemiologic studies, it appears that an elevated serum urate level is an independent risk factor for kidney disease, hypertension, and cardiovascular disease. The precise underlying mechanisms remain unclear; and there is a need for sufficiently large studies to convincingly demonstrate the risk of these potentially severe complications of hyperuricemia. Again, the treatment of hyperuricemia is currently not indicated in patients with hypertension, kidney disease, or heart disease except in the treatment of gout and of uric acid kidney stones.

Considering the growing incidence of cardiovascular risk factors such as obesity in Ghana and the potential link between hyperuricemia and cardiovascular complications, we are of the opinion that attention should be given to the evolving prevalence of hyperuricemia as well.

Limitations:

A number of limitations should be borne in mind when interpreting the results of this study. First, this was a cross-sectional study and therefore a causal relationship between clinical parameters and risk of hyperuricemia cannot be established. When used as mono therapy or with a start in, niacin increases Gout or uric acid levels[51]. Given the unique nature of the study population, it is quite probable that some patients could be exposed to niacin. However, niacin status of study participants was not evaluated. Other clinical aspects that could be evaluated include, participants' kidney function, alcoholism and micronutrient status, exposure to thiazide diuretics, high purine diet and presence of gout all of which have been known to affect serum uric acid levels[52-54].

Conclusions

In summary, our results show that hyperuricemia may not be a rare condition in the Kumasi Metropolis of Ghana and in similar urban settings. In fact strong relations of hyperuricemia to central obesity, diabetes mellitus and hypertension and other conditions of increasing importance in low middle income countries (LMIC) imply that the clinical significance of hyperuricaemia could have been underrated in the past. Considering the increasing prevalence of non-communicable diseases such as cardiovascular disease in Ghana, the potential impact of hyperuricemia deserves closer attention especially in the management of obesity, diabetics and hypertensives.

Competing interests

All the authors declare that in the past years none of us has been a beneficiary of fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future. We do not hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future. Further, we are not currently applying for or bearing any patents relating to the content of the manuscript? And we have neither received, fee reimbursements, funding, nor salary from any organization that holds or has applied for patents relating to the content of the manuscript. In addition, we hold no political, personal, religious, ideological, academic, intellectual, commercial or any such non-financial competing interests to declare in relation to this manuscript.

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Tables

Table 1: Characteristics of the study population stratified by gender

Parameter (units)	**Total**	**Male**	**Female**	**P**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**t test**
Number (%)	372	145 (39.0)	227 (61.0)	
Age (years)	49.9 (13.8)	49.0 (14.6)	50.4 (13.3)	0.33
Weight (kg)	68.8 (14.6)	68.7 (11.4)	68.9 (16.4)	0.85
Height (m)	1.62 (0.08)	1.68 (0.06)	1.58 (0.06)	**<0.0001**
BMI (kg/m^2)	26.3 (5.5)	24.3 (3.6)	27.5 (6.1)	**<0.0001**
WHR	0.90 (0.10)	0.90 (0.07)	0.90 (0.11)	0.98
WC(cm)	89.3 (12.6)	86.4 (10.5)	91.1 (13.5)	**<0.001**
HC(cm)	99.2 (11.1)	95.7 (7.2)	101.4 (12.5)	**<0.0001**
SBP (mmHg)	133.6 (22.9)	135.6 (24.1)	132.3 (22.1)	0.18
DBP (mmHg)	84.5 (12.2)	84.5 (12.5)	84.4 (12.1)	0.93
SUA (μmol/L)	333.8 (80.8)	367.8 (110.2)	312.1 (108.8)	**<0.0001**
FBG (mmol/L)	8.2 (4.4)	8.1 (4.6)	8.3 (4.3)	0.59

BMI: body mass index; WHR: waist-to-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; WC: waist circumference, HC: hip circumference; SUA: serum uric acid.

Table 2: Clinical characteristics of study participants stratified by gender

Parameter (units)	**Total**	**Male**	**Female**	**p**
	N (%)	**N (%)**	**N (%)**	**$\chi 2$ test**
Only DM (%)	86 (23.1)	27 (18.6)	59 (26.0)	0.10
Only HPT (%)	83 (22.3)	34 (23.5)	49 (21.6)	0.67
DM-HPT (%)	137 (36.8)	58 (40.0)	79 (34.8)	0.31
No DM-No HPT (%)	66 (17.7)	26 (17.9)	40 (17.6)	0.94
All DM (%)	223 (60.0)	85 (58.6)	138 (60.8)	0.68
All HPT (%)	220 (59.1)	92 (63.5)	128 (59.4)	0.18
Hyperuricaemia (%)	111 (29.8)	44 (30.3)	67 (29.5)	0.87
BMI≥30 (%)	82 (22.0)	7 (4.8)	75 (33.0)	**<0.001**
High WHR (%)	275 (73.9)	74 (51.0)	201 (88.6)	**<0.001**
High WC(%)	215 (57.8)	38 (26.1)	177 (78.0)	**<0.001**

DM: diabetes mellitus; HPT: hypertension; BMI: body mass index; WHR: waist-to-hip ratio; WC: waist circumference.

Table 3: Characteristics of participants stratified by uric acid status

	Total	Normal	Hyperuricaemia	p
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**t test**
Number (%)	372	261 (70.2)	111 (29.8)	
Age (years)	49.9 (13.8)	48.6 (13.6)	52.8 (13.9)	**<0.01**
Weight (kg)	68.8 (14.6)	67.2 (14.0)	72.6 (15.2)	**<0.01**
BMI (kg/m^2)	26.3 (5.5)	25.6 (5.1)	27.8 (6.0)	**<0.001**
WHR	0.90 (0.10)	0.89 (0.07)	0.93 (0.13)	**<0.001**
WC (cm)	89.3 (12.6)	87.6 (12.0)	93.3 (13.1)	**<0.001**
HP (cm)	99.2 (11.1)	98.5 (10.3)	100.9 (12.6)	0.06
SBP (mmHg)	133.6 (22.9)	130.6 (22.1)	140.6 (23.2)	**<0.001**
DBP (mmHg)	84.5 (12.2)	83.3 (11.9)	87.2 (12.7)	**<0.01**
FBG (mmol/L)	8.2 (4.4)	8.4 (4.7)	7.9 (3.8)	0.31
Uric Acid (μmol/L)	333.8 (80.8)	278.9 (71.8)	462.9 (80.8)	<0.0001

BMI: body mass index; WHR: waist-to-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; WC: waist circumference, HC: hip circumference.

Table 4: Distribution of hyperuricaemia among study participants according to various clinical characteristics

	Total	Normal	Hyperuricaemia	p
	N (%)	**Mean (SD)**	**Mean (SD)**	**χ2 test**
Females (%)	227 (61.0)	160 (61.3)	67 (60.4)	0.87
Only DM (%)	86 (23.1)	70 (26.8)	16 (14.4)	<0.01
Only HPT (%)	83 (22.3)	60 (23.0)	23 (20.7)	0.63
DM-HPT (%)	137 (36.8)	74 (28.4)	63 (56.8)	<0.00001
No DM-No HPT (%)	66 (17.7)	57 (21.8)	9 (8.1)	<0.01
All DM (%)	223 (60.0)	144 (55.2)	79 (71.2)	<0.01
All HPT (%)	220 (59.1)	134 (51.3)	86 (77.5)	<0.001
BMI≥30 (%)	82 (22.0)	51 (19.5)	31 (27.9)	0.07
High WHR (%)	275 (73.9)	182 (69.7)	93 (83.8)	<0.01
High WC (%)	215 (57.8)	142 (54.4)	73 (65.8)	0.04

DM: diabetes mellitus; HPT: hypertension; BMI: body mass index; WHR: waist-to-hip ratio; WC: waist circumference

Table 5: Univariate linear regression analysis with uric acid as the outcome variable

	R	CI	P
Gender	-55.76	-78.61 – 32.91	**<0.001**
Age	0.71	-0.12 – 1.54	0.09
Weight	1.67	0.91 – 2.44	**<0.001**
Height	235.63	84.88 – 386.37	**<0.01**
BMI	1.29	1.22 – 5.36	**<0.01**
WHR	217.13	98.67 – 335.58	**<0.001**
WC	1.71	0.82 – 2.61	**<0.001**
HC	0.93	-0.11 – 1.96	0.08
SBP	1.08	0.59 – 1.57	**<0.001**
DBP	1.52	0.60 – 2.45	**<0.01**
FBG	-3.03	-5.61 – -0.45	**0.02**

BMI: body mass index; WHR: waist-to-hip ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; FPG: fasting plasma glucose; WC: waist circumference, HC: hip circumference.

Table 6: Univariate logistic regression analysis with high uric acid as the outcome variable

	OR	CI	P
Gender	0.96	0.61 – 1.51	0.87
Age	1.02	1.01 – 1.04	**<0.01**
BMI≥30	1.60	0.95 – 2.67	0.08
High WHR	2.24	1.27 – 3.96	**<0.01**
High WC	1.61	1.01 – 2.55	**0.04**
DM	2.01	1.24 – 3.23	**<0.01**
HPT	3.26	1.96 – 5.41	**<0.001**

BMI: body mass index; WHR: waist-to-hip ratio; WC: waist circumference; DM: diabetes mellitus; HPT: hypertension;

Figures

Figure 1: Prevalence of Hyperuricaemia by age group in Females

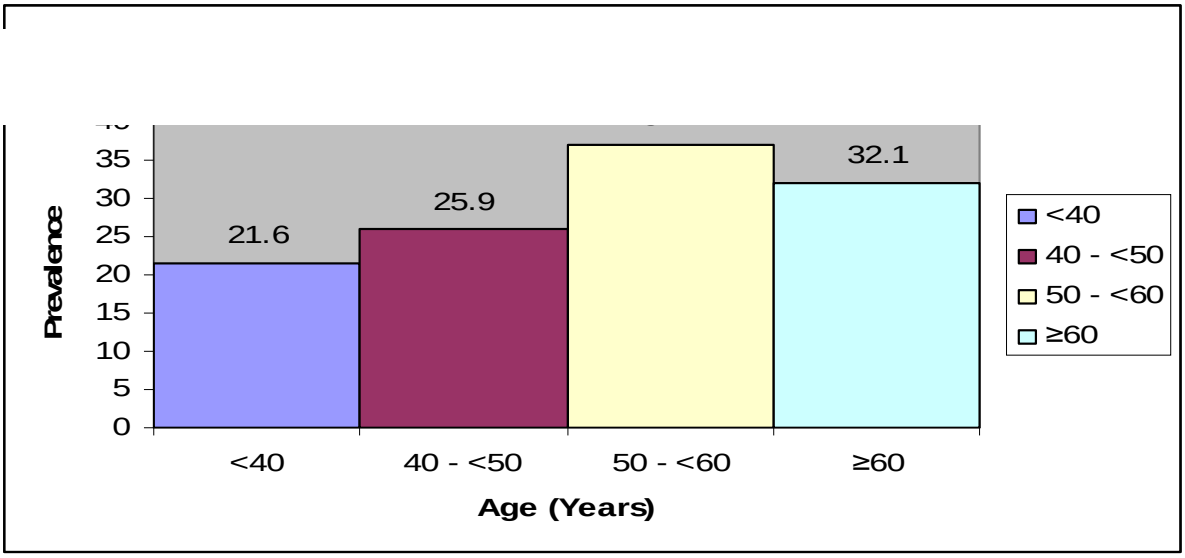

Figure 2: Prevalence of Hyperuricaemia by age group in Males

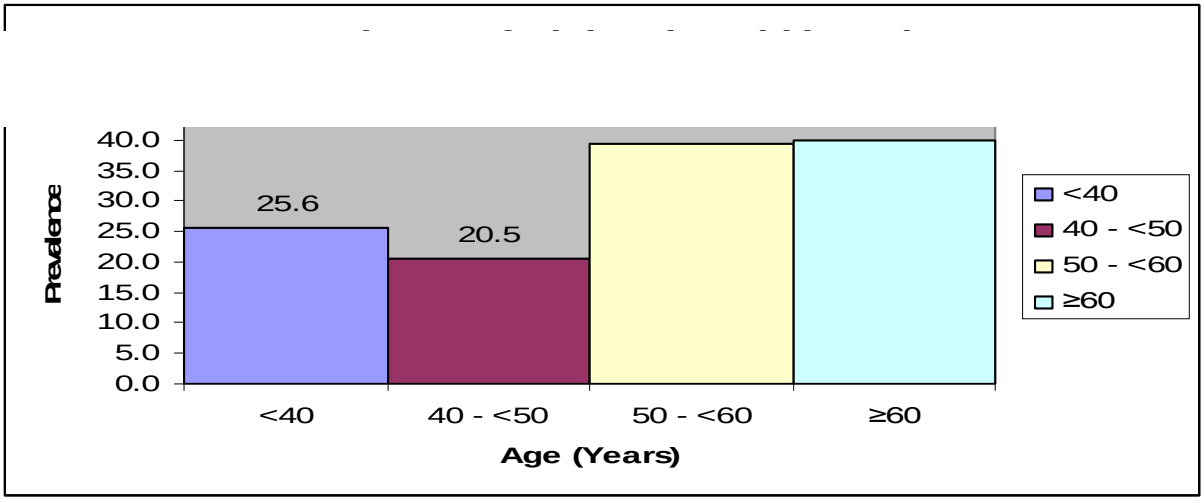

Figure 3: Scatter plot of serum uric acid levels against age by gender