JMSCR Volume||2||Issue||6||Page 1261-1269 ||June 2014 2014

www.jmscr.igmpublication.org Impact Factor 1.1147
ISSN (e)-2347-176x

IGM Publication Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Association of Hyperuricemia and Dyslipidemia-A Potent Cardiovascular Risk Factor

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Absract
Hyperuricemia is becoming a universal risk factor for CVD complications as it is associated with dyslipidaemia, obesity, hypertension and metabolic syndrome. India is a country with variations of culture, life style, food habits and epidemiological report on CVD risk factor may alter in different geographical areas. Hence the present study was on Kodavas, a minority community mainly living in Coorg district of Karnataka. They are now distributed to other places in India and abroad. Ethnic Kodavas have high prevalence of CVD risk factors as they consume diet rich in fat, meat along with alcohol. The investigation was carried out on kodavas living in Mysore Karnataka. Out of 418 subjects enrolled in the study, 28.94% of subjects suffered from hyperuricemia condition and men were affected more than women. High LDL and Hypertriglyceridemia were more prevalent in hyperuricemics. The subjects with both dyslipidemia and hyperuricemia had significant increased levels of novel CVD markers like Lp(a),homocysteine, ApoB and ApoB/ApoA1 ratio(P Keywords: ApoA1, ApoB, Dyslipidemia, Homocysteine, Hyperuricemia, Lp(a)

1.INTRODUCTION

Hyperuricemia is defined as the excessive uric acid production in the body which leads to gout. But in recent times, hyperuricemia has attained prime position and is becoming a important cause for metabolic diseases and CVD[1]. Its prevalence is increasing not only in developed countries but

also in developing countries [2]. There are reports on hyperuricemia condition that it is associated with metabolic syndrome such as obesity, dyslipidemia and hypertension [3]. Lipid disorders especially hypertriglyceridemia have always been linked with hyperuricemia [4]. Hyperuricemia has been extensively studied and their relationship with gout is well known, studies have shown that elevated serum uric acid is also related to cardiovascular diseases [5]. Hyperuricemia is caused by the improper excretion or excess production of uric acid. Over production may be caused due to genetic defect such as Lesch nyan syndrome and health conditions such multiple myeloma, where there is high production of cellular nucleotides. Further consumption of alcohol, smoking and diet rich in red meat, organ meat (liver and spleen) promotes the hyperuricemia condition. Our present study is on Kodava community who are mainly living in Kodagu district, Karnataka. They are mostly agriculturist but now many have migrated to urban areas for education and job prospects. The kodavas life style and food habits differ from other South Indians and most of them consume a diet rich in pork meat along with alcohol [6]. Therefore the sedentary lifestyle seen in urban population makes them prone to hyperuricemia coupled with dyslipidemia which becomes a main CVD risk factor. There are several studies related to metabolic syndrome and hyperuricemia but very few studies are done to find the effect of hyperuricemia in combination with dyslipidemia on non traditional CVD markers.

The rationale of the study is to examine the prevalence of hyperuricemia in this community and its association with dyslipidemia and patterns of mixed dyslipidemia. Further to ensure whether the association of hyperuricemia and dyslipidemia, increases the CVD risk

2. METHODOLOGY

2.1. Study Design

The study was conducted in Mysore during June 2012 to February 2013 Around 418 Kodava subjects from 25 to 85 age groups participated in the study program Campaigning was done with the help of area associations and Kodava Samaj, Mysore. The subjects were from urban area and educated. Informed consent form was signed by all participants. A standardised questionnaire related to their medical history especially regarding hyperuricemia, diet, medications, alcohol consumption, smoking status and physical activities were noted down. The study was approved by Institutional Ethical Committee (IOE), Anthropological Survey of India, Kolkata.

2.2. Anthropometric data

Body weight, height, waist and hip circumference were measured. Height was measured using Holtain Anthropometric scale and weight was checked using weighing scale with or without shoes. Waist circumference was measured using a flexible inextensible tape placed horizontally at the midpoint between the lowest rib and the iliac crest The hip circumference (HC) at the widest circumference over the major trochanters with the subject standing erect and waist hip ratio was calculated using these measurements. Body fat percentage, Body Mass Index (BMI), was measured using Omron fat monitor with the subject standing erect without shoes. Blood pressure was measured using mercury Sphygmomanometer in sitting position.

2.3. Laboratory analysis

After 10-2h of overnight fast, the venous blood was drawn from the subjects and was collected in EDTA vacutainers. The plasma was separated by centrifugation and tested for Uric acid using liquid stable reagent kit by Randox which is based on uricase PAP method on trinder's reaction. The

fasting glucose, HDL, LDL, Triglyceride and total Cholesterol were measured using Transasia kit using fully automated biochemical analyser EM360. The CVD markers like CRP, ApoA1, ApoB and Lp(a) were measured using Randox kits by immunoturbidometry method in biochemical analyser EM360 Transasia. Homocysteine was measured using homocysteine kit in Immulite 1000 using antigen antibody reaction.

2.4. Defining variables

For serum lipids, we referred to National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) guidelines. According to these standard guidelines, hypercholesterolemia is defined as TC>200mg/dl, Hypertriglyceridemia as TG>150mg/dl, high LDL-C as >100mg/dl and low HDL-C as <40mg/dl for women and <35mg/dl for men[7]. For uric acid,in men >7mg/dl and in females >6mg/dl were considered hyperuricemic[8]. For Lp(a)(>30mg/dl), ApoB (>139mg/dl for men and >130mg/dl for women) ApoA1 (<106mg/dl), ApoB/ApoA1 (<0.8mg/dl), Homocysteine (>15mg/dl), CRP(>1mg/dl) we referred to kit ranges.

2.5. Statistical Analysis

The data were arranged and checked twice before entering into the excel spread sheet. The statistical analysis was done using SPSS 19, The variables were expressed as mean and stanadard deviation. Their means were compared using independent T test. Comparison of quantitative data was done using chi square test. P value <0.05 was considered significant.

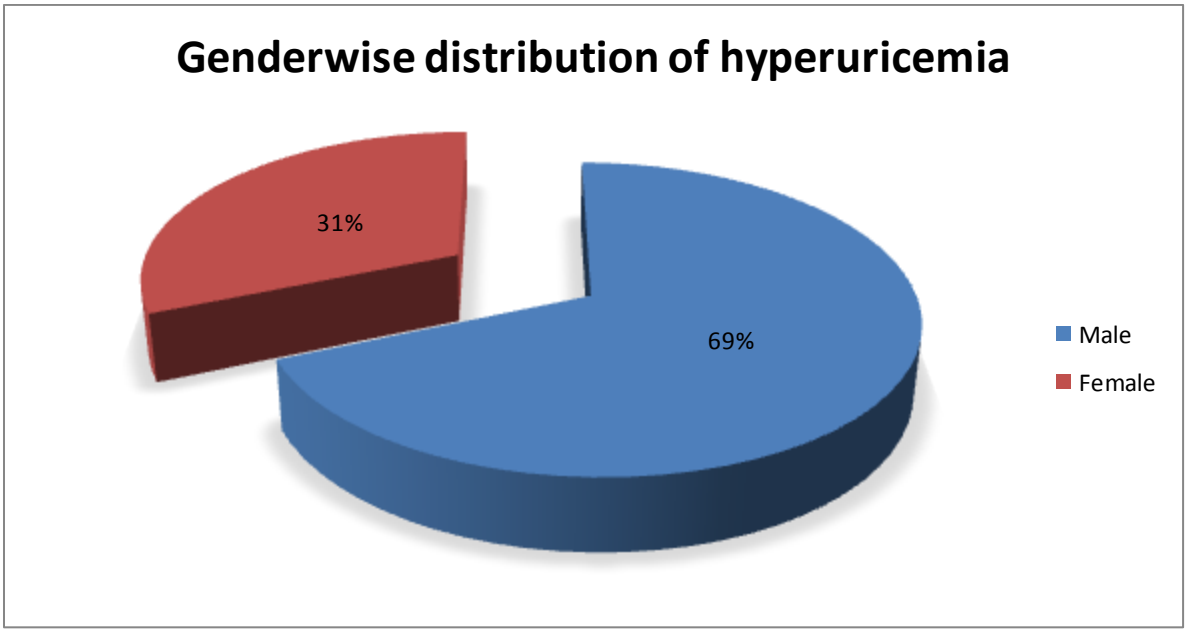

Figure 1: Gender wise Distribution of hyperuricemia among Kodavas

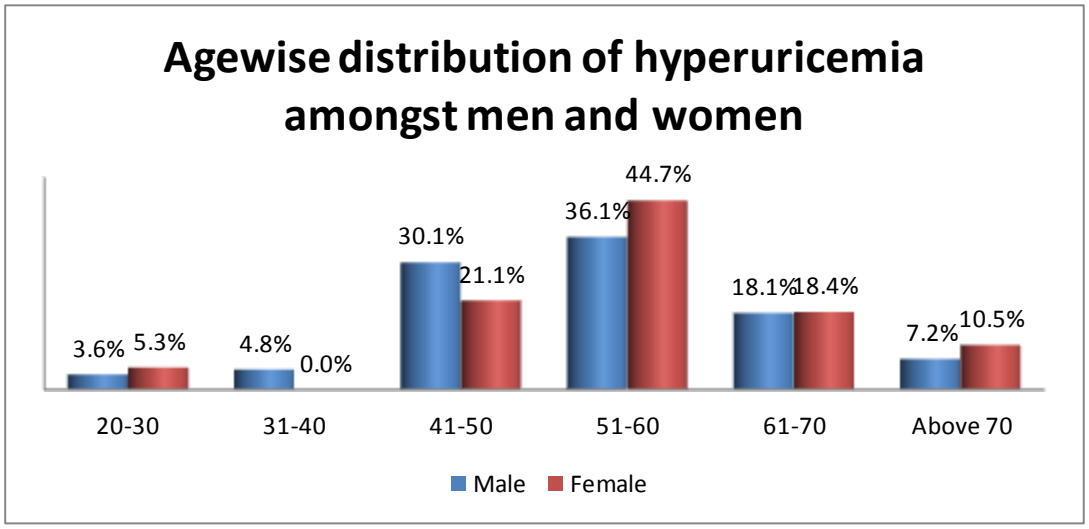

Figure 2: Age wise distribution of hyperuricemia

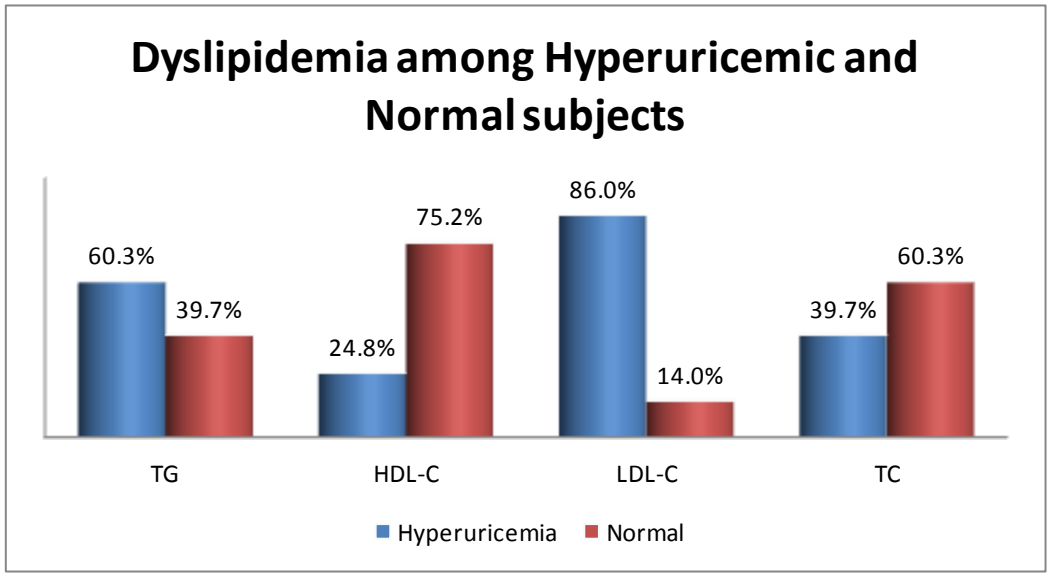

Figure 3: Dyslipidemia amongst hyperuricemics and normal subjects

P value by chi square analysis:0.00, 0.033, 0.021, 0.010 respectively

Table 1: Characteristics of hyperuricemics and normal Kodava subjects

	Hyperuricemics	Normal Subjects	P Value
Age	54.68±10.97	53.10±11.40	0.197
Sex Male Female	 83 38	 111 186	 0.000 0.000
BMI	26.67±3.47	25.83±3.71	0.033
Body fat%	31.36±6.49	33.11±6.43	0.012
Waist circumference	94.07±8.16	87.81±10.65	0.000
WHR	0.94±0.06	0.88±0.10	0.000
LDL	132.43±30.89	120.81±29.32	0.000
HDL	43.91±10.67	47.11±11.32	0.008
Triglyceride	214.04±83.22	144.71±52.67	0.000
Total Cholesterol	187.70±41.06	177.48±38.38	0.016
Fasting Plasma glucose	116.48±46.44	112.85±50.44	0.495
SBP	136±16	132±22	0.123
DBP	88±10	84±10	0.000
Alcohol intake	79	122	0.000
Smoking status	19	20	0.000

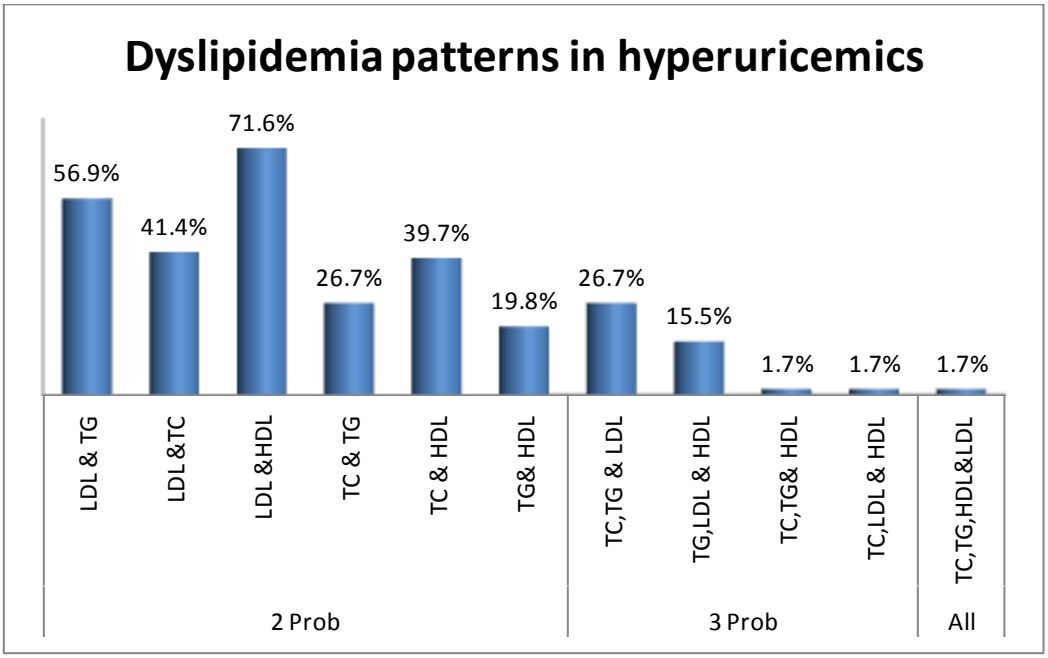

Figure 4: Patterns of dyslipidemia in hyperuricemia

Table 2: Comparison of mean lipid values and CVD markers in subjects with both hyperuricemia and dyslipidemia and one of the problem

CVD markers	Both hyperuricemia & dyslipidemia	Either hyperuricemia or dyslipidemia	P value
CRPmg/dl	1.71	1.87	0.318
Lp(a) mg/dl	47.05	40.11	0.013*
ApoB mg/dl	102.22	95.19	0.064*
ApoA1 mg/dl	129.90	135.97	0.142
ApoB/ApoA1ratio	0.78	0.63	0.000*
Homocysteine	16.46	14.50	0.05*

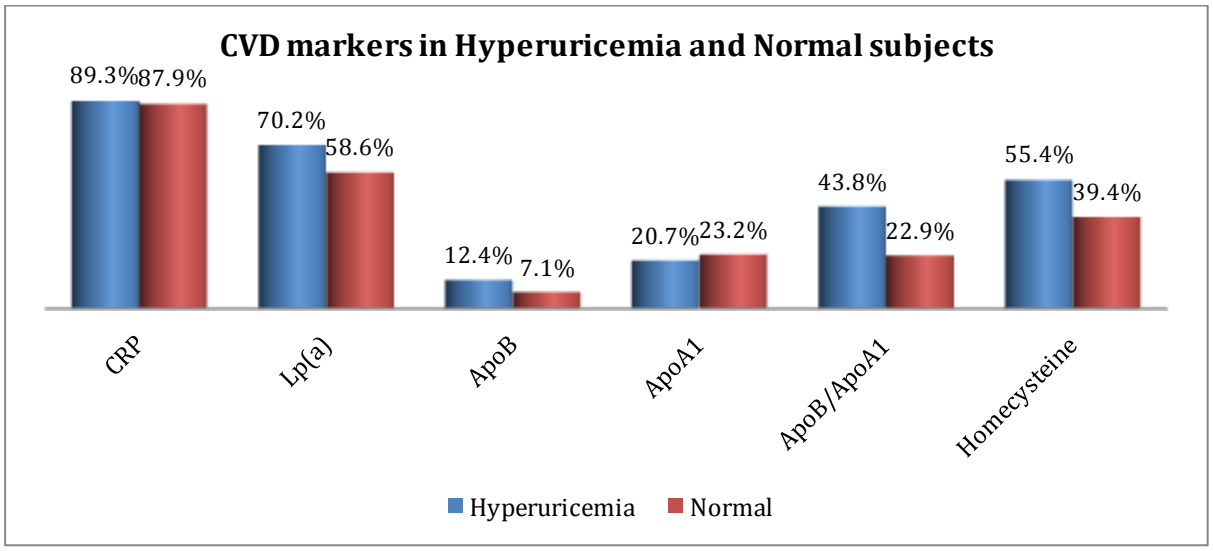

Figure 5: Comparison of CVD Markers in hyperuricemics and normal subjects

P value by chi square analysis is 0.741, 0.027*, 0.086, 0.607, 0.000*,0.003* respectively.

RESULTS

Figure 1 and Table 1 shows that the overall prevalence of hyperuricemia is 28.94% and was significantly high in men than women (34.53% in men and 16.51% in women, $p<0.05$). Among them 17(4%) subjects reported previous history of hyperuricemia in which 9 were still on drugs and others were not under any medication But 104 subjects (24.88%) were newly diagnosed with hyperuricemia and could be considered for therapeutic and dietary modifications. Figure 2 indicates that the highest prevalence of hyperuricemia in males and females was in 51-60 age groups. Out of 121 subjects, 116 had at least one or the other form of dyslipidemia and their prevalence was as seen in Figure 3, whereas hypertriglyceridemia and high LDL-C was the

most common symptom among hyperuricemics. However the patterns of dyslipidemia exhibited by hyperuricemics showed high LDL with low HDL followed by hypertriglyceridemia with high LDL as the recurrent problem (Figure 4). Table 2 shows subjects with combination of dyslipidemia and hyperuricemia had elevated levels of CVD markers especially Lp(a),homocysteine, ApoB and ApoB/ApoA1 ratio.

DISCUSSION

In the recent period there is renewed concern about hyperuricemia and its associated disorders like dyslipidemia, obesity, hypertension, diabetes, and CVD[9]. This study ascertains the relationship between hyperuricemia, dyslipidemia and CVD risk. Uric acid is the catabolic end product of purine nucleotides degradation and is usually caused due to the overproduction or under excretion and usually latter forms the leading cause. Diet rich in purines such as organ meat, red meat and excessive consumption of alcohol and low alcoholic drinks such as beer is one of the reasons for hyperuricemia condition, The Kodavas consume excess of meat and alcoholic drinks and hence our investigation was concentrated on this community This is the novel study done on an Indian community and only few information is available about hyperuricemia and related disorders in India.

The prevalence of hyperuricemia was in 28.94%,among the study population which is of serious concern and is higher than study done on Arabians[10] where only 23.9% were affected however it was almost similar to Japanese study (25.8%,)[11]. In the study population the prevalence of hyperuricemia almost doubled among men (34.53%) than women (16.51%) which is comparable to study done on Japanese-Brazilians where 46% of men and 26% of women had hyperuricemia[12] In another Indian study obesity associated with hyperuricemia also showed similar pattern of results wherein 50% of males were effected and only 21.7% of female suffered[13]. This effect may be due to influence of fat rich diet and sedentary lifestyle causing obesity; however genetic defects cannot be neglected. There were noteworthy differences in anthropometric measurements such as BMI, body fat%, waist circumference and waist hip ratio. Our results are comparable to previous reports on obesity which causes increase in uric acid production and reduces its excretion leading to accumulation in the body [14].

In our study hyperuricemia was the highest in 51-60 age group and both men and women, were equally effected which is similar to Nepalgunj study report as high incidence of hyperuricemia was seen in 50 age group and above [15].Dyslipidemia that is abnormality in the levels of one or the other type of lipids is frequently associated with hyperuricemia, In the present findings hypertriglyceridemia shows highest correlation with hyperuricemia Among the study population 60.3% subjects had hypertriglyceridemia and 86% had high LDL[16]. Previous studies have shown that hyperuricemics have abnormal lipid profile with high TG (44%) and no correlation was observed with lp(a) levels[17] In contrast in our findings there was significant difference in lp(a) values.(p=0.013)

Much studies are not undertaken to compare the CVD markers in hyperuricemics and normal subjects, In the present result there was a significant difference in Lp(a),homocysteine and ApoB/ApoA1 ratio probably correlating the CVD risk. Previous study on hypertensives showed 30% of hyperuricemics and and 19%normal subjects had high homocysteine levels These results are comparable to our report (55.4% in hyperuricemia and 39.4% in normal subjects)[18].There was no significant difference in the ApoB and ApoA1 levels and is comparble to report on apolipoproteins and hyperuricemic subjects[19].

Thus our study noticeably indicates that presence of both dyslipidemia and hyperuricemia doubles the CVD risk as there is escalation in the levels of CVD markers. Although uric acid is an antioxidant, in the presence of dyslipidemia and in atherosclerotic environment it acts as a prooxidant and brings about the oxidation of lipoproteins resulting in plaques[20].This shows that the association of hyperuricemia with lipid disorders is a deadly huddle for CVD.

CONCLUSION

Our study highlighted the high prevalence of hyperuricemia associated with dyslipedemia as one of the CVD risk factor in the kodavas. It is a life style disorder and Men are more susceptible than women. The lipid profile is abnormal in most of the subjects suggesting evaluation at regular intervals The non traditional CVD markers show a distinct difference between normal and hyperuricemic subjects Thus from our present study we conclude that dyslipidemia and hyperuricemia are risk factors for cardiovascular diseases and the association further increases the CVD risk by twofold. Thus it is of paramount importance that hyperuricemic patients must restrict their high fat diet and bring lifestyle modifications to avoid the wave of CVD risk in kodava population

ACKNOLEDEGEMENT

I would like to thank Anthropological Survey of India, Head office, Kolkata for funding the project and all my subjects for participating in the study.

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