

# **HYPERURICEMIA AND CORRELATES IN CORONARY HEART DISEASE**

Pages with reference to book, From 90 To 94

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## **Abstract**

Serum Uric Acid (SUA), cholesterol, Ponderal Index (PI) and smoking behaviour were studied in 27 patients with coronary heart disease (CHD) and 30 sex, physique and ethnic group matched controls. Mean SUA was significantly raised ( $P < 0.01$ ) in the coronary group. Mean serum cholesterol, although within normal range in both the groups, was higher in the coronary group than in controls ( $P < 0.05$ ). The difference of PI was also highly significant ( $P < 0.001$ ) indicating preponderance of obesity in the coronary group. No correlation, was found between SUA and either cholesterol or ponderal index. (JPMA 37 90, 1987).

## **INTRODUCTION**

The association between hyperuricemia and accelerated atherosclerotic arterial disease is well known 1-3 Many epidemiological studies have shown significantly raised SUA levels in CHD patients than in controls 4 1 0 Coronary Drug Project Group reported twice as higher a risk of early coronary mortality in hyperuricemic CHD patients as compared to normouricemias. Davis reported urate deposits on heart valves in rare cases of gout. Later, urate crystal induced endothelial injury was reported to initiate coronary artery thrombosis 2 Since then many studies have demonstrated platelet stimulation and activation of initial coagulation pathways by hyperuricemia both in-vivo and in vitro and reversal of these changes by lowering SUA with uricosuric agents 4 1 9 The object of the present study was to assess the status of SUA in coronary risk profile and to study its correlation with other risk factors as obesity and hypercholesterolemia in our population.

## **MATERIAL AND METHODS**

A total of 30 patients of CHD admitted during the year 1983-84 to the Department of Medicine, Unit IV of Allama Iqbal Medical College, Lahore could fulfil all criteria laid down below and qualified for the study. Thirty age, sex, physique and ethnic group matched controls were selected from the patients attendants or hospital employees. Data of three coronary patients on final analysis was found incomplete hence statistical analysis in coronary group was reduced to 27 patients only.

## **CRITERIA FOR SELECTION**

CHD patients with typical history and ECG changes and raised cardiac enzymes in cases of myocardial infarction were included in the study. Those with atypical history and the ones with non-specific ST-T changes, Left Bundle Branch Block or Left ventricular hypertrophy were excluded. Patients having any of the conditions known to be associated with hyperuricemia like myelo and lymphoproliferative disorders, malignancy, psoriasis, sarcoidosis, chronic renal failure, congestive cardiac failure or on drugs as diuretics, methyldopa, reserpine, low dose salicylates, ethambutol, pyrazinamide were excluded from the study.

$$PI = \frac{\text{Height in inches}}{\sqrt[3]{\text{Weight in lbs}}}$$

A questionnaire was given to each subject which also included items on educational and vocational achievements, smoking, alcoholism and high purine dietary fads etc. A complete history was taken and general and systemic examination done on each subject. Height was recorded in inches (without shoes) and weight in pounds (lbs). Ponderal Index was calculated for each subject, which is a quotient of height in inches to cube root of weight in lbs.

Related inversely to body physique, P1' is a measure of body build. A value approaching 10 reflects laterality of build or obesity while a figure approaching 14 indicates linearity of build or leanness<sup>4</sup>. Haemoglobin, urinalysis and total and differential white cell count were obtained in each subject. An X-Ray chest, P.A.view, was taken in all coronary patients for the evidence of cardiomegaly and wherever indicated in control group. A resting 12 lead ECG was recorded in each subject and whenever necessary 'Master's Double Step Stress Test' was administered. Sera of all the cases was immediately refrigerated for the determination of SUA, creatinine and cholesterol. Hemolysed sera were discarded. SUA was determined by uricase enzyme spectro -photometric method<sup>20</sup> and serum cholesterol by 'Abell Kendal Method'<sup>21</sup>. Fasting and 2 hours post prandial blood glucose was determined in all on capillary blood by Ferricyanide Method. All laboratory determinations except fasting blood glucose were done within a week of drawing blood.

Statistical analysis was done by student's 't' test and 2 tailed test of significance. Taking SUA, a dependent variable, its correlation with Serum Cholesterol and Ponderal Index was determined by calculating its correlation co-efficient vis-a-vis, the other 2 independent study variables.

## RESULTS

For statistical analysis subjects were divided into Coronary and control groups. Coronary group consisted of 19 males and 8 females (sex ratio 2.37:1) against 21 males and 9 females in the control group (sex ratio 2.33:1). Age  $\pm$  SD for all the study groups is summarized in table I.

**TABLE I**  
**Age and Sex in the two Groups.**

Study Group	n	Mean Age (in years)	SD	Simple Range (in years)
Coronary Males	19	50.89	11.68	34 – 75
Control Males	21	51.87	11.25	31 – 69
Coronary Females	8	52.50	5.97	35 – 70
Control Females	9	50.97	8.78	35 – 72

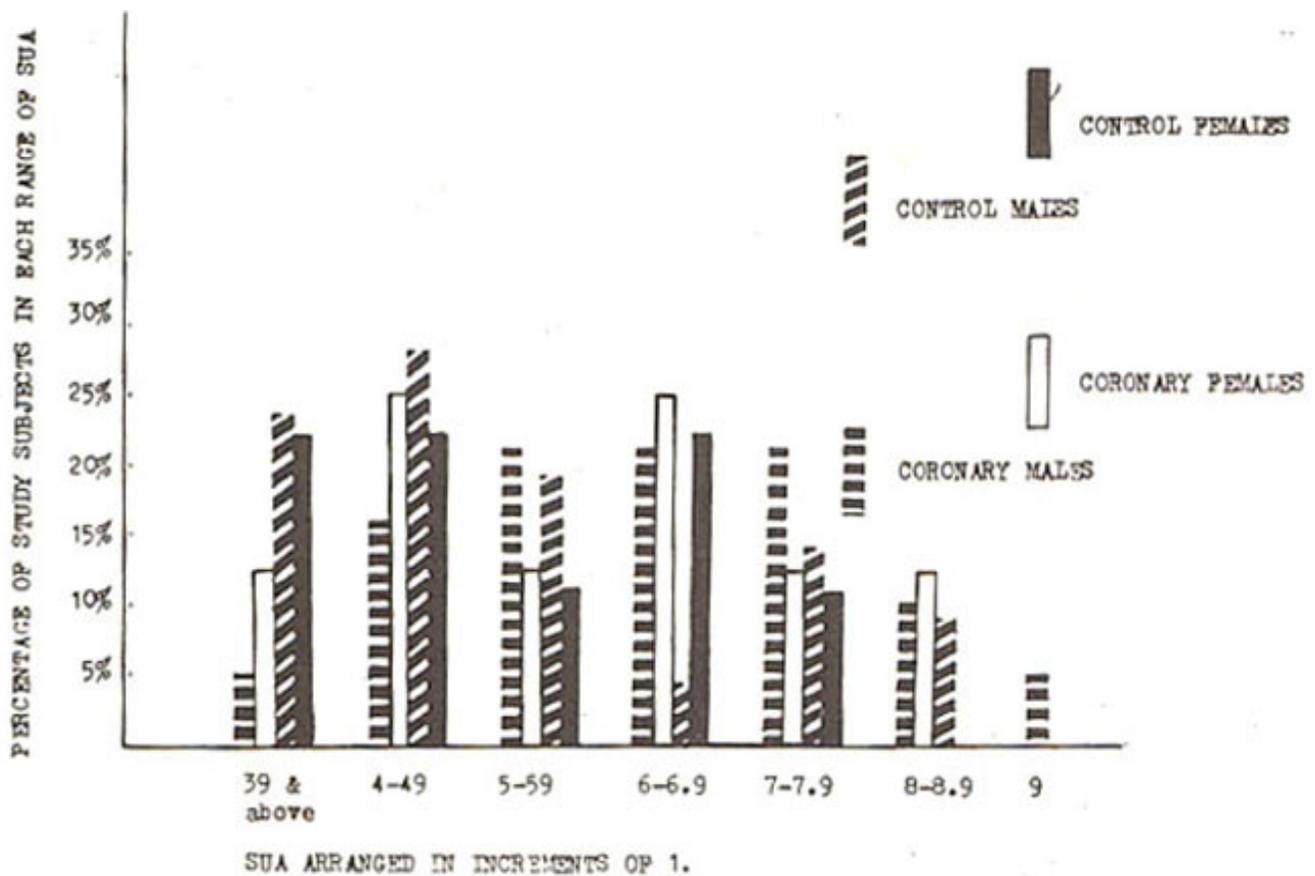
**TABLE II**  
**SUA, Ponderal Index and Cholesterol.**

Study Group	*S.U.A.		PONDERAL INDEX		CHOLESTEROL	
	Mean (mg / dl)	SD	Mean	SD	Mean (mg / dl)	SD
Coronary Males	7.40	2.61	12.53	0.67	215.00	42.02
Coronary Females	6.90	1.73	11.30	1.93	190.00	7.29
Coronary Group (M + F)**	7.15	2.43	11.91	1.18	202.00	37.08
Control Males	5.43	2.51	13.81	0.43	193.86	45.38
Control Females	4.89	1.78	11.99	0.89	179.91	21.04
Control Group (M + F)**	5.16	2.14	12.90	0.58	187.00	29.65

\* S.U.A = Serum Uric Acid

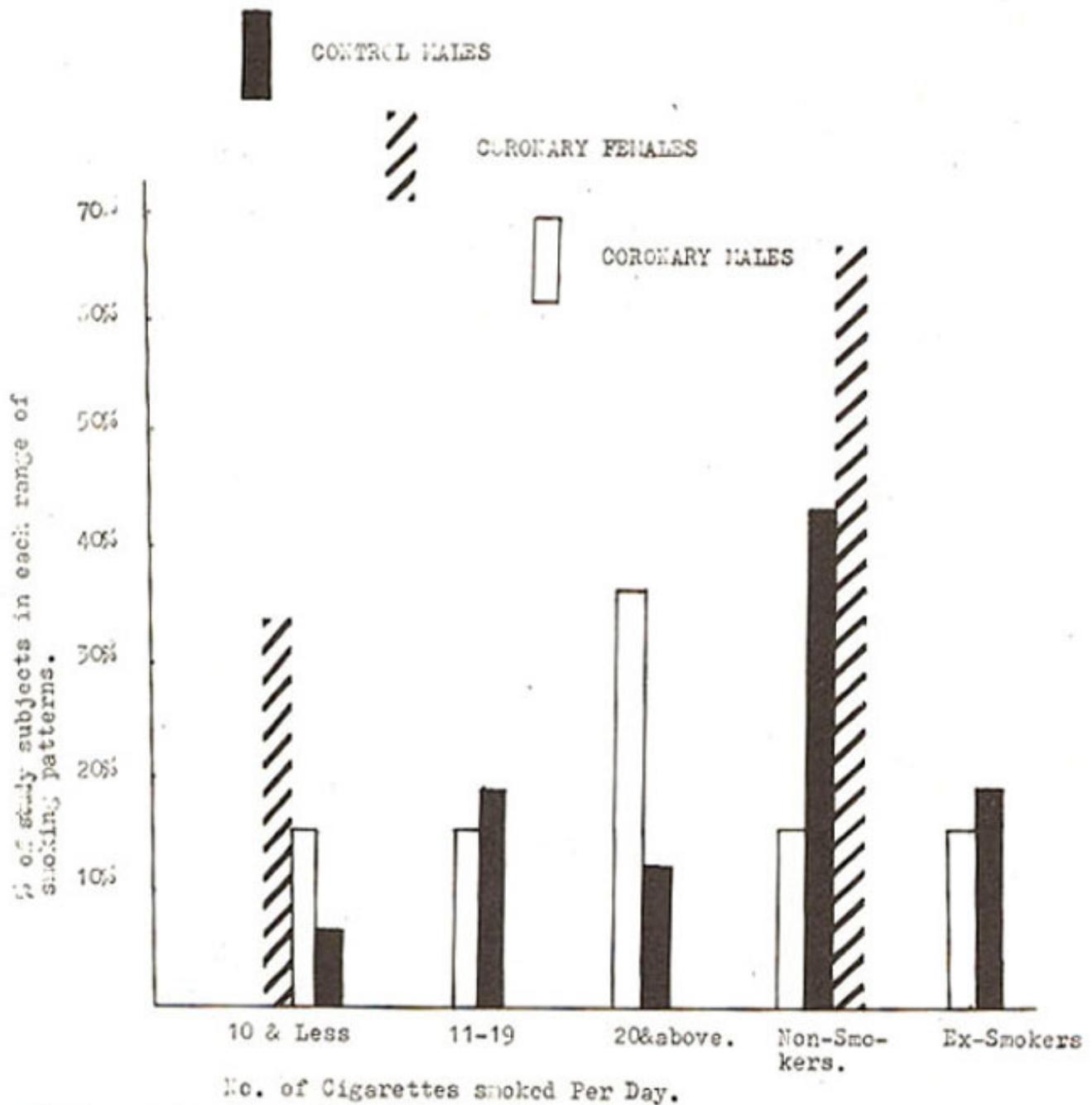
\*\* (M+F) = Male plus Female data pooled

Table II sums up means  $\pm$  SD of the 3 study variables i.e., SUA, P1 and S. Cholesterol (sexwise and pooled figures) in different groups. Frequency distribution of SUA arranged in increments of 1 against percentage of study subjects falling in each range is shown in Figure 1 for all the study groups.



**Figure 1.** Frequency distribution of Sua in terms of percentage of study subjects falling in different ranges of SUA values.

There was a preponderance of smokers in the coronary group as compared to the controls. While 36.84% of coronary males smoked 20 or more cigarettes a day, only 12.5% of control males smoked that heavily. Among males 43.75% controls and 15.78% patients were non smokers (Figure 2).



**Figure 2. Smoking pattern in coronary & control.**

None of the control females smoked so their data is not shown in the figure 2.

There was a significant difference in mean SUA levels and P1 in control and coronary groups (Table III).

**TABLE III**  
**Comparison of Coronary vs Control for SUA, Ponderal Index & Cholesterol.**

Study Variable	Coronary Group	Control Group	t	df	P
*SUA	7.15±2.43	5.16±2.14	-3.26	55	0.01
Ponderal Index	11.91±1.18	12.9±0.58	3.96	55	0.001
Cholesterol	202 ±37.08	187±29.65	-1.67	55	0.05

\*SUA: Serum Uric Acid  
t = Student's t test  
df = Degree of freedom  
P = Level of significance

Cholesterol was normal in both groups.

## DISCUSSION

Many diverse conditions influence SUA either by increasing uric acid synthesis (overproduction - hyperuricemia) or by decreasing its renal excretion (under-excretion -hyperuricemia). Examples of the former include all myelo and lymphoproliferative disorders, malignancies, sarcoidosis, psoriasis, cytotoxic agents, radiotherapy etc., (i.e. all conditions characterized by increased cell turn-over), while examples of the latter include all types of acidosis, chronic renal insufficiency, all oedematous conditions, diabetes, CCF, most diuretics, low dose salicylates, methyl dopa, reserpine, guanethedine, suiphipyrazone, ethambutol, pyrazinamide, alcohol. A sizeable percentage of coronary patients would have one or the other of above mentioned associates on admission. All these for obvious reasons had to be excluded, making patient selection very difficult.

Mean age in coronary females (52.50. ± 5.97) was slightly higher than their male counter parts (50.89 ± 11.68) indicating possibly a slight cardioprotective role of female sex hormones at least until menopause. Mean SUA in the present study was 7.40 ± 2.61 for coronary males and 6.9 ± 1.73 for coronary females. Comparable figure of Mc-Ewin and colleagues<sup>9</sup> in a study of 300 Australian patients with myocardial infarction was 7.24 ± 1.18 mg/dl and 6.60± 2.01 for males and females respectively. In the control group mean SUA was 5.43 ± 2.51 in males and 4.89 ± 1.78 in females. A comparable figure in Evan County study<sup>23</sup> was 5.7 ± 1.2 and 4.8 ± 1.2 for males and females respectively. Figures of

Framingham study<sup>5</sup>, Yano and associates<sup>7</sup> and Haider et al<sup>26</sup> were similar. Lower means for SUA in females of both the study groups indicate presumably a depressant effect of oestrogens on SUA.

Frequency distribution of SUA and ponderal index did not reveal any consistent trend whatsoever except that 37.5% of coronary females had 'P1' 10 and below vis-a-vis 22.22% of control females, indicating a preponderance of obesity in former compared to the later notwithstanding the fact that females in both the groups were bulkier as compared to males.

'SUA' has been reported to be dependent on age, ponderal index, serum cholesterol, fasting blood glucose and social status<sup>5,27</sup>. In the present study no correlation was found between SUA and age or social status. These findings are in agreement with those of Yano and associates<sup>7</sup>. No regular association between SUA and educational or vocational achievements was found in the present and other study<sup>7</sup> while a positive correlation between SUA and vocational and/or educational achievement was found by them<sup>24,25</sup>. As diabetics were excluded from the present study hence effect of blood glucose on SUA could not be studied. As for influence of serum cholesterol and ponderosity on SUA, correlation-co-efficient of each of these 2 variables with 'SUA' was calculated, and represented as an 'r' value (Table IV). An 'r' value

**TABLE IV**  
**Correlation of Serum Uric Acid with**  
**Other 2 Variables.**

	*r	P
SUA vis-a-vis Ponderal Index	-0.02	NS
SUA vis-a-vis Cholesterol	-0.003	NS

\*r = Correlation co-efficient.  
SUA = Serum Uric Acid.

approaching zero indicates no correlation, while a value of +1 indicates a direct positive and 1 a direct negative one. In this study SUA vs 'P1' had an 'r' value of -0.02 and is in complete harmony with many other epidemiological studies<sup>5,2,2,2,6</sup> while other studies showed a positive correlation<sup>4,27</sup>; A similar comment applies to the correlation between SUA and cholesterol (r=-0.003) and is in agreement with many similar studies.<sup>2,9-1</sup> Many other studies have reported a direct positive correlation between SUA and cholesterol<sup>17,22,23</sup>. In Framingham study<sup>5</sup> this correlation could not reach statistical significance. Contrary to the controversial association between SUA and cholesterol an association between SUA and triglycerides is clearly defined and is a real one. Halpurn et al<sup>12,2</sup> reported a direct positive correlation between SUA and triglycerides. Many other epidemiological

studies corroborate this point.<sup>32,7</sup> It appears that the association between SUA and triglycerides is a direct and true one, that between cholesterol and SUA is uncertain and needs further work. Findings of this study suggest hyperuricemia to be a risk factor on its own merits in CHD, not being interdependent on obesity or hypercholesterolemia.

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