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Research Article

Increased Serum Uric Acid Association with Hypertension

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Background

Hypertension is the leading form of cardiovascular disease amongst adults, it's prevalence rises with age resulting in an increased morbidity and mortality through complications such as stroke, myocardial infarction, renal failure and heart failure [1-4]. It is defined as a sustained elevation of systemic arterial pressure[5]. Blood pressure is considered to be elevated when the systolic blood pressure is greater than or equal to 140mm Hg and/or diastolic blood pressure is greater than or equal to 90 mmHg [6]. Essential or primary hypertension is of multifactorial origin and accounts for about 95% of cases [7].

The gene for uricase in human beings was lost several million years back and since uricase is the enzyme which converts uric acid into a soluble form, without this enzyme allantoin and uric acid are left as the end products of purine metabolism in human beings [8,9]. Consequently, we have higher uric acid levels than other mammals possessing the enzyme uricase. Conventionally, normal uric acid levels in the body are defined as <7 mg/dl in men and <6 mg/dl in women, based on the solubility limits of monosodium urate in serum at body temperature [10]. The reason for this difference has been connected to the uricosuric action of estrogens in women [11].Being a powerful antioxidant, uric acid has been proposed to be protective against cardiovascular disease as well as some cancers [12]. But although it may seem to possess antioxidant activity in the extracellular compartment, its effects are quite detrimental once it enters cells such as vascular smooth muscle cells [13,14].These adverse effects include initiation of platelet aggregation [15], pro-inflammatory actions [16] and an inhibitory effect on the production of nitric oxide [17]. Various studies have proposed that hyperuricemia is associated with hypertension, and serum uric acid levels were reported to act as an independent predictor for the development of hypertension [18-20]. Regardless of ethnicity, a relationship was found to exist between serum uric acid levels and blood pressure amongst African- Americans, whites and Asians [21,22]. A series of hypotheses aimed to shed some light on this unexpected positive association, in the process elaborating on the upregulation of renin release and the subsequent decrease of endothelial function [23].

According to a recent review, the prevalence of hypertension in Pakistan has been on the rise and this fact along with the prediction that by 2020, non-communicable diseases such as cardiovascular problems will constitute a major chunk of morbidity and mortality in developing nations, as high as four times the deaths due to communicable diseases, warrant that importance be attached to the separate risk factors for hypertension [24,25]. Hyperuricemia can leadto hypertension in many studies shown in human. Hypertension can be decreased by using drugs that lowers serum acid levels [26,27]. Increased serum uric acid levels are an indirect marker of having Chronic Kidney Disease (CKD) [28]. For effective prevention, all possible interactions between hypertension and other risk factors should be analyzed in detail and dealt with accordingly. Since there is not enough data regarding the link between uric acid and hypertension from Pakistan, this study was conducted to investigate the aforementioned relationship.

Materials and Methods

Means were compared using the t-test for hypertension and uric acid levels. For the comparison between hypertension and acute gout attacks, the chi square test was used.Patients of Chronic kidney disease was excluded, laboratory done urea Creatinine was normal as no chronic kidney disease were enrolled, patients were labeled as hypertension by applying JNC 8 guidelines follows,

mostly paramedic staff of the hospital as we had taken data from them.

Results

A total of 82 patients were included in this study, men 39% (n=32) and women 61% (n=50) with a mean age of 48 years with standard deviation of 16.25 years. 7.3% (n=6) of people had reported acute gout attacks with pain, redness and swelling and an average serumUric Acid (UA) level of 9.62 and a standard deviation of 4.43.

Accounting for confounding variables some interesting observations were made. Adjusting for patients who had chronic kidney disease, patients with history of hypertension complained of no acute gout attacks, although it was not statistically significant. The average of UA level for patients with hypertension was 6.72±2.65 vs. 6.47±1.48 for those who had no history of hypertension, the means did not correlate to the presence of hypertension in patients.When data is adjusted for people with diabetes mellitus (n=7), there still was no relationship seen between hypertension and acute gout attacks. The UA levels in patient categories of hypertensive vs normotensive were also not significantly correlated.

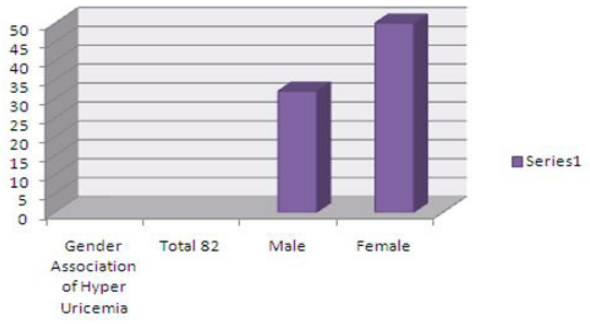
While our study failed to show any relation between hypertension and acute gout attacks or UA levels. A larger study is recommended with higher sample size to more accurately find any correlations between hypertension and acute gout attacks/UA levels.

Gender Association of Hyper Uricemia	
Total 82	
Male	32
Female	50

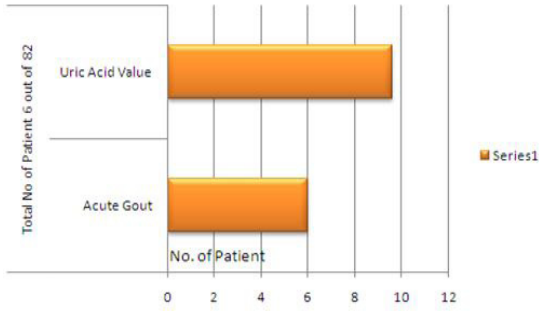
Table 1: Gender Association with Hyperuricemia.

Total No of Patient 6 out of 82	Acute Gout	6
	Uric Acid Value	9.6

Table 2: Number of Patients Reported with Acute Gout.



Graph 1: Gender Association with Hyperuricemia.



Graph 2: Number of Patients Reported with Acute Gout.

Discussion

Experimental data suggests that serum uric acid may instigate the development of hypertension using various mechanisms such as inducing oxidative stress, activating the renin-angiotensin system and inhibiting nitric oxide. The aforementioned mechanisms may be a consequence of the development of renal arteriolar disease coupled with infiltration by T-cells and macrophages, resulting in renal vasoconstriction and ischemia in due course [29, 30]. A number of studies conducted previously have suggested to consider rising levels of serum uric acid as a risk factor for developing hypertension [18-22], similar to the risks posed by obesity and age [31,32].

Given that not all epidemiological data supports the establishment of uric acid as an autonomous risk factor for the development of hypertension [33,34] and the sparse amount of data regarding this association which was available in Pakistan was the reason why we conducted this observational study.

According to our findings, there was no significant association between serum uric acid levels and blood pressure. The mean levels of serum uric acid were similar in both normotensive and hypertensive patients, and neither was there any significant association when age and sex were analyzed in respect to serum uric acid levels. This is similar to studies which suggest likewise that serum uric acid may not play an important role in hypertension [33, 34]. A staunch 7rgument which supports these studies is reliant on Gene Wide Association Studies (GWAS). Data from these studies has linked urate transporter polymorphisms with hyperuricemia as well as gout but not with hypertension [35]. A suggested explanation which may account for this is that serum uric acid by itself may not be a determining factor for hypertension, rather it is the level of intracellular uric acid which may be of more significance in this regard. In a GWAS study, the levels of intracellular uric acid and serum uric acid are dissociated and therefore better conclusions can be drawn [36]. Kosugi and colleagues also reported that when allopurinol was administered in type 2 diabetic mice which had normal or low serum uric acid levels, there was a de-

crease in blood pressure which suggests that it is intracellular uric acid rather than extracellular which results in the development of raised blood pressure [37]. Data from two prospective cohort studies using Mendelian randomization estimates also demonstrated a similar trend, that elevated uric acid does not affect the risk of having elevated blood pressure [38].

For quite some time now, there has been a considerable debate on the significance of the relationship between serum uric acid levels and hypertension as well as cardiovascular disease and as yet it is not clear whether uric acid is in itself a causal, coincidental or compensatory variable. But in contrast to this, the protective action of uric acid against the development of atherosclerosis, due to its antioxidant nature, has been reported [33].

Limitations

This study has several limitations which deserve mention. The present study had several limitations. Firstly, this was an observational study and therefore it does not allow us to determine any sort of causal relationship between serum uric acid and hypertension. Second, we have relied on hypertension that was self-reported and therefore systolic and diastolic values of blood pressure are not available for a detailed analysis of changes in both with respect to serum uric acid levels. Third, the sample size was quite limited which also decreased the power of the analysis, therefore if this study is repeated with a larger sample size, better and more accurate conclusions can be drawn. Lastly, regarding the patients' use of anti hyperuricemic medications was not available, which may have led us to underestimate the extent of hyperuricemia.

Conclusion

Overall, we found no evidence signaling towards a significant association between serum uric acid levels and hypertension. We recommend a large-scale study to further explore this vista and determine if increased uric acid levels do in fact contribute to the development of hypertension.

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