Editorial

Hyperuricemia and its Management: An Emerging Public Health and Clinical Practice Challenge

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Hyperuricemia and gout has traditionally been regarded as the disease of the affluent, being associated with unhealthy lifestyle including alcohol consumption. It has been identified as a disease entity since early period of Egyptian civilization and was known to Hippocrates.[1] It is now emerging as a serious public health and a clinical practice challenge for a variety of reasons. Unfortunately, it has so far been very narrowly seen in the limited context of gout and urolithiasis. Traditionally, the role of diet has rightly assumed a central and key position in the management of hyperuricemia but unfortunately with lesser value attached to drug therapy for its more aggressive control.

Emerging evidence shows increased disease burden resulting in increased economic costs. This situation mandates calls for more aggressive measures, to reduce uric acid excess for treatment of acute gout and prevention of further attacks, which leads to chronic gout, gouty arthropathy and tophaceous gout.[2] The gouty arthropathy results in joint damage and chronic pain, mandating a much earlier proactive approach, based on aggressive uric acid lowering. Unfortunately, available evidence suggests inadequate uric acid control among treated patients. [3]

Hyperuricemia is now being associated with enhanced cardio-metabolic risk. Pathophysiologic basis for such associations is now becoming clear. Hyperuricemia is shown to have association with hypertension, diabetes, renal and cardiovascular disease, including coronary heart disease and stroke.[4-9] This emerging evidence mandates a change in the approach for the management of hyperuricemia. It's time that clinicians should consider cardio-metabolic risks in addition to gout in the management plan of hyperuricemia.

In animal models, hyperuricemia can be induced and lowered. It demonstrates a rise in blood pressure with a rise in serum uric acid levels, which is lowered once hyperuricemia is corrected.[4] Apart from animal studies, meta-Analysis of data based on 55,607 participants demonstrates a relative risk of 1.41 for hypertension, among those having serum uric acid at 6.8 mgs/dl. There is an additional relative risk of 1.13 for hypertension for rise of 1 mg/dl of serum uric acid above this level.[5] A crossover study of adolescents, with newly diagnosed hypertension, treatment with allopurinol resulted in reduction of Blood Pressure. This evidence calls for a more broad based and aggressive therapeutic approach to identify and treat hyperuricemia.[6]

A recent meta-analysis of prospective cohort studies has provided strong evidence that hyperuricemia is an independent risk factor for developing diabetes mellitus in middle-aged and older people.[7] The meta-analysis demonstrates a relative risk of 1.56 for Diabetes Mellitus in highest in comparison to lowest quartile of serum uric acid levels.

Hyperuricemia is independently associated with a decline in renal function. Meta-analysis suggests a relative risk of 1.18 for chronic kidney disease (CKD) for rise of 1 mg/dl of serum uric acid. Stronger association in hypertensive individuals may indicate that hypertension mediates the association between serum uric acid and CKD.[8]

Hyperuricemia may modestly increase the risks of both stroke incidence and mortality.[9] Meta-analysis suggests a relative risk of 1.18 for stroke mortality for rise of 1 mg/dl of serum uric acid above 6.8 mgs/dl. Hyperuricemia is also independently associated with cardiovascular mortality. These risks increase with rising uric acid concentrations.[10] Hyperuricemia increases the risk of coronary heart disease events, independently of traditional risk factors. Meta-analysis shows relative risk of 1.16 for coronary heart disease mortality for serum uric acid level above 5.6 mg/dl and 4.7 mg/dl in men and women respectively.[11]

Serum uric acid level should be lowered sufficiently to counter unfavorable health related outcomes.[12] Further research is also required to understand underlying pathophysiologic mechanisms that may provide better therapeutic approaches. Emerging and available evidence with regards to adverse health related consequences of hyperuricemia are posing a public health challenge. Approaches to identifying and managing hyperuricemia require more aggressive measures.

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