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Original Research Article

Serum urea: an independent risk factor for cataract

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ABSTRACT

Background: Elevated levels of blood urea/blood urea nitrogen in serum is considered an independent risk factor for the occurrence of cataract. Estimation of these levels can be used as a predictor for the occurrence of cataract.
Methods: This was a hospital-based prospective case control study conducted in the department of ophthalmology at SKIMS MCH, Srinagar from January 2023 to June 2023. We evaluated 25 patients admitted for cataract surgery in our department for serum urea and BUN levels and compared their results with 25 age and sex-matched controls admitted for causes other than cataract. The cases with significantly elevated levels of urea were further screened for possible renal impairment using Glomerular filtration rates and urine albumin.
Results: 7 out of 25 cases had elevated levels of serum urea with a mean of 44.2±16.19 mg/dl whereas all 25 patients of the control group had normal serum urea levels with a mean of 28.84±4.3 mg/dl. The mean levels of urea were significantly higher in the cases than controls with $p<0.0001$. 4 out of the 7 patients in the case group with elevated serum urea levels showed impaired glomerular filtration rates and clinically significant levels of urine albumin.
Conclusions: The study suggested a statistically significant correlation ($p<0.0001$) between serum levels of urea and BUN with cataract.

Keywords: Urea, Blood urea nitrogen, Cataract, Hyperuricemia

INTRODUCTION

Lancet Global Health in 2020 reported that cataract remained the largest cause of blindness worldwide, responsible for approximately 45% of cases (over 15 million cases in 2020).[1] Although cataract prevalence has declined due to increased surgical interventions, avoidable blindness caused by cataract in people older than 50 years nevertheless increased from 2010 to 2019, likely due to aging populations.[1,2] Given the large global health burden and limited resources, identifying risk factors is crucial for developing novel strategies to prevent cataract progression. As a multifactorial oculopathy, cataract is affected by individual, metabolic, and environmental factors.[3] Age, sex, race, and genes are important but non-modifiable factors for cataract formation.[3] Thus, special attention should be paid to modifiable risks, like diet and systemic diseases.[4] For instance, cataract is more common in individuals with high-glycaemic diets or those exposed to ultraviolet-B radiation.[5-7] Diabetes patients have higher cataract morbidity even at a younger age.[8] Renal impairment and metabolic disorders also strongly accelerate cataract formation.[9,10] However, although clinical cohort research has been conducted, microenvironmental changes in the aqueous humour related to cataract have rarely been studied. Previously, we reported that uric acid levels in the aqueous humour and serum were strongly correlated with cataract incidence; however, the precise underlying mechanism remains unknown.[11]

Uric acid (UA), as the end product of purine degeneration, was formerly considered to be an antioxidant in hydrophilic environments.[12] Hyper-uricemia is associated with gout, cardio vasculopathy, and kidney disorders; elevated UA can trigger inflammatory or immune reactions.[13-15] The pro-inflammatory nature of UA is related to the crystallization of monosodium urate (MSU); this has been clearly demonstrated in gout [13], which is a form of inflammatory arthritis characterized by increased white blood cells in the synovial fluid, resulting from the deposition of MSU crystals within joints.[13] The exact process by which MSU crystals induce inflammation was unclear until 2006, when Fabio Martinon et al identified the role of the NLRP3 (nucleotide-binding oligomerization domain–like receptor pyrin domain containing-3) inflammasome.[16] Upon stimulation with elevated UA, NLRP3 oligomerizes and binds to ASC (apoptosis-associated speck-like protein containing a caspase recruitment domain), an adapter protein, and effector pro-caspase-1, ultimately forming the NLRP3 inflammasome.[17] In this cytoplasmic, multiprotein complex, pro-caspase-1 is cleaved into caspase-1, which then activates cytokines IL-1β and IL-18 in macrophages.[17] Consequently, persistent NLRP3 dysregulation leads to chronic inflammation, potentially resulting in pathological changes. The lens, as an avascular organ, is susceptible to changes in its metabolism and the transparency of the adjacent aqueous humour.[18] Any alteration in the composition of the aqueous humour can trigger or accelerate cataract development. Our previous findings indicated a strong association (r=0.9) between hyper-uricemia and excessive UA in the aqueous humour, as well as urate deposition in the lens cortex.[11] We speculated that elevated UA levels contribute to the progressive clouding of the originally clear lens by activating the NLRP3 inflammasome.

METHODS

This was a hospital-based prospective study conducted in the Department of Ophthalmology, SKIMS MCH Srinagar from January 2023 to June 2023. Ethical clearance for the study was obtained from IEC, SKIMS MCH, Srinagar.

Inclusion criteria

25 cataractous eyes of 25 patients were included in the study (figure 1). The control group included 25 age and sex-matched patients admitted for causes other than cataract (figure 2).

Exclusion criteria

Diabetic and hypertensive patients were excluded from the study. Patients with history of alcohol and cigarette smoking were excluded from the study.

All patients underwent a standard history and examination protocol. All patients underwent a complete ophthalmic examination including BCVA (best corrected visual acuity), fundus examination, SLE (slit-lamp examination), IOP (intra-ocular pressure) etc. Subsequently the study participants were tested for the levels of serum urea using standard biochemical testing available in the hospital. The cases that showed elevated levels of serum urea were then screened for renal impairment using glomerular filtration rates and urine albumin levels.

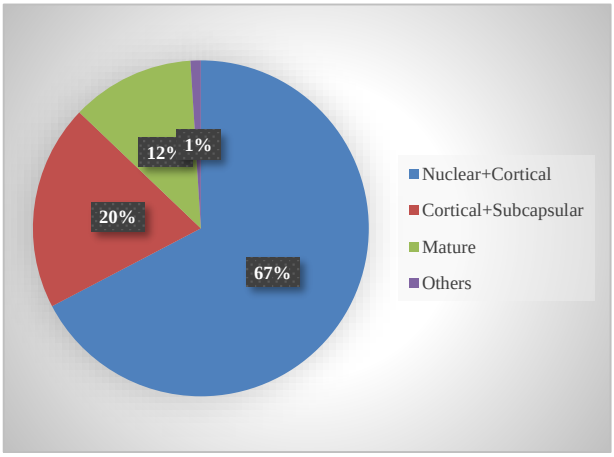

Figure 1: Distribution of case group.

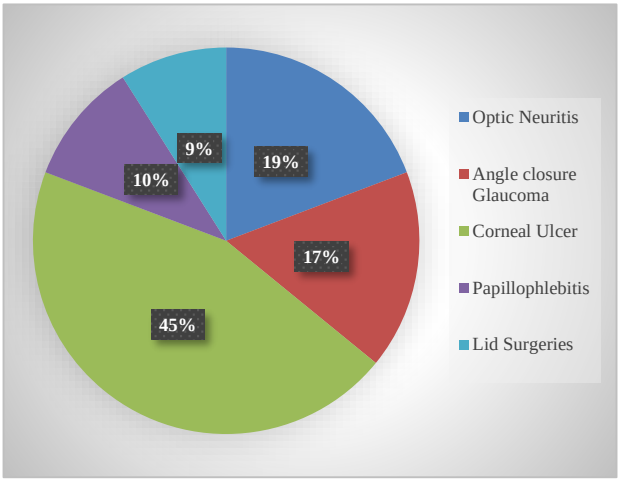

Figure 2: Distribution of control group.

RESULTS

Out of the 25 cases, 14 (56%) were males and 11 (44%) were females with a mean age of 69.27±8.1 years. In the control group, age and sex-matched patients were taken with a mean age of 68.9±7.67 years (Table 1).

Both cases and controls were examined for serum urea levels using standard biochemical testing. Among the cases, 7 participants had serum urea levels greater than 45 mg/dl with mean levels of 44.2±16.19 mg/dl. The mean level of serum urea in the control group was estimated to

be 28.84±4.3 mg/dl with no control showing level greater than 45 mg/dl. The difference between cases and controls was statistically significant with p<0.0001 (Table 2).

Table 1: Patient profile.

Parameters	Cases (N=25)		Controls (N=25)	
Mean age ±SD (years)	69.27±8.1		68.9±7.67	
Sex, N (%)	**Male**	**Female**	**Male**	**Female**
	14 (56)	11 (44)	14 (56)	11 (44)

Table 2: Serum urea levels.

Parameters	Cases	Controls	P value
Normal range, N (%)	18 (72)	25 (100)	<0.0001
Raised, N (%)	7 (28)	0	
Mean±SD (mg/dl)	44.2±16.19	28.84±4.3	

Table 3: Serum BUN levels.

Parameters	Cases	Controls	P value
Normal range, N (%)	18 (72)	25 (100)	<0.0001
Raised, N (%)	7 (28)	0	
Mean±SD (mmol/l)	19.71±7.2	12.86±1.9	

The level of serum BUN was estimated from the serum urea by multiplying it with a factor of 0.446. The average level of serum BUN in the cases was estimated as 19.71±7.2 mmol/l and the controls as 12.86±1.9 mmol/l. The difference in the two groups was statistically significant with p<0.0001 (Table 3). Although the levels of serum urea levels were elevated in only 7 cases but the mean difference between the two groups was statistically significant with the cases showing notably higher levels of urea than the controls. 4 cases that showed urea levels greater than 45 mg/dl were subsequently screened for renal impairment. These patients recorded elevated levels of urine albumin and impaired glomerular filtration rates.

DISCUSSION

Cataract is a leading cause of preventable blindness worldwide and measures must be taken for its early detection and subsequent treatment.[1] Our study tries to establish a relationship between elevated levels of serum urea or serum BUN with the occurrence of cataract. Considering the possibility of hyperuricemia as a risk factor for the occurrence of cataract can help intercept early cases and its rectification slow down the progression. This will result in reduction of the overall burden of the disease. In this study, 25 patients were included in the case group, of which 14 (56%) were males and 11 (44%) were females with a mean age of 69.27±8.1 years. In the control group, 25 age and sex-matched patients were taken with a mean age of 68.9±7.67 years. Out of 25 cases, we observed that 7 patients had serum urea levels greater than 45 mg/dl with mean levels of 44.2±16.19 mg/dl. The mean level of serum urea in the control group was estimated to be 28.84±4.3 mg/dl. None of the control group showed levels greater than 45 mg/dl. Our study revealed a statistically significant difference with a p<0.0001 between cases and controls. Mirsamadi et al conducted a similar case-control study and established the correlation of serum urea and other blood biochemical agents with the occurrence of cataract.[19]

They evaluated 155 cataract patients and 155 age and sex-matched controls for serum urea, cholesterol, glucose, albumin, creatinine, sodium, potassium, and calcium levels. Mean levels of these elements including serum urea differed significantly between cases and controls with cataract patients showing a statistically significant increase in urea levels. They also found that patients with a cortical cataract had the highest level of urea, differing significantly from other subgroups and controls.

Another case-control study was conducted by CA Donelly et al to look for differences in plasma constituents between age and sex-matched cataract cases and controls.[20] The individual cases were further divided into subcategories based on the type of cataract. They observed that nuclear cataract was significantly associated with raised plasma alanine aminotransferase and bilirubin, posterior subcapsular cataract was associated with increased calcium and urea, cuneiform with reduced potassium, mature/hypermature with raised potassium and reduced total carbon dioxide. In our study, 4 out of 7 cases showing urea levels greater than 45 mg/dl were subsequently screened for renal impairment. The said patients recorded elevated levels of urine albumin and impaired glomerular filtration rates and were subsequently put on nephrology follow-up. This further suggests a correlation between renal impairment and cataract. Liu et al conducted a cohort study to establish the same correlation.[21] It was found that increased levels of BUN and serum creatinine associated with renal failure were directly associated with an increased incidence of cataract. This study indicates a relationship between CKD and cataract, and suggests that the risk for cataract increases with the severity of renal impairment. The limitation of the study is in the small sample size.

CONCLUSION

Our study concludes that there exists a statistically significant relationship between elevated levels of serum urea and cataract. By excluding diabetics and hypertensives from the study and using age-matched controls, we were able to establish a near-independent causal association between cataract and serum urea levels which could further act as a modifiable risk factor for the occurrence and subsequent progression of cataract.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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