A case series on *Averrhoa bilimbi* induced acute oxalate nephropathy; an experience from a tertiary center in Kerala, India

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ABSTRACT

**Background:** *Averrhoa bilimbi* is a commonly used fruit in South India for various home preparations and as a traditional remedy for hypercholesterolemia and hypertension. As it belongs to Oxalidaceae family, fruit has high oxalate content, causing calcium oxalate crystal deposition in renal tubules, resulting in acute oxalate nephropathy (AON) when consumed in large quantities.

**Case Series:** We present a series of 24 patients from 11 hospitals in the State of Kerala who developed acute renal failure after some days of intake of *Irumban puli* fruit juice. Seven patients needed hemodialysis while the other three improved with conservative management.

**Conclusions:** We conclude that it is not safe to consume high oxalate containing fruits, especially in concentrated forms, that too in large quantities.

Implication for health policy/practice/research/medical education:

*Irumban Puli* (*Averrhoa bilimbi*) is commonly used as an ingredient of various South Indian dishes. It is also used in various other South East Asian countries for the indigenous method of treatment of diseases like hypertension, diabetes and hypercholesterolemia. Consumption of highly concentrated fruit juice can lead to acute renal failure due to acute tubular necrosis. The high oxalate content leads to Intra-tubular oxalate crystal deposition and renal failure. Hence, we conclude that it is not safe to consume such fruits with high oxalate content, especially in concentrated forms.

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1. **Background**

Secondary oxalosis can be due to increased ingestion, increased production, or decreased excretion of oxalate, leading to excessive oxalate accumulation and subsequent oxalate nephropathy. As oxalate has urinary excretion, increased oxalate load can lead to renal insufficiency (1,2). Case reports describing excessive intake of star fruit (*Averrhoa carambola*) juice (3,4) and peanut intake (5) leading to oxalate nephropathy are available. *Irumban puli* (*Averrhoa bilimbi*), belonging to the same genus as *A. carambola*, also has high oxalic acid content. It has commonly seen in South India and is used in various preparations. Excessive ingestion of fruit juice results in increased serum oxalate level. Calcium oxalate crystals are deposited in renal tubules and finally results in acute renal failure. We present a series of 24 cases from 11 different hospitals in the state of Kerala, during the study period 2010-2013, who developed acute oxalate nephropathy (AON) after consumption of *Irumban puli* juice.

2. **Materials and Methods**

We conducted a retrospective study on 24 patients from 11 different hospitals in Kerala, whose renal biopsies were sent to our laboratory for histopathological examination. We analyzed the following parameters; Age, gender, symptoms, comorbidities, blood pressure, ultrasonography findings of kidney, urine analysis with microscopic examination, serum creatinine levels,
quantity of fruit juice consumed, time for recovery and detailed histology along with the follow up. The details of the cases are illustrated in Tables 1, 2 and 3.

3. Results

Majority of the cases were males (M: F = 7:1) and belonged to the age group of 40-60 years. However, there were cases as young as 25 years to as old as 75 years. All of them had consumed the *A. bilimbi* juice as a traditional remedy for either hypertension or dyslipidemia except for a group of 3-4 youngsters, who had consumed wine prepared using the same fruit. Regarding the comorbidities, 8 patients had hypertension, two had diabetes mellitus, one had hypertension and diabetes mellitus, one had dyslipidemia along with hypertension and two had dyslipidemia only. Rest of the patients were devoid of any comorbidities. Oliguria and edema were seen only in minority of cases. This variation could be due to lack of data received from referring hospitals. Majority had urinary oxalate crystals (16/24 cases). Serum creatinine values varied from 2.4–14.5 mg/dL. Around 19 patients had creatinine more than 5 mg/dL. Moreover, 58% cases underwent hemodialysis and renal biopsy, while 42% were treated conservatively. All of the 15 cases with renal biopsy showed features of AON. The photomicrographs of a representative case are given in Figure 1.

Ultrasonographic findings were normal in all the cases except for changes due to comorbidities like presence of diabetes, in respective patients. The proportion of fruits consumed varied from 20-100 mL/d. Majority had consumed it as concentrated juice 100-400 mL/d, either as single dose or as multiple doses, as a traditional remedy for their comorbidities, mostly on empty stomach.

4. Follow up of case series

All 15 patients who had hemodialysis recovered soon within few days. Creatinine levels normalized within 6-8 weeks. All those who were managed conservatively also recovered.

5. Discussion

Oxalate nephropathy can be of two types as primary hyperoxaluria and secondary hyperoxaluria. Primary

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HTN; hypertension, BP; blood pressure, DM; diabetes mellitus, Y; yes, N; no.

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HTN; hypertension, BP; blood pressure, DM; diabetes mellitus, Y; yes, N; no.
Hyperoxaluria is an autosomal recessively inherited enzyme deficiency disorder that leads to the increased urinary excretion of oxalate. There is a reduction of alanine-glyoxylate transaminase (AGT) activity in liver, leading to the accumulation of oxalate in type 1 primary hyperoxaluria. While, type 2 primary hyperoxaluria occurs due to a mutation of glyoxylate reductase/D-glycerate dehydrogenase, resulting in increased excretion of L-glyceric acid as well as oxalate.

The causes for secondary hyperoxaluria are increased dietary oxalate intake, enteric hyperoxaluria and increased production of oxalate. Enteric hyperoxaluria usually results from fat malabsorption. Enteric hyperoxaluria occurs in orlistat therapy, Roux-en-Y gastric bypass surgery, celiac disease, and Crohn's disease. Increased production of oxalate is mainly due to glyoxylate accumulation, which is associated with ethylene glycol ingestion, and less commonly ascorbic acid.

Deposition of calcium oxalate crystals within the renal tubules results in acute renal failure in AON. *Averrhoa bilimbi* (commonly known as *bilimbi*, *Irumban Puli*, *Chemmeen Puli*, *bimbul*) is a fruit-bearing tree of the genus *Averrhoa*, family *Oxalidaceae*. *Bilimbi* tree grows 5-10 m in height. It is widely cultivated in the tropical countries. Fruits are produced in clusters, cylindrical with five broad rounded longitudinal lobes. *Averrhoa bilimbi* fruits are very sour, and are used in the production of vinegar, wine, pickles, jams and jellies and in the preparation of South Indian dishes.

*Averrhoa bilimbi* is commonly used as a natural remedy for the treatment of hyperlipidemia, hypertension and diabetes in different parts of India, especially the leaves, flowers and fruits. In rats, it has been shown that this fruit has a cholesterol lowering effect. The fruit is also used to treat tinea versicolor, mumps, rheumatism, beriberi, cough, and scurvy. The oxalate content of the fruit was found to be 25.1 mg/100 g of fruit when analyzed in our laboratory which is very high
compared to other fruits (Table 4). The high levels of oxalic acid found in bilimbi are probably responsible for its extremely low pH (0.9-1.5).

Various renal and neurological side effects like muscle weakness, intractable hiccups, mental confusion, seizures can develop after ingestion of star fruit (Averrhoa carambola) (14,15). However, acute tubular necrosis due to A. bilimbi ingestion is being reported for the first time. Oxalic acid damages the renal tubules and interstitium. Oxalate crystals get endocytosed by renal epithelial cells which damage renal epithelial cells and stimulate specific genes in renal tubular cells by the crystals, including the connective tissue growth factor gene, finally causing interstitial fibrosis.

All our patients had a history of intake of Averrhoa bilimbi juice. Calcium oxalate crystals detected in the urine of 8 patients. Intratubular polarizable crystals of oxalate were detected in 15 patients, with kidney biopsy.

6. Conclusions

Irumban puli (Averrhoa bilimbi) is commonly used as an ingredient of various South Indian dishes. It is also used in various other South East Asian countries for the indigenous method of treatment of diseases like hypertension, diabetes and hypercholesterolemia. Consumption of highly concentrated fruit juice can lead to acute renal failure due to acute tubular necrosis. The high oxalate content leads to intratubular oxalate crystal deposition and renal failure. Hence, we conclude that it is not safe to consume such fruits with high oxalate content, especially in concentrated forms.

Authors’ contribution

SNV, AJ and ZS designed and performed the research. Zuhara Shemin and Seethalekshmy collected the histopathological data. ZS, SNV and AJ analyzed data and wrote the manuscript. All authors reviewed, edited and approved the final manuscript.

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Conflicts of interest

The authors have no conflicts of interest to declare.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patients had given their informed consent regarding this case series report.

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References


