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Calcium Urolithiasis: Role of Lipid Peroxidation and Antioxidants

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Abstract

The aim of present study was to assess the levels of malondialdehyde (marker of lipid peroxidation), vitamin E and selenium (natural antioxidants) in serum samples of patients with calcium containing kidney stones and in control subjects in order to observe their role in the pathogenesis of calcium containing kidney stones. For this purpose 80 subjects including 40 confirmed cases of calcium containing kidney stones and 40 age and gender matched control subjects with no personal or family history of urolithiasis were recruited from the OPD of Liaquat University Hospital Jamshoro and Isra University Hospital Hyderabad during June 2012 to December 2012. Serum malondialdehyde (MDA), vitamin E and selenium levels were measured by spectrophotometric methods using commercially available kits. Serum MDA levels were found to be significantly higher ($p < 0.001$) and of vitamin E and selenium significantly ($p < 0.001$) lower in calcium containing kidney stone patients as against the control subjects. A weak positive correlation (which was not statistically significant) was seen between serum MDA and vitamin E levels and between MDA and selenium levels. The results of present study suggest that lipid peroxidation owing to decreased amounts of antioxidants seems to play a major role in the pathogenesis of calcium containing kidney stones.

1. Introduction

Calcium lithiasis in kidney is a very common urological finding in Pakistan as well as in many developing and developed countries of the world [1-5]. It costs the society a huge amount of money each year, both on medical treatment and due to loss of work days. The economic consequences of this disorder are enormous as majority of the kidney stone patients are males of 20-40 years age [1] (an important socio-economic group of any population) and the recurrence rate within ten years of the first episode is 50%. [6]

The mechanism of formation of calcium containing kidney stones is a complex phenomenon not yet fully understood. Supersaturation of urine, crystal nucleation, and crystal attachment to the surface of injured renal epithelial cells are considered as initiating events involved in the genesis of calcium containing kidney stones [7, 8]. It is now well established that increased lipid peroxidation owing to overproduction of reactive oxygen species (ROS) and / or decreased activity of antioxidant system are involved in the pathogenesis of calcium containing kidney stones [9]. The chemical process of lipid peroxidation is mostly initiated by a free radical or any other reactive

oxygen species (ROS), which removes a hydrogen atom from the carbon chain of an unsaturated fatty acid, leaving a carbonyl radical [4] which can bind an oxygen molecule, yielding a peroxy radical [10]. Peroxy radicals so produced are themselves amply reactive to remove further hydrogen atoms from an adjacent fatty acid, resulting in the formation of lipid peroxide. Lipid peroxidation in this way promulgates as a chain reaction causing functional irregularity of several cellular organelles [11]. Moreover, lipid peroxides themselves are unstable and breakdown to yield a range of toxic aldehydes that are capable of damaging membrane proteins [12]. Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxide in cells and the serum level of this is used as a biomarker to measure the level of oxidative stress in an organism [13].

Vitamin E, the most important lipid soluble antioxidant protects cell membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction [14, 15].

Selenium, an essential mineral and a natural antioxidant, delays the oxidation of polyunsaturated fatty acids in cell membranes and thus preserves elasticity of tissues [15]. Any significant alteration in selenium concentration would cause changes in the activity of seleno-enzymes (which have antioxidant function) and thus have important consequences on the susceptibility of tissues to oxidative stress [16].

In the present study serum levels of malondialdehyde (used commonly as an indicator of lipid peroxidation), selenium and vitamin E (two antioxidants) were measured in patients with calcium containing kidney stones and in controls (with no personal or family history of urolithiasis) matched for age and gender.

2. Material & Methods

This study was carried out in the Postgraduate Research Laboratory of Isra University Hyderabad, and Hi-tech Laboratory, University of Sindh, Jamshoro, during the period June 2012 to December 2012. In all 80 adults of 30-50 years age, including 40 confirmed cases of calcium containing kidney stones and 40 gender matched control subjects with no personal or family history of urolithiasis were recruited from the OPD of Liaquat University Hospital Jamshoro and Isra University Hospital Hyderabad. None of the recruited subjects were on vitamin supplementation or have any disease which can cause changes in serum levels of parameters measured. After getting written informed consent from the study population, 5ml fasting blood sample was drawn from every subject and allowed to clot. The clotted

blood was then centrifuged at 3,000 rpm for ten minutes to separate serum for analysis of malondialdehyde (MDA), vitamin E and selenium levels by spectrophotometric methods using commercially available kits.

3. Statistical Analysis

The results are presented as Mean \pm SD. Student's unpaired 't' test was used to compare the mean values of the parameters measured between patient group and the control group. Pearson's correlation analysis was done to see any association between MDA and vitamin E levels and between MDA and selenium levels. A p-value of less than 0.05 was taken as statistically significant.

4. Results

Table 1 shows gender wise distribution of cases and control subjects. The data shows that majority (72.5%) of calcium containing kidney stone patients were males. In Table 2, serum levels of MDA, vitamin E and selenium are shown. Serum MDA levels were found to be significantly higher ($p < 0.001$) in patient group as against the control group ($26.03 \pm 7.84 \mu\text{mol/L}$ Vs $1.88 \pm 0.62 \mu\text{mol/L}$). In contrast to this, the mean serum levels for both vitamin E and selenium were seen to be significantly lower ($p < 0.001$) in patient group compared to the control group ($0.38 \pm 0.15 \text{mg/dL}$ Vs $1.06 \pm 0.17 \text{mg/dL}$) and ($38.40 \pm 14.10 \mu\text{g/L}$ Vs $84.50 \pm 10.22 \mu\text{g/L}$) respectively.

Table 1. Gender-wise distribution of calcium stone patients and control subjects.

Gender	Patients n = 40	Controls n = 40
Male	29 (72.5%)	26 (65%)
Female	11 (27.5%)	14 (35%)

Table 2. Comparison of serum MDA, vitamin E and selenium levels between calcium stone patients and control subjects.

	Patients n = 40	Controls n = 40	Level of significance
MDA ($\mu\text{mol/L}$)	26.03 ± 7.84	1.88 ± 0.62	$p < 0.001$
VitaminE (mg/dL)	0.38 ± 0.15	1.06 ± 0.17	$p < 0.001$
Selenium ($\mu\text{g/L}$)	38.40 ± 14.10	84.50 ± 10.22	$p < 0.001$

Results are presented as Mean \pm Standard Deviation

Pearson Correlation Co-efficient between MDA and vitamin E levels (Figure 1) and between MDA and selenium (Figure 2) levels in patients with calcium containing kidney stones were weakly positive.

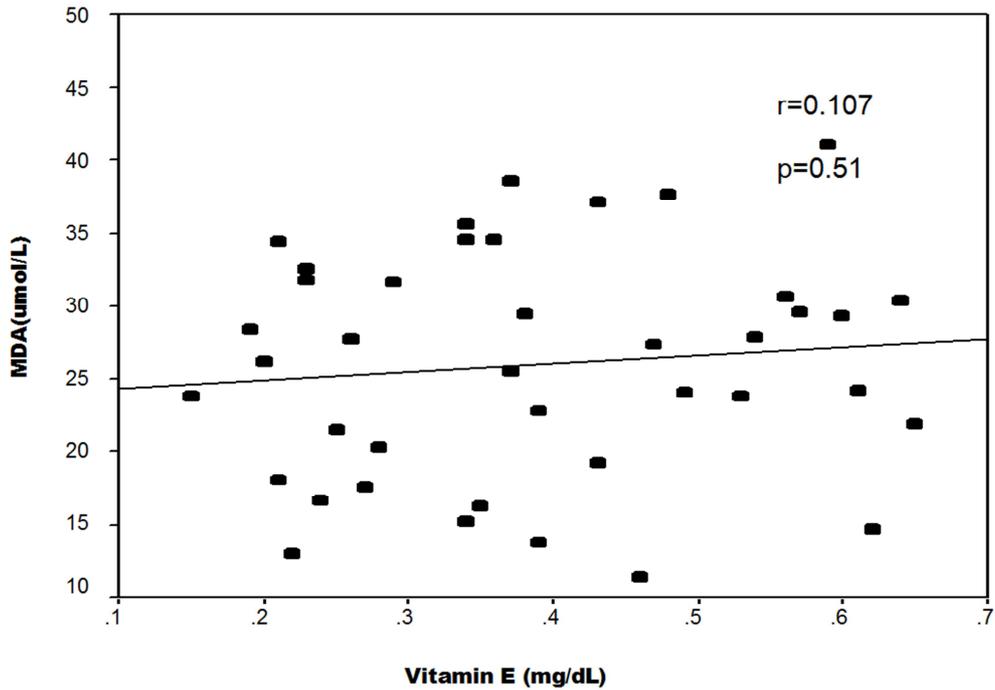


Figure 1. Correlation coefficient between MDA and vitamin E levels in the calcium stone patients.

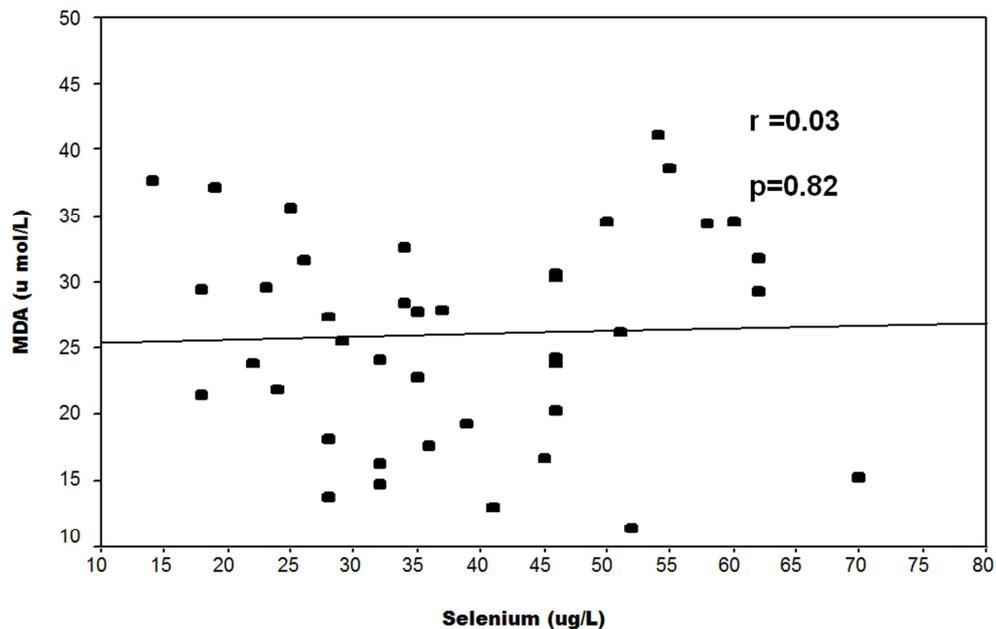


Figure 2. Correlation coefficient between MDA and selenium levels in the calcium stone patients.

5. Discussion

In the present study, calcium containing kidney stones were found to be more common in males than in females. All reports available in literature show that calcium lithiasis in kidney is predominantly a male disease. A possible cause for high incidence of calcium containing kidney stones in adult males could be increased level of blood testosterone, which promotes urinary oxalate excretion and suppresses osteopontin expression in the kidneys [17].

Excessive production of oxalate may cause supersaturation

of urine that may lead to crystallization, crystal aggregation and hence stone formation. This is suggested because oxalate has no metabolic role in human body and is removed from the body via filtering mechanism of the kidneys.

Calcium oxalate, the major component of calcium containing kidney stones has been shown by various investigators to induce free radical generation which results in peroxidation injury to renal epithelial cells [18, 19].

Age group of early 20's and late 40's is considered to be most active period in life. Increased physical activity in this age group has been shown to induce several fold increase in

plasma xanthine oxidase level that in turn could produce oxidative stress to filtering renal tissue [20].

In this study, a significant increase in serum MDA levels ($P < 0.001$) were found in patient group compared to control group. This finding is in accordance with the reports by many investigators [21, 22].

Increase in serum MDA levels could be due to increase in oxidative stress in kidney's caused by increased production of reactive oxygen species or decrease in antioxidant defense mechanism and vice-versa.

Vitamin E is a well-known chain breaking antioxidant, which protects the cell – membranes from oxidative stress. In present study significantly lower levels of serum vitamin E ($P < 0.001$) and of selenium ($P < 0.001$) were seen in calcium containing kidney stone patients compared to controls.

It is not very clear at this stage as to whether the reduction seen in levels of vitamin E & selenium in present study is cause (because of reduced dietary intake) or consequence of disease process (because of increased utilization of vitamin E and selenium as antioxidants during oxidative stress).

6. Conclusion

From this study, it may be concluded that lipid peroxidation owing to decreased antioxidants and / or increased level of oxidants do play a major role in the pathogenesis of calcium containing kidney stones.

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