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A STUDY TO EVALUATE THE TOTAL ORGANIC ACID CONTENT IN URINE OF CALCIUM OXALATE RENAL STONE FORMERS AND NON STONE FORMERS

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ABSTRACT: Renal stones disease is the most common disease of the urinary tract affecting about 10% of the global population. Renal stone disease is a common disorder that develops when the urine becomes overly saturated with certain microscopic substances that bind into hardened mineral deposits known as renal stones. The objective of our current study is to evaluate the total organic acids of urine of calcium oxalate stone formers and compare it with that of non stone formers, to investigate whether the difference between the property studied in two groups really exists or not. The study was conducted on 50 patients divided into two groups- Group I consist of 25 idiopathic patients having calcium oxalate renal stone *i.e.* stone formers (SF) and Group II consists of 25 controls *i.e.* non stone formers (NSF) having no clinical evidence of renal stones. Each patient and control collected a 24 h urine, which was kept unrefrigerated, using thymol as preservative. It was found from our studies that evaluation of Total organic acids can be used as a test to separate a SF from NSF.

INTRODUCTION: Urine is a very complex polyionic solution and contains various inhibitors and promoters of crystallization [1]. Important ions and molecules in relation to renal stone formation are Ca^{2+},oxalate, phosphate, Na^+, K^+, H^+, OH^-, Mg^{2+}, SO_4^{2-} citrate, amino acids, glycolsamino-glycans (GAGs) *etc* [2]. The loss of balance between the urinary promoters and inhibitors and super saturation of urine with stone forming ions has been suggested to increase the risk of stone formation more than disturbance in any single substance as renal stone formation is a multifactorial problem [3].

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Kidney stones are solid crystals that are formed from dissolved minerals in urine, can be caused by both environmental and metabolic problems [4]. Of all the renal stones, calcium oxalate and calcium phosphate stones account for almost 70% in economically developed countries [4]. Renal stones can develop anywhere in urinary tract. Most of the patients had renal stones (66%), followed by ureteral stones (25%) followed by vesical and urethral stones (9%) [5].

All type of stones are formed due to imbalance between fluid and certain wastes in urine causing a high concentration of stone forming salts *i.e.* calcium oxalate, calcium phosphate, uric acid and struvite [6]. Renal stones may grow over months and even years before causing problem. Normally the stone that is very small in size will move through the urinary tract and pass out in the urine. Large stones do not always pass through and may require a procedure or surgery to remove them [7].

These stones can result in extreme pain, burning sensation during urination, blood in urine, can stop the flow of urine and in some cases may lead to high blood pressure [8] and increase the risk for coronary artery disease and diabetes mellitus [9]. The renal stone oxalate production [14]. Further, renal stones formation is a recurrent problem and around half of all people who previously had a kidney stone will develop another one within five years [10]. The recurrence rate without preventive treatment is approximately 10% at 1 year, 33% at 5 years and 50% at 10 years [11]. Another visible change was the variation in the gender of the affected people [12]. Although in the beginning the disease was limited to men, now-a-days it also affects the women. Peak age of renal stone found in men is 30 years and women are 35-55 years [13]. Incidence of formation of stones is 3 times higher in men than women. This is due to lower testosterone levels providing protection for women and children against developing oxalate stones, as testosterone may increase hepatic develop frequently in people with a family history of stones than in those without a family history [15].

Relative mobility of the ions present in the urine imparts conductance property to the urine. In our previous study, we had studied specific gravity, pH [16] and surface tension and viscosity [17]. In the current paper, we will study total organic acids of urine of calcium oxalate stone formers and compare with that of non stone formers, to investigate whether the difference between two groups really exists or not so that a new simple method may be developed to distinguish the stone formers from non stone formers rather than the various imaging techniques used now-a-days [18]. We present a study of 50 patients. Group I consist of 25 idiopathic patients of various ages and both sexes having Calcium oxalate renal stone disease *i.e.* stone formers (SF) and Group II consists of 25 controls *i.e.* non stone formers (NSF) with matched age and sex having no family history of kidney stone.

MATERIALS AND METHODS:

Preparation of Patients and Controls: Patients and controls were put on equal calorific diet/kg body weight and equal amount of water for 2 days. On third day, they were asked to collect 24 h urinary sample. 24 h collection is still the gold standard for metabolic evaluation in renal stone disease [19].

Collection of 24 h Urine: Each patient is provided with two 2.5 l collecting bottles and for urine preservation 10 ml of 5% thymol in isopropyl alcohol is added into each bottle. On the day of urine collection, patients were asked to empty the bladder completely upon awakening and discard this urine. This is the start date and time. Write it on the collection container. After that, all urine should be collected in the bottle (also during the night) for the next 24 h. Always store the collecting bottles in a cool place. The last urine collected should be that voided upon awakening the second day, at the same time as the start time [20].

Experimental: The total organic acids in urinary sample in both the groups was evaluated by Van Slyke and Palmer method. The individual values of each observation of each subject in both the groups are shown in **Table 1**.

TABLE 1: EXPERIMENTAL VALUES OF ORGANIC ACIDS OF STONE FORMERS AND NON STONE FORMERS

Stone Formers	Organic acids (meq/L)	Non stone Formers	Organic acids (meq/L)
1	16.5	26	34.75
2	17.34	27	25.57
3	32.34	28	52.5
4	28.4	29	39.75
5	34.95	30	56.20
6	38.05	31	48.40
7	13.08	32	76.24
8	29.7	33	72.7
9	32.35	34	44.40
10	37.65	35	29.60
11	36.7	36	22.40
12	35.95	37	39.84
13	35.65	38	52.56
14	39.61	39	35.89
15	30.29	40	49.78
16	38.39	41	47.33
17	39.98	42	60.78
18	50.2	43	44.20
19	36.45	44	46.7
20	52.5	45	65.54
21	27.05	46	72.31
22	38.39	47	67.55
23	18.85	48	75.2
24	39.95	49	62.7
25	36.7	50	54.55

Statistical Methods: Significance of mean value differences between the two groups *i.e.* Group-I and Group-II were tested using student t-test. The results of total organic acids of 24 h urinary sample in the two groups were shown in **Table 2**.

TABLE 2: RESULTS OF TOTAL ORGANIC ACIDS OF 24 h URINARY SAMPLE IN THE TWO GROUPS

Subjects	Evaluated Range	Evaluated Mean	Evaluated Standard Deviation
Stone Formers (Group-I)	13.08-52.5	33.481	± 9.306
Non Stone Formers (Group-II)	22.40 - 76.24	51.097	± 15.107

t value = 4.86

RESULTS AND DISCUSSION: The present study was conducted on 50 patients divided into two groups- Group I consist of 25 patients having calcium oxalate renal stone *i.e.* stone formers (SF) and Group II consists of 25 controls i.e. non stone formers (NSF). 24 h urine was collected from each patient and control. It was found during study that total organic acids of Group I range from 13.08 to 52.5 with a mean value of 33.481 ± 9.306 as shown in **Fig. 1**.

Corresponding value in Group II ranges from 22.40 to 76.24 with a mean value of 51.097 ± 15.107 as shown in **Fig. 2**. Comparison of total organic acids in both the groups is shown in **Fig. 3**. By applying student t-test, t value comes out to be 4.86 which is statistically highly significant.

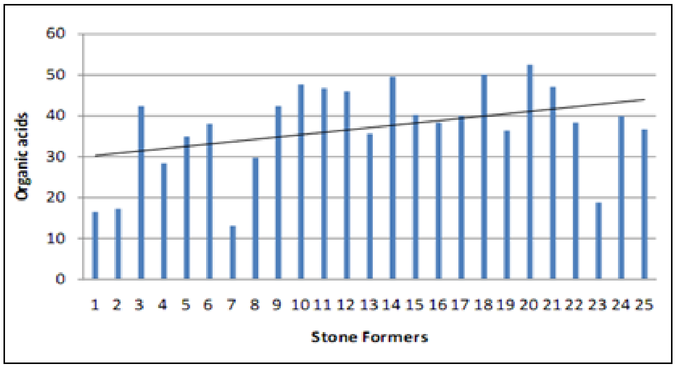

FIG. 1: GRAPH SHOWING ORGANIC ACIDS OF STONE FORMERS

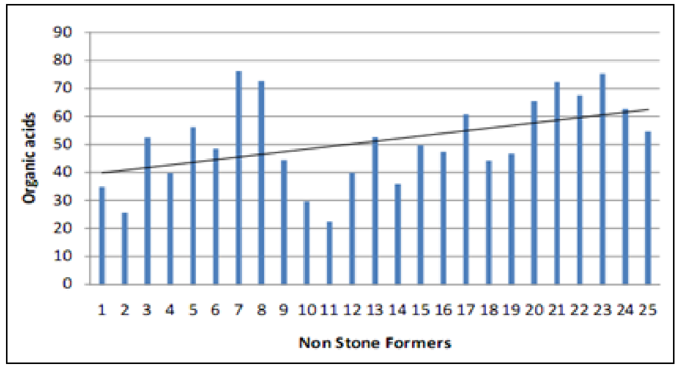

FIG. 2: GRAPH SHOWING ORGANIC ACIDS OF NON STONE FORMERS

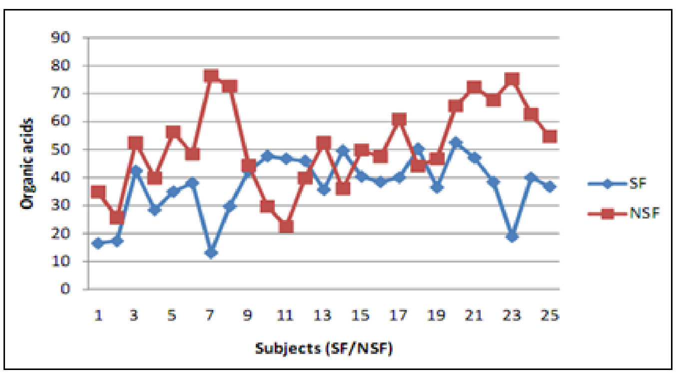

FIG. 3: GRAPH SHOWING COMPARISON BETWEEN ORGANIC ACIDS OF STONE FORMERS AND NON STONE FORMERS

CONCLUSION: It was concluded from the studies that evaluation of total organic acids in urinary samples of stone formers and non stone formers can be used as a clinical test to separate a SF from NSF. Reduced organic acids in stone formers may be due to defective metabolic pathways in the kidneys as most of the organic acids in urine belong to the acids of glycolytic and citric acid pathways. Patients with calcium oxalate renal stone have found to excrete less organic acid as found by the experiments. This is due to the fact that citric acid content is less in stone formers. Citric acid is the most important inhibitor of stone formation. It inhibits stone formation by forming complex with calcium, thus reducing the concentration of calcium ions and inhibiting spontaneous nucleation and crystal growth.

As citric acid content is less in stone formers, chances of formation of stones are more whereas in non stone formers, organic acid content is more, so there is less or no chance of formation of stones. Thus, both groups could be separated on basis of total organic acid content in urine.

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CONFLICT OF INTEREST: Nil

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