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Risk Factor of Cystinuria and Applicable of Reliable Screening Test

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Abstract:

One approach is to calculate the proportion of patients (pediatrics) with cystinuria disorder and know the efficacy of reliable cyanide nitroprusside test. We can say that a significant relationship between family history, and recurrence of urinary stone with cystinuria disorder. On the other hands, cyanide – nitroprusside test is simple to perform and should be carried out in the routine examination of cystinuria since early diagnosis of a cystinuria enables to timely treatment and family counseling, helps the patients in avoiding incorrect treatment, prevents the recurrence of renal stone and a serious a consequence of renal failure.

Cystinuria is an inherited metabolic disorder categorized by the abnormal transport of some amino acids such as cystine, lysine, arginine, and ornithine. However, untreated cystinuria can cause the formation of calculi in the urinary system. The serious feature of cystinuria associated with stone disease which caused by defect in the intestinal absorption of cystine.

In clinical practice the test of cystinuria was carried out using sodium nitroprusside test. The specimens which include 110 urine samples was collected from pediatrics from ESWL unit in Al- Sader medical city and others.

Our results are limited to the behavior of the cystinria in pediatrics. Thus there are 15 cases were positives and 95 cases which are negatives. Prevalence was reported to be 14 % in studied population of Iraq country. Our plan to conduct through investigation of the risk factors associated with this disorder, such as family history and previous history of renal stone occurrence. As already stated, an analysis of results shows increased prevalence of cystinuria in persons whom belongs to the families afflicted with renal stone, since results demonstrated that RR = (1.58) (CI 95% = 0.87-2.22) and OR = (2.70)(CI 95% = 0.78-10.13) , and the prevalence = 45.5 %, additionally to that previous history occurrence exhibited RR = (2.30) (CI 95% = 1.37-2.92), OR = (7.52) (CI 95% = 1.79-36.37) and the prevalence = 41. % .

Keywords: Cystinuria, Sodium nitroprusside test, prevalence, Odd ratio.

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Introduction

Cystinuria can be defined as an autosomal recessive disease which is occurred because of the imperfect transport of the amino acid cystine and other amino acids such as lysine, ornithine and arginine in the gastroentric tract and renal tubules [1,2] , thus low solubility of cystine will enhance its deposition in the urinary tract [3]. The insufficient reabsorption of cystine during the glomeruli filtration for amino acid , causing an immoderate amounts of it in urine and eventually cause the development of stone particularly when the urine is neutral or acidic [4].

The treatment of cystinuria is based on two aspects the first is to change the urine features that the major amount of cystine discharged is preserved in a soluble state, so as to avoid its precipitation while the second is to decrease the absolute amount of cystine excreted [5,6].

Methods

The samples were collected during the routine medical care for the pediatrics in the ESWL unit. The information was both personal and familial taken in our consideration. As a screening study for the cystinuria, a freshly voided specimens (110 cases) of urine from pediatric in Al- Sader teaching hospital and others. The samples was examined on the patient's first visit to the laboratory of ESWL unit, respected the obvious data, the analysis was carried out for cystinuria. The screening test was achieved by using cyanide- nitroprusside test. Cyanide –nitroprusside test was standarized using a standard curve ranged from 6 to 30 mg/dl. For accurate results calling used to order the patients for collecting typical sample.

Results

The simplest case to consider is when patients can be classified into two groups according to the results of an investigation, a clinical signs, the presence or absence of family history about stone disease and if the current patients have previous renal stone disease. Table (1) show that descriptive of enrolled data about averages ages of patients according to their sex, stone location, radiological activity of stone and their percentages. Our results studied family history as a risk factor for cystinuria, it was found the odd ratio (OR =2.70, CI 95 % = 0.78-10.13) and relative risk was RR = 1.58. Additionally, the results explained the significant ($p< 0.01$) relationship between cystinuria and recurrent of stone (OR = 7.52, CI 95% = 1.79-36.37) and RR = 2.30 as shown in table 3.

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Table 1: Descriptive data of children with urinary stones in studied population.

	Age (mean ± SD)	No.	Range	Percent
Sex:				
Male	5.53 ± 3.38	75	1-12 year	68 %
	6.37 ± 2.94	35	1.5-12 year	32%
Position of urinary stone:		No.		Percent
Unilateral stone:		88		80%
Left kidney		50		46 %
Right kidney		38		35 %
Bilateral stone		8		7%
Vesical stone		7		6%
Ureteric stone		7		6 %
Radiological activity:				
Radiopaque		78		86%
Radiolucent		24		22%

Table 2: Family history as a risk for developing cystinuria in children in the studied population.

RR=1.58(0.87-2.22 OR=2.70(CI 95% 0.78-10.13) P value >0.05

		Family history		Total
Result of screening test		Yes	No	
	yes	10	5	15
	No	40	55	95
Total		50	60	110

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Table 3: Evaluating recurrent stone by cystinuria screening test.

		Recurrent of urinary calculi		Total
Result of screening test		present	absence	
	yes	12	3	15
	No	33	62	95
Total		45	65	110
OR RR P value		7.52(1.79-36.37) 2.30(1.37-2.92) < 0.01		
Evaluating test data		percentage		
Prevalence Sensitivity Specificity PPV NPV		41% 27 % 95 % 80 % 65%		

OR: odds ratio , RR: relative risk, PPV: positive predictive value , NPN: Negative predictive value

Discussion

Cystinuria is a rare but important cause of urinary stone disease because of the formation of cystine urinary calculi [(7)]. In normal persons there are 0.4% of filtered cystine is lost in the urine[(8)]. Two transport mechanisms, a high and a low-affinity system, are responsible for cystine reabsorption in the proximal tubular cells. In cystinuria the absorption of cystine, along with the three other dibasic amino acids, ornithine, arginine & lysine, via the high affinity process is reduced [(9, 10)] It is the insolubility of cystine that leads to the pathological process of calculus formation.

The current study seems at first sight to be linked of family history and cystinuria as suggested by study the odd ratio. The results show a significant relationship between them, and this study reports that children who are belong to afflicted family with urolithaisis are nearly one and half (1.58 times) as likely to suffer a cystinuria disease if they have urinary calculi.

Cystinuria is a hereditary disease, if your parents or other relatives have it, you then have a higher chance of having it than another person who does not have a relatives with cystinuria. Early studies suggested that families with affected members that there are at least three types of cystinuria [(11)]. Three

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types are based on measurements of urinary cystinuria in the parents of affected children, as well as of the patients themselves. Cystinuria has been described as one of the most common genetic disorders in amino acid transport. prevalence was reported to be 14 % in studied population of Iraq country.

The prevalence of cystinuria globally is 1 per 7000 with widespread variation UK 1:2000; Australia 1:4000; Japan 1:18 000; Sweden1:100 000; Libyan Jews 1:2500.It accounts for 6-8% of urinary stones in paediatric patients and 1-2% of urinary stones in adults[(11)]. The widespread variation suggest that unless it is known that the diagnosis is almost always correct, it is wise to evaluate a diagnostic test on the patients with the same prevalence of the disease as those for whom the test will be analysed. Cystinuria has been recognized in the medical history for almost two centuries. The authors postulated the cause of cystinuria being a defective common transport mechanism of the dibasic amino acids (including cystine, lysine, arginine and ornithine) in the renal tubules[(12,13)].

In the current study we observed that the sensitivity and specificity of the sample 27 % and 95 % respectively. We can consider three ways of categorizing patients: their true condition, the diagnosis and the test results. When we calculate the sensitivity and specificity of the test we do this in relation to the diagnosis, but we do not necessary know that the diagnosis is always correct. Unless the diagnosis is perfect, so that it always gives the patient's true status (positive or negative), we are evaluating the test's ability to predict the diagnosis rather than the patient's true disease status. Sensitivity and specificity of the test in relation to the true state are related to the prevalence of abnormality.

Cystinuria is basically a renal disease. Cystinuric patients, when symptomatic, can form stones since their early lives. 41% of these patients will have their first stone identified in the first decades of life. Stones formation recurs throughout their lives and the life time risk of having bilateral urolithiasis can be as high as 7%. In the past, cyanide nitroprusside test had been used as a screening test, a Cyanide cleaves cystine into cysteine; the nitroprusside then binds with the sulfide moiety of cysteine, producing a purple colour when cystine was present. This study suggested that cyanide nitroprusside used as a simple and economic test for cystinuria as a screening test. However, urine samples were analyzed in our laboratory using the obvious test after compared with a gold standard. On the other hand, it is important to take the test limits of specificity and sensitivity in our consideration, by this test we able to discern 14 % of cystinuria in 110 cases of our population an addition to that the false positive results are found in homocystinuria, acetonuria, and patients taking ampicillin or other sulfur-containing medication[(14)]. With the advancement of other investigation modalities, this test has been out of favor. Successful diagnosis of cystinria often requires clinical information (i.e., detailed record of patient's history, presentation and clinical examination findings), results of relevant clinical/radiological diagnostic tests, and results of routine laboratory tests, in addition to those specific for inherited metabolic diseases. Therefore, good communication between clinical and laboratory staff is important in improving the chances of correct diagnosis. If clinical manifestation strongly indicates the presence of cystinuia, it would be advisable to seek assistance of well-established for the determination of cystine concentration in urine. Such confirm a diagnosis will guide to intensity of future management to the treatment and prevention of cystinuria[(15)].

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In conclusion, the cyanide-nitroprusside test is important screening test for identification the cystinuria. Perfect diagnosis is basically depends on the patient`s true status, regarding to the interference with other drugs and others diseases. In such as cases we were advised to repeat test and ordered to get the typical sample. With the advisement of the current analysis we are advise to applied the cyanide-nitroprusside test as a routine screening test for cystiniuria.

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