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Prevalence and Risk Factors of Urolithiasis in Children with Cerebral Palsy

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Authors' contributions

This work was carried out in collaboration among all authors. Author GEE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MAEG and AKAS managed the analyses of the study. Author AHD managed the literature searches. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Introduction: Cerebral palsy (CP) is due to damage occurring to the developing brain. This damage can occur during pregnancy, delivery, the first month of life, or less commonly in early childhood. Cerebral palsy is one of the most common causes of physical disability in childhood. Rates of cerebral palsy appear to be similar in both the developing and developed world. The overall CP morbidity rate will automatically increase unless a substantially improved outcome in survivors can be achieved. Children with CP are predisposed to many complications including renal stones.

Aim of the Study: The aim of this study was detection of prevalence and risk factors of urolithiasis in children with cerebral palsy.

Subjects and Methods: This cross sectional case control study was conducted on forty children suffering from cerebral palsy who were attending the Pediatric Neurology Unit of Tanta University Hospital through the period from March 2018 to March 2019. Forty age and sex matched children were taken as a control group.

Inclusion Criteria: Children suffering from different types of cerebral palsy at any age.

Exclusion Criteria: Children whose parents refuse to participate in the study, children receiving drugs that can cause renal stones.

A- Hematological Investigations: Total serum calcium, serum uric acid, serum creatinine.

B- Urinary: Complete urine analysis, urine culture,and urinary chemistry.

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C - Imaging Study: Plain X-ray of abdomen. Pelvic and renal ultrasonography.
Results: Renal stone were detected in 12.5% of children with CP. Urinary tract infection, immobilization, hypercalcemia, hypercalciuria and hyperuricemia were the risk factors detected in this study.
Conclusion: Children with CP are liable to develop renal stones more than normal children.

Keywords: Urolithiasis; cerebral palsy; brain damage; postural dysfunction.

1. INTRODUCTION

Cerebral palsy (CP) is a heterogeneous group of permanent, non-progressive clinical syndromes that are characterized by motor and postural dysfunction. These conditions, which range in severity, are due to abnormalities of the developing brain resulting from a variety of causes. Although the disorder itself is not progressive, the appearance of neuro-pathologic lesions and their clinical expression may change over time as the brain matures [1]. Beside the motor impairments, sensation, perception, cognition, communication, behavior, epilepsy and muscle-skeletal problems are also accompany to CP [2].

In the past few decades, the global incidence of urolithiasis in children, which is associated with considerable morbidity and recurrence, has increased considerably. Many causes, such as metabolic, genetic, anatomical, dietary and environmental risk factors, have been attributed to this increase [3].

Indeed, the increase in urolithiasis can be accounted for in changes in nutrition patterns (including increased consumption salty fast foods or high-protein diets), increasingly sedentary lifestyles,and the global rise in obesity, global warming and climate changes. Furthermore, improved and increasingly systematic screenings for metabolic risk factors for urolithiasis have likely contributed to the inflation of incidence [4].

There were some limitations of this study because of the small sample size and there was no facilities to perform more serum and urinary investigations because of high cost, but our aim was to attract the attention toward the importance of investigating children with CP for urolithiasis which can cause many problems to the child as pain or hematuria without awareness of the parents or medical personnels.

1.1 Aim of the Work

The aim of this study was detection of prevalence and risk factors of urolithiasis in children with cerebral palsy.

2. SUBJECTS AND METHODS

This cross sectional case control study was conducted on forty children suffering from cerebral palsy who were attending the Pediatric Neurology Unit of Tanta University Hospital through the period from March 2018 to March 2019. Forty apparently healthy children of matched age and sex served as a control group.

2.1 Inclusion Criteria

The presence of children that are suffering, from different types of cerebral palsy, at any age.

2.2 Exclusion Criteria

- Children whose parents refuse to participate in the study.
- Children receiving drugs that can cause renal stones e.g. topiramate (antiepileptic drug), ephedrine (used to treat asthma and congestion), sulfamethoxazole – trimethoprim and carbonic anhydrase inhibitors.

2.3 Methods

All children in this study were subjected to the following after an informed consent from their parent and approval from the Ethical Committee of Tanta University Hospital:

- History taking.
- Demographic data: name, age, sex, consanguinity, and socioeconomic status.
- Obstetric history, developmental history, dietetic history and family history.
- Carful physical and neurological examination.
- Gross motor function classification system (GMFCS) to classify the severity of functional impairment in children with cerebral palsy [5].
- Specific investigational studies [6].

2.3.1 A- Hematological investigations: [6]

- Total serum calcium.
- Serum uric acid.
- Serum creatinine.

2.3.2 B- Urinary investigations

2.3.2.1 Complete urine analysis

(RBCs, pus, cast, crystals, proteinuria) [7].

Midstream morning samples were collected in sterile wide mouth containers under complete aseptic conditions.Samples were subjected immediately to laboratory examinations or kept at 4 c.

2.3.2.2 Urine culture

A urine culture is a test to detect and identify organisms (usually bacteria) that may be causing a urinary tract infection. Samples were cultured to blood agar media with the surface streak method for detection of bacteria. They also were cultured with disposable measured loops in order to count pure cultures. The urine cultured within one hour of collection if not refrigerated. However, refrigerated samples stored up to 24 hours before plating the sample [8].

Urine culture is quantitative procedure. A calibrated inoculating loop that holds 0.01 or 0.001 ml of urine is inserted vertically into the urine sample and used to transfer the urine to a sterile agar plate. The urine is spread evenly across the plate with a glass rod as opposed to streaking the plate with the loop. This procedure is usually performed on plates of 5% sheep blood agar, which detects growth of most organisms, and on plate of MacConkey agar or other selective and differential medium for isolation of gram-negative organisms [9].

Urine is normally sterile and there should be no growth. Greater than 100.000 CFU/ml of any single colony type is considered significant in some patient population and clinical setting as supra pubic aspiration [10].

2.3.2.3 Urinary chemistry

- Urinary calcium.
- Urinary creatinine.
- Urinary magnesium.

Although the measurement of urinary calcium excretion using 24 hr urinary analysis is essential for the diagnosis of hypercalciuria, the procedure is often difficult to apply in young children. Thus, random urinary calcium/creatinine ratio (UCa/Cr) has been used to overcome such difficulties. The 24-hour urine calcium excretion could be predicted with reasonable confidence from the calcium/creatinine concentration ratio of the second urine specimen passed in the morning [11].

2.3.3 C - Imaging study

- Plain X-ray of abdomen.
- Pelvic and renal ultrasonography.

The study was approved by the local ethical committee of Faculty of Medicine, Tanta University. Written patient consent was obtained from the parents of all included children.

2.4 Statistical Analysis

The data were coded, entered and processed on computer using SPSS (version 18) (Levesque, 2007).

3. RESULTS

There was no statistically significant difference between children with CP and control children regarding Age, Sex and Consanguinity.

This table showing that types of C.P were spastic (80%), atonic (7.5%), extra pyramidal (2.5%) and mixed (10%). Regarding causes prematurity was (55%), post anoxic (25%), meningioencephaletic (15%) and congenital malformations (5.0%). Regarding associated manifestation epilepsy was (37.5%), hearing impairment (12.5%), visual impairment (15%) and intellectual disability (75%). Regarding gross motor function classification system level II was (2.5%), level III (5%), level IV (10%) and level V (82.5%).

There was statistically significant increase in total serum calcium, serum uric acid and serum creatinine among children with CP than control children.

There was no statistically significant difference between children with CP and control children regarding RBCS, casts and protinuria.

There was statistically significant difference between children with CP and control children regarding pus cells and crystals (higher among children with CP).

Urine culture was positive (greater than 100.000 CFU/ml) in 17.5% (7 out of 40) in children with CP and 7.5% (3 out of 40) in control children (Escherichia coli and Klebsiella pneumonia was detected).

Table 1. Demographic data of the studied groups

Object	Parameter	Children with CP	Control children	Statically test	P. value
Age (years)	Range	3 – 14	3 – 14	t.test= 0.108	0.744
	Mean±SD	8.30 ± 2.98	8.08 ± 3.15		
Sex NO. (%)	male	28(70.0%)	23(57.5%)	X^2=1.352	0.245
	female	(30.0%)12	(42.5%)17		
Consanguinity No.(%)	-ve	(87.5%)35	(95.0%)38	1.409	0.235
	+ve	5(12.5%)	(5.0%)2		

*X^2 =chi square test, t. test=Student's t-testSignificant * < 0.05*

Table 2. Clinical characteristics of children with CP (Types, Causes, Associations and Gross motor function classification system)

Object	Parameter	Children with CP	
		No.	%
Type of C.P	Spastic	32	80
	Atonic	3	7.5
	Extra pyramidal	1	2.5
	Mixed	4	10
Causes	Prematurity	22	55
	Post anoxic	10	25
	Meningioencephaletic	6	15
	Congenital brain malformations	2	5
Associated manifestation	Epilepsy	15	37.5
	Hearing impairment	5	12.5
	Visual impairment	6	15
	Intellectual Disability	30	75
Gross motor function classification system (GMFCS)	II	1	2.5
	III	2	5
	IV	4	10
	V	33	82.5

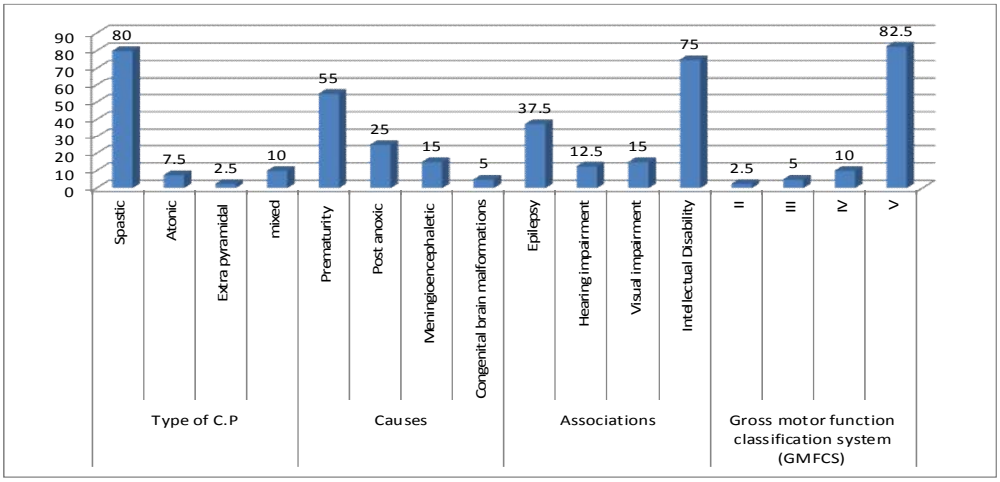

Fig. 1. Types of C.P, causes, associated manifestation and gross motor function classification system (GMFCS) among Children with CP

There was statistically significant increase in urinary calcium / creatinine ratio level in children with CP than control children.

There was no statistically significant difference between children with CP and control children regarding urinary magnesium / creatinine ratio.

This table showing regarding to plain X ray of abdomen no abnormal data in (87.5%) and positive stone was present in (12.5%) regarding to renal ultrasound no abnormal data in (87.5%) and positive stone was present in (12.5%).

From this study we concluded: Children with CP are liable to develop renal stones. Renal stones were found in 12.5% of children with CP included in this study. Urinary tract infection, immobilization, hypercalcemia, hypercalciuria and hyperuricemia were the risk factors detected in this study.

4. DISCUSSION

CP is a chronic motor disorder that various efforts failed to prevent its occurrence. In most cases, the cause is unknown and prematurity remains the most common risk factor. Children with CP suffer from multiple problems and potential disabilities such as mental retardation, epilepsy, feeding difficulties, vision, and hearing impairments. Screening for these conditions should be part of the initial assessment [12].

Also, children suffering from CP may suffer from other complications that can pass unnoticed including the development of renal stones.

Therefore, this study aimed to investigate children with cerebral palsy for the possible urolithiasis.

In the current study, there was no statistically significant difference between children with CP and controls as regard to age and sex This is consistent with El-Tallawy et al. [13] who aimed to determine the prevalence and subtypes of CP and risk factors for the disease among children and adults in El-Quseir City, located in the Red Sea Governorate in Egypt.

Table 3. Hematological investigations of the studied groups

Variable	Parameter	Children with CP	Control children	t. test	P. value
Total serum calcium mg/dl	Range	10 – 13	9 – 11	8.392	0.001*
	Mean±SD	11.32 ± .95	9.89 ± 0.51		
Serum uric acid mg/dl	Range	1.34 – 6.3	3.12 - 4.40	5.913	0.017*
	Mean±SD	4.10 ± 1.07	3.66 ± 0.39		
Serum creatinine mg/dl	Range	0.66 – 1.70	0.50 – 1.0	5.050	0.001*
	Mean±SD	0.95 ± 0.27	0.70 ± 0.13		

*Significant * < 0.05, t. test=Student's t-test*

Table 4. Complete Urine analysis of studied groups

Variable	Parameter	Children with CP No.(%)	Control children No. (%)	X^2	P. value
RBCS	< 5/HPF	34(85.0%)	36(90.0%)	0.4570	.4990
	+ve (>5/HPF)	6(15.0%)	4(10.0%)		
Pus cells/HPF	< 5/HPF	32(80.0%)	37(92.5%)	6.135	0.013*
	+ve (>5/HPF)	8(20.0%)	3(7.5%)		
Casts	Nill	38(95.0%)	40(100.0%)	2.051	0.152
	+ve	2(5.0%)	0(0.0%)		
Crystals	Nill	34(85.0%)	40 (100.0%)	6.486	0.011*
	+ve	6(15.0%)	0(0.0%)		
Protinuria	Normal < 4 ml/m^2/hr.	39(97.5%)	40(100.0%)	1.013	0.314
	+ve	1(2.5%)	0(0.0%)		

*X^2 =chi square test, Significant * < 0.05*

Table 5. Urine culture among studied groups

Variable	Concentrations	Children with CP No. (%)	Control children No.(%)	X^2	P. value
Urine culture	< 100.000 CFU/ml	33 (82.5%)	37 (92.5%)	1.829	0.176
	> 100.000 CFU/ml	7 (17.5%)	3 (7.5%)		

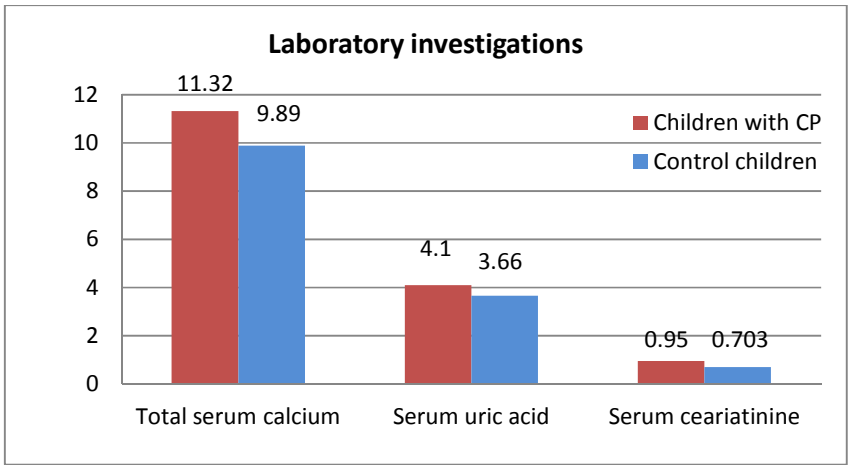

Fig. 2. Laboratory investigations of the studied groups

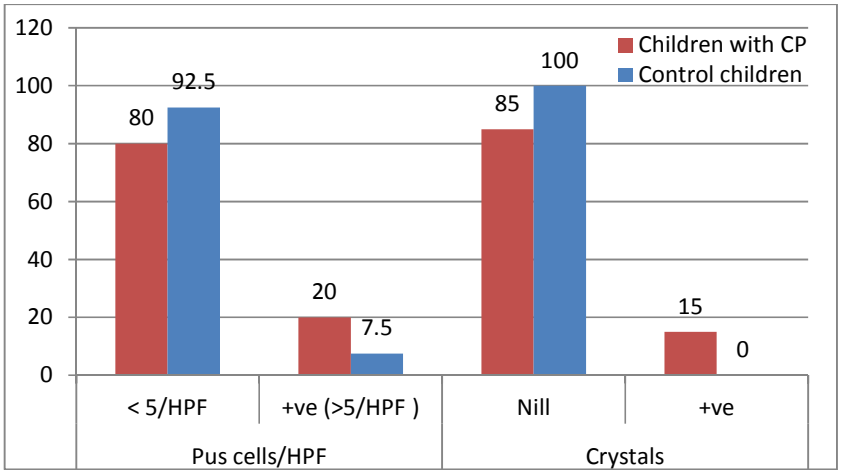

Fig. 3. Pus cells and crystals of the studied groups

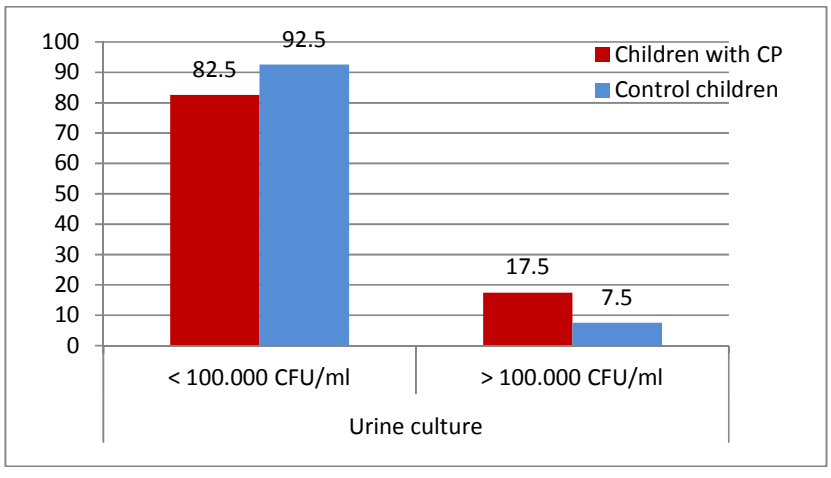

Fig. 4. Urine culture among studied groups

Table 6. Urinary chemistry among the studied groups

Variable	Parameter	Children with CP	Control children	t. test	P. value
Urinary calcium / creatinine ratio	Range Mean±SD	0.00 - 0.26 0.16 ± 0.06	0.01 - 0.19 0.010 ± .003	16.483	0.001*
Urinary magnesium/ creatinine ratio	Range Mean±SD	0.05 - 0.11 0.07 ± 0.016	0.02 - 0.12 0.07 ± 0.029	0.005	0.996

*Significant * < 0.05, t. test=Student's t-test*

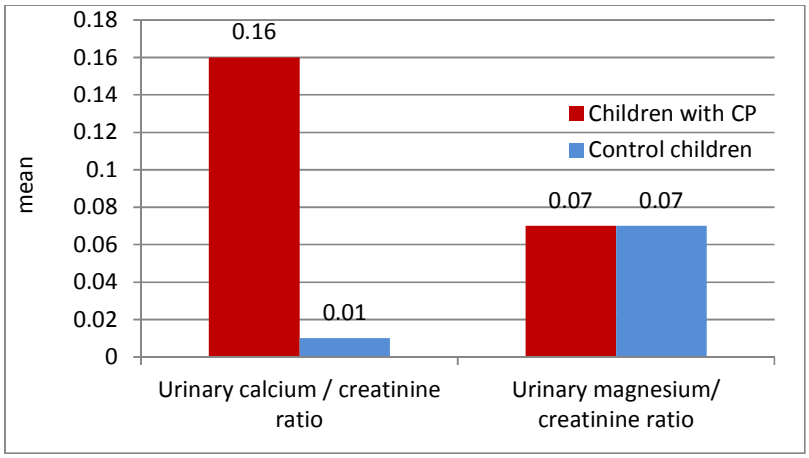

Fig. 5. Graphical representation of urinary chemistry among the studied groups

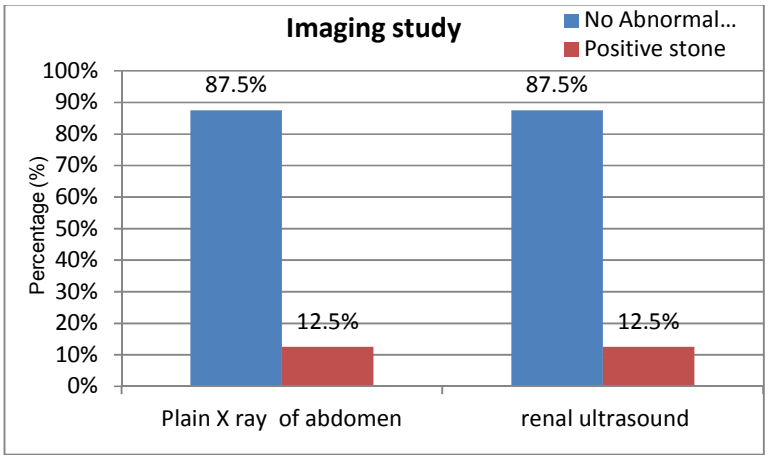

Fig. 6. Graphical representation of imaging study (Plain X ray of abdomen and renal ultrasound) among children with CP

Table 7. Imaging study (Plain X ray of abdomen and renal ultrasound) among children with CP

Criteria	Result	Children with CP	
		No.	%
Plain X ray of abdomen	No Abnormal Data	35	87.5
	Positive stone	5	12.5
Pelvic and renal ultrasound	No Abnormal Data	35	87.5
	Positive stone	5	12.5

*X^2 =chi square test, Significant * < 0.05*

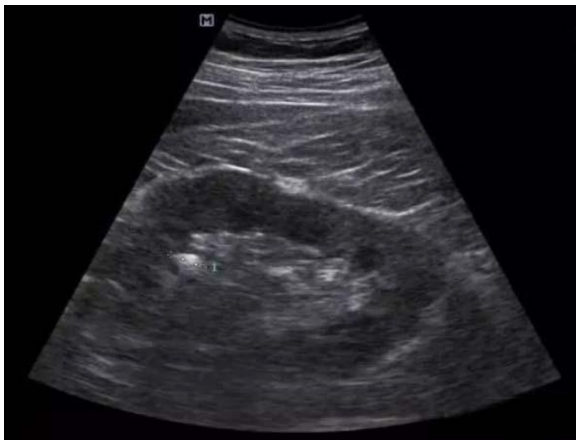

Fig. 7. Pelvi abdominal ultrasound examination of male patient aged 7 years showing a small echogenic stone seen within the upper renal calyx of right kidney with no associated backpressure changes

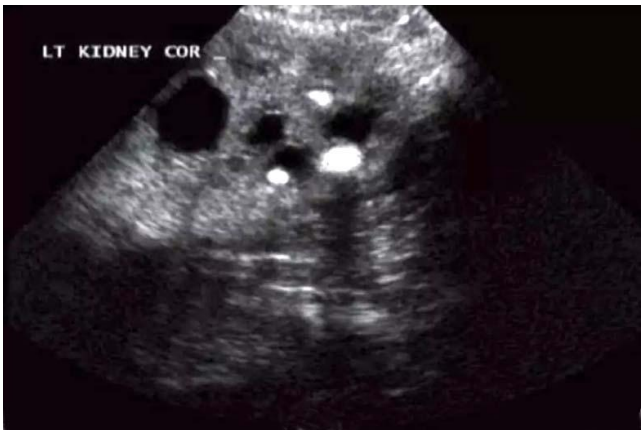

Fig. 8. Pelvi abdominal ultrasound examination of female patient aged 5 years showing cortical renal cysts and three echogenic stones seen within the middle renal calyx and renal pelvis of left kidney (nephrocalcinosis) with associated minimal backpressure changes

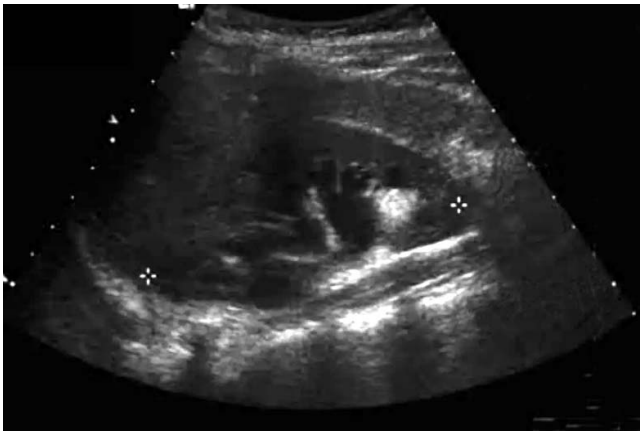

Fig. 9. Pelvi abdominal ultrasound examination of male patient aged 9 years showing a rounded echogenic stone seen within the lower renal calyx of left kidney with no associated backpressure changes

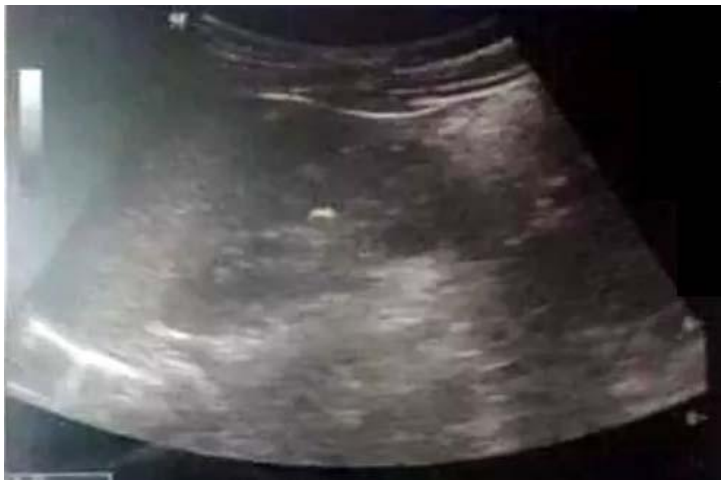

Fig. 10. Pelvi abdominal ultrasound examination of male patient aged 6 years showing a small echognic stone seen in the upper renal calyx of left kidney with no associated back pressure changes

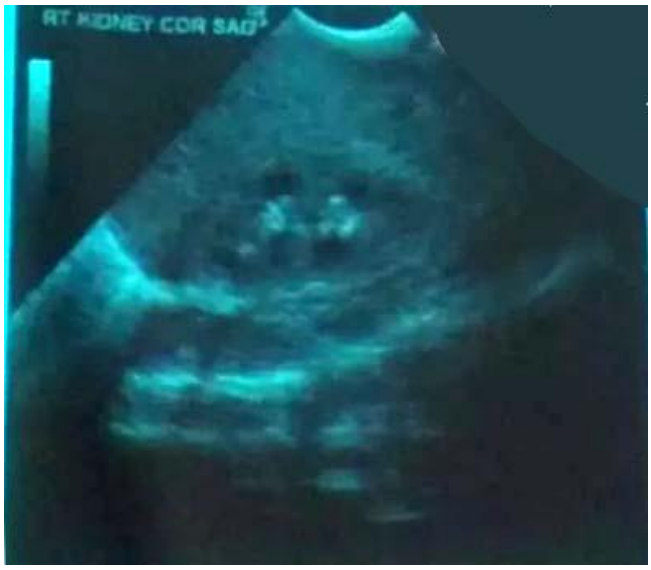

Fig. 11. Pelvi abdominal ultrasound examination of male patient aged 5 years showing multiple variable sized echogenic renal stones seen within the pelvi calyceal system of left kidney with associated minimal back pressure changes

The results of the present study revealed that the incidence of CP was higher in boys than girls. Boys represented 70% and girls represented 30% of cases. This accords with the results of Aggarwal et al. [14] who reported a high male to female ratio (4:1). They stated that the male preponderance may be attributed to reporting bias due to male preference and female neglect in local population.

These results were also convenient with the findings of Yasin and Abd-elaazem [15] who reported that the ratio was higher among boys than girls in Bani_Mazar, Minya, Egypt. They explained their results due to neglection of periodic caring for mothers with girls sex of fetus.

These findings weren't convenient to El-Tallawy et al. [13] who stated that the prevalence rate of CP was higher among girls than boys in El-Kharga District- new Valley (Egypt).

The present study showed that, types of CP were Spastic (80%, mostly diplegia), atonic (7.5%) and

mixed (10%). The higher incidence of spastic CP in our study is mostly due to the high incidence of prematurity in our cases.

This is in agreement withh Abas et al. [16] who aimed at identifying the prevalence and the disability profile and associated comorbidities of CP cases in a prospective cross-sectional study from referral centres of physiotherapy and rehabilitation in Bani-Mazer district, Elminia Governorate, Egypt. They found spastic CP in (72.5%), dyskinetic (16%), ataxic (7%) and hypotonic (4.5%) and also agrees with [13].

Also, Aggarwal et al. [14] found that spasic CP was the most common type of CP in their study. They reported that higher incidence of spastic diplegic CP may be attributed to higher preterm survival in developed countries compared to developing countries. There was no correlation between the types of CP with gestational age as compared to western studies, which have shown diplegic CP is more common in preterm compared to term children. They attributed this to the lower incidence of preterm children in their study.

Skrablin et al. [17] reported that, possible causes of CP related to prematurity involve development of the brain. Babies born too early are at risk for intraventricular hemorrhage, Periventricular leukomalacia, which reflects injury to the white matter of the brain, is also more likely in babies born prematurely than in those born at term. Both intraventricular hemorrhage and periventricular leukomalacia increase the risk of CP. In addition, children born preterm have a combination of antenatal and perinatal risk factors, and possible combination of interdependent risk factors was observed more often [18]. Therefore, early intervention programs such as the massage intervention developed by Guzzetta et al.,[19] based on manipulation of the extrauterine environment, have been used in preterm infants with the aim of improving development and functional outcomes.

This study showed that, regarding associations, Epilepsy was present in (37.5%). Hearing impairment present in (12.5%). Visual impairment present in (15%). Intellectual Disability present in (75%). These accords with the results obtained by Sellier et al. [20].

The higher incidence of epilepsy in this study was attributed to the increased number of cases of spastic CP which has a higher rate of epilepsy than in other types of CP.

This was explained by the fact that children with CP might suffer extensive brain injury including the cortex, deep white matter, and central nuclei, and therefore they are liable to develop epilepsy. Andersen et al. [21] Epilepsy in children with CP also has been related to impaired intellectual performance [22].

In the current study, the majority of children with CP (82.5%) had severe motor disability (GMFCS V).

Dalvand et al. [23] stated that GMFCS could be considered as a gross proxy for evaluating the cognitive deficit and Hundozi-Hysenaj [24] suggested thatepilepsy was correlated to the level of GMFCS.

The present study revealed that five out of forty (12.5%) children suffering from CP had renal stones detected by plain X ray and ultrasonography. Four were males and one was a female and two of them had positive family history of renal stones.

It should be mentioned that in this study we excluded children who were receiving topiramate for the treatment of epilepsy because it increases the risk of urolithiasis [25].

We did not find any published literature that assessed the occurrence of renal stones in children with CP to compare the results of this study with them.

However, Gnessin et al. [26] performed aretrospective analysis of patients with musculo-skletal anomalies including cerebral palsy who underwent nephrolithotomy between April 1999 and June 2009 and had follow-up 24-hour urine studies was performed. Patients with musculo-skletal anomalies included spinal cord injury, myelomeningocele, muscular dystrophy, multiple sclerosis, cerebral palsy, or other clinical syndromes causing kyphoscoliosis and contractures.

Gnessin et al. [26] reported that stones were infectious in etiology in 18.4% and 6.2% in musculo-skletal and control groups, respectively. Thus, most patients harbored stones of metabolic origin. Metabolic stones in the musculo-skletal group were composed of 52.7% hydroxyapatite, 10.5% calcium oxalate, 7.9% brushite, 2.6% uric acid, 0% cystine, and 7.9% other. Metabolic stones in the control group were 50.5% calcium oxalate, 16.4% hydroxyapatite, 11.5% brushite, 10.8% uric acid, 4.3% cystine, and 0.3% other.

Gnessin et al. [26] concluded thatalthough patients with musculo-skletal anomalies are traditionally thought to harbor infection-related calculi, most will be found to have calculi of metabolic etiology. The incidence of calcium phosphate stones is high in this group of patients, perhaps reflecting their high urinary pH.

In this study renal stones were formed more in males than in female patients (4:1). This concurs with the previous findings of male preponderance of renal calculus disease. Males on average have a larger body size and a three-fold higher lifetime risk of stone formation than women [27].

On the other hand, other studies reported a higher incidence of renal stones in females than males. Scales et al. [28] observed a dramatic increase from 1997 to 2002 of the adjusted rate of discharges for stone disease in females in a representative sample of United States population with a change in the prevalence by gender of treated stone disease from a 1.7:1 to 1.3:1 male-to-female ratio. The increasing incidence of nephrolithiasis in females might be due to lifestyle associated risk factors, such as obesity.

Also, Lieske et al. [29] reported a decrease from 3.1 to 1.3 male-to-female ratio during the last 30 years. The male-to-female ratio of the incidence of symptomatic ureteral stones was different between the Hispanic (1:1) and the Caucasian (2.5:1) population whereas no significant sex differences were noted in the symptomatic presentation of kidney stones [30].

In developing countries the male-to-female ratio range from 1.15:1 in Iran [31] and 1.6:1 in Thailand [32] to 2.5:1 in Iraq [33] and 5:1 in Saudi Arabia [34].

Kidney stones often have no definite, single cause. Several factors may increase the risk. Kidney stones form when urine contains more crystal-forming substances, such as calcium, oxalate and uric acid, than the fluid in urine can dilute. At the same time, urine may lack substances that prevent crystals from sticking together, creating an ideal environment for kidney stones to form. Any child who has had a kidney stone is at increased risk of developing another stone in the future [35].

Pediatric urolithiasis is an important medical problem, which has seen an increasing incidence in developing countries [36].

VanDervoort et al. [37] documented a similar trend in that the incidence of urolithiasis in the pediatric population had augmented nearly five folds during the last decade in USA.

In this study we performed some hematological and urinary investigations, trying to detect some of the possible causes of renal stones in the studied children with CP.

In the current study the percentage of Pus cells and Crystals was higher among CP children and urine culture was positive in 17.5% of cases indicating urinary tract infection in those children.

This agrees also with other studies such as Ryakitimbo et al. [38] who aimed to determine the burden of UTI among children with CP in Moshi. This was an analytical cross-sectional study that was conducted from September 2016 to March 2017 at Comprehensive Community Based Rehabilitation in Tanzania Moshi and Kilimanjaro Christian Medical Centre Neurological Pediatrics Outpatient Clinic Pediatric Health, Medicine and Therapeutics. The study included all children aged 2-18 years who were diagnosed to have CP (99 children with CP). UTI was detected in 13.1% of cases. This agrees also with other previous studies [5,39].

Children with a UTI have an increased risk of developing urolithiasis. Bacteria with urease activity such as Proteus spp., Klebsiella spp. and Staphylococcus aureus can increase the risk of urolithiasis because urease increases urinary pH, which promotes the supersaturation of urine with magnesium ammonium phosphate (as in struvite stones) and calcium phosphate (as in apatite stones). Struvite stones account for approximately 2.1– 24% of all urolithiasis cases in children [40].

Although patients with UTI are at increased risk of stone formation, the treating clinician must discriminate between infection-induced stones and a urinary stone merely accompanying an infection. Unfortunately, this distinction is not always easily achieved. However, stone analysis might be useful to make the distinction: struvite stones, which are difficult to treat and have tendency to recur, cause serious morbidity [4].

This study revealed that children with CP had statistically significant higher levels of serum calcium than controls. This is in agreement with Tasdemir et al. [41] who found significantly

higher serum calcium levels in children with CP than those of controls [41].

This study also revealed that children with CP had statistically significant higher levels of urinary calcium, detected by CA/creatinine ratio, than controls.

This accords with Shaw et al., [42] who demonstratedhypercalciuria in children with CP and Gnessin et al., [26] who found higher calcium/ creatinine ratio in children with musclo-skletal disorders including CP.

Müller et al. [43] suggested that Immobilization causes bone dissolution because it increases bone calcium resorptionleading to hypercalcemia and hypercalciuria in children. They reported a case of a 10-year-old boy who developed 2 stones in the pelvis of his left healthy kidney after only 8 days of immobilization. He was on bedrest after pyeloplasty done for a ureteropelvic junction obstruction on the right side. Compared to references in literature this patient showed stone formation very early during the course of immobilization. This may be applied to children with CP who have difficult mobilization especially those with severe motor disability level (V) who were the majority of our cases.

On the other hand Unay et al. [44] found that serum levels of calcium were not significantly different between the studied CP group and control group.

Most kidney stones are calcium stones, usually in the form of calcium oxalate. Oxalate is a naturally occurring substance found in food and is also made daily by the liver. Some fruits and vegetables, as well as nuts and chocolate, have high oxalate content [45].

Dietary factors, high doses of vitamin D, intestinal bypass surgery and several metabolic disorders can increase the concentration of calcium or oxalate in urine [46].

Calcium stones may also occur in the form of calcium phosphate. This type of stone is more common in metabolic conditions, such as renal tubular acidosis [45].

This study revealed that children with CP had higher levels of serum uric acid than controls. This hyperuricemia may result in hyperuricosuria which may increase the risk of stone formation, but we did not assess urinary uric acid.

Uric acid stones can form in people who don't drink enough fluids or who lose too much fluid, those who eat a high-protein diet, and those who have gout. Certain genetic factors also may increase the risk of uric acid stones [47].

Uric acid can result from a diet high in purines, which are found especially in animal proteins such as beef, poultry, pork, eggs, and fish. The highest levels of purines are found in organ meats, such as liver and fish. Eating large amounts of animal proteins can cause uric acid to build up in the urine. The uric acid can settle and form a stone by itself or in combination with calcium. It is important to note that a person's diet alone is not the cause of uric acid stones. Other people might eat the same diet and not have any problems because they are not prone to developing uric acid stones [47].

In our community, the usual belief of mothers of any handicapped child is to give high quality food to the child aiming to improve his general condition and subsequently his disability. Even if the child can not swallow the mother gives regular feeds through the nasogastric tube. This high quality diets often includes meat, vegetables, fish, milk, and fruits which are rich in proteins.

Also, these children are usually given vitamins in high doses especially vitamin D which may also cause hypercalcemia and calciuria.

Children with cerebral palsy are also predisposed to frequent infections and usually given frequent antibiotics, mostly including ceftriaxone and ampicillin which may increase the risk of stone formation [25].

The presentstudy did not show statistically significant difference in urinary magnesium detected by magnesium/ creatinine ratio between children with CP and controls.

Magnesium is an inhibitor of calcium crystal growth, and contributes to urinary calcium oxalate and calcium phosphate supersaturation. However, low urinary magnesium in isolation has not been identified as a common cause of kidney stones, nor has magnesium supplementation been proven as an effective therapy for stone prevention [48].

In the current study, there was statistically significant increase in serum ceriatinine among CP children than controls.

In the present study we could not assess the composition of renal stones by the metabolic workup because non of the affected children performed nephrolithotomy.

Renal stone formation is a complex process that depends on several factors, including the urinary concentration of stone-forming ions, urinary pH and flow rate, various metabolic factors of crystallization and anatomic factors that encourage urinary stasis. Predisposing causes for urolithiasis have been recognized in >75% of children with urinary tract calculi [49].

In some studies in pediatric patients, especially in those from European centers, the primary cause of urolithiasis is often cited as infection [50] However, the etiologic paradigm for urolithiasis in children has shifted from predominantly infectious to metabolic causes [51].

Studies over the past few decades have identified metabolic disorders in 33-95% of pediatric patients with urolithiasis, whereas structural urinary abnormalities and infection were found in 8-32% and 2-24% of cases, respectively [4].

Renal stone disease is a significant medical problem, which has experienced an increasing incidence worldwide. This may be due to the increased awareness of the entity or to the routine use of ultrasonography in children presenting with specific or nonspecific symptoms for urolithiasis [36].

Factors that place a child with CP at increased risk for developing kidney stones are:

- Family history of stones.
- Decreased water intake or long periods of dehydration.
- Repeated urinary tract infection.
- Diet high in sodium and/or protein.
- Obesity.
- Decreased activity level.
- Defects in the urinary tract.
- Use of certain medications.

There were some limitations of this study because of the small sample size and there was no facilities to perform more serum and urinary investigations because of high cost, but our aim was to attract the attention toward the importance of investigating children with CP for urolithiasis which can cause many problems to the child as pain or hematuria without awareness of the parents or medical personnels.

5. CONCLUSION

From this study it can be concluded that;

- Children with CP are liable to develop renal stones.
- Renal stones were found in 12.5% of children with CP included in this study.
- Urinary tract infection, immobilization, hypercalcemia, hypercalciuria and hyperuricemia were the risk factors detected in this study.

6. RECOMMENDATIONS

From this study it can be recommended that:

- It is important to investigate children with CP for the possibility of urolithiasis.
- A future study should be done on a larger number of children and adolescents with cerebral palsy to evaluate prevalence and risk factors of urolithiasis in children with cerebral palsy.
- Further study should be done to investigate the composition of renal stones in children with CP to give them the chance of proper treatment and prevention.

CONSENT AND ETHICAL APPROVAL

All children in this study were subjected to the following after an informed consent from their parent and approval from the Ethical Committee of Tanta University Hospital: History taking, carful physical and neurological examination, gross motor function classification system (GMFCS), specific investigational studies.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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