ULTRASOUND MASS SCREENING OF NEONATES WITH CONGENITAL ANOMALIES OF THE KIDNEY AND URINARY TRACT (CAKUT)

By

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ABSTRACT

Background: Congenital anomalies of kidney and urinary tract represent the most common cause of end stage kidney disease in infant and children. Early detection of these changes allows timely initiation of more specific diagnostic studies, and of therapeutic interventions**.**

Objective: This study was done to detect the incidence and risk factors of (CAKUT) in neonate.

Patients and methods: This study was carried out on 390 neonates in the incubator of Al-Matariya Teaching Hospital and Al-Hussein University Hospital during the period from July 2014 to July 2015.All neonates were included except those with apparent congenital anomalies, surgical emergency orinborn errors of metabolism. All neonates after parent consents were subjected to full history, clinical examination and investigated by pelvi-abdominal ultrasound, serum creatinine level, and some cases subjected to more investigations in the form of computed tomography scan with intravenous urographin contrast medium, ascending cystourethrography and TC 99m DTPA dynamic renal scan.

Results: The overall incidence of congenital anomalies of kidney and urinary tract was 3.3%. Positive family history of renal anomalies together with maternal history of diabetes mellitus and maternal age above 35 years were considered predictors for renal anomalies by binary logistic regression.

Conclusion: Congenital anomalies of kidney and urinary tract (CAKUT) were major health issues and were the leading cause of ESRD in pediatric population.

Key words: Ultrasound, neonates, CAKUT.

INTRODUCTION

Congenital anomalies of kidney and urinary tract (CAKUT) comprise a spectrum of malformations that occur at the level of the kidney as hypoplasia and dysplasia, collecting system as hydronephrosis and megaureter, bladder as ureterocele and vesicoureteral reflux, or urethra as posterior urethral valves(**Song and Yosypiv, 2011**).

Cases of CAKUT were detected in3.7 % of kidneys in one ultrasound examination at the following points of time at least: (i) prenatally in 18.2 % of newborns (ii) 3 - 7 days postnatally in 65.2 % and (iii) 17 %during the 6-month follow-up (**Richter et al., 2012**).

The main etiologic factor of chronic kidney disease in children is represented by CAKUT(**Harambat et al.,2012).**

Genetic as well as environmental factors that are present before or during pregnancy are presumed to be involved in

deficient kidney development (**Schwaderer et al., 2007**)

Every child who suffers from CAKUT was born with a different set of nephrons. Our duty as pediatricians is to preserve as long as possible the function, avoiding a worse dysplasia caused by obstruction and recurrent UTIs(**Rodriguez, 2014**).

Practical criteria for surgical intervention in CAKUT are recurrent UTIs, especially in children under 1 year of age, children with VUR of high bilateral grade, worsening hydronephrosis > 3 cm or with noticeable changing during the follow-up, bilateral dilation and pain symptoms. Surgical correction involves preferably endoscopic, laparoscopic and robotic approach(**Arlen and Cooper, 2015).**

The aim of this work was to detect the incidence and risk factors of CAKUT.

PATIENTS AND METHODS

This study was carried out on 390 neonates in the incubator of Al- Matariya Teaching Hospital and Al-Hussein University Hospital during the period from July 2014 to July 2015.

Inclusion criteria: All neonates (preterm and term) of both genders (male and female) from 3 days to 30 days.

Exclusion criteria: 1- Apparent congenital anomalies. 2- Inborn errors of metabolism 3-Neonates with surgical emergencies.

After parent consents, all those neonates were subjected to full history, clinical examination, serum creatinine level and pelvi-abdominal ultrasound for congenital anomalies of kidney and urinary tract. By using Simens–Adara ultrasound machine – Japan, we measured the kidneys as regard length, width, thickness, corticomedullarydifferentiation. Also, detection of any urinary tract abnormalities and renal pelvic measurement were included.

Selected cases were subjected to further investigations in the form of:

- Computed tomography (CT) scan with intravenous urographin contrast medium, after skin sensitivity test.

- TC 99m DTPA dynamic renal scan.

- Ascending cystourethrography.

Statistical methodology: Analysis of data was done by IBM computer using SPSS (statistical program for social science version 16) as follows:

● **Description** of quantitative variables as mean, SD and range.

● **Description** of qualitative variables as number and percentage.

● **Unpaired t-test** was used to compare two groups as regard quantitative variables.

● **Chi-square test was** used to compare two groups as regard qualitative variables.

● **Fisher exact** test was used instead of chi-square when one expected cell less than or equal 5.

Binary logistic regression was used for detection of independent predictors by using enter technique.

● P<0.05 was significant.

RESULTS

Statistical analysis of the demographic data of the studied cases showed that the male gender was more than female.Gestational age was between 37-

42 weeks, and maternal ages of studied cases were in the age group 20-35 years, with more cases delivered by cesarean section**.** The body weight of studied cases was in the category of 2.5-3.99 kg. There was an irrelevant prenatal history (Table 1).

Table (1): Statistical analysis of the demographic data of the studied cases

Count / Variables	No.	%
1) Gender		
Males	218	56%
females	172	44%
2) Gestational age (weeks)		
$\leq$28	16	4.1%
29-32	58	14.9%
33-36	128	32.8%
37-42	188	48.2%
3) Post natal age (days)		
3-7	247	63.3%
8-30	143	36.7%
4) Maternal age (years)		
Less than 20	24	6.1%
20-35	290	74.4%
More than 35	76	19.5%
5) Mode of delivery		
Vaginal	130	33.3%
Cesarean section	260	66.7%
6) Body weight (kg)		
$\leq$1	15	3.8%
1-1.49	53	13.6%
1.5-2.49	114	29.2%
2.5-3.99	205	52.6%
>4	3	0.8%
7) Prenatal history		
Consanguinity	65	16.6%
Medical history		
Irrelevant	334	85.6%
Diabetes mellitus	21	5.4%
Hypertension	20	5.1%
Rheumatic heart	7	1.8%
Epilepsy	3	0.8%
Asthma	5	1.3%

MOFTAH M. RABEEA *et al.*

Pelvi-abdominal ultrasound of the studied cases showed that the overall incidence of congenital anomalies of kidney and urinary tract was 3.3% (Table 2).

Table (2): Pelvi-abdominal ultrasound of the studied cases

Count / Ultrasound	Number	Percent
Normal	377	96.7%
Abnormal	13	3.3%

Distribution of different types of congenital anomalies of kidney and urinary tract among abnormal cases showed that mild hydronephrosis was considered the most frequent congenital anomaly of UT among the studied cases (Table 3).

Table (3): Distribution of different types of congenital anomalies of kidney and urinary tract

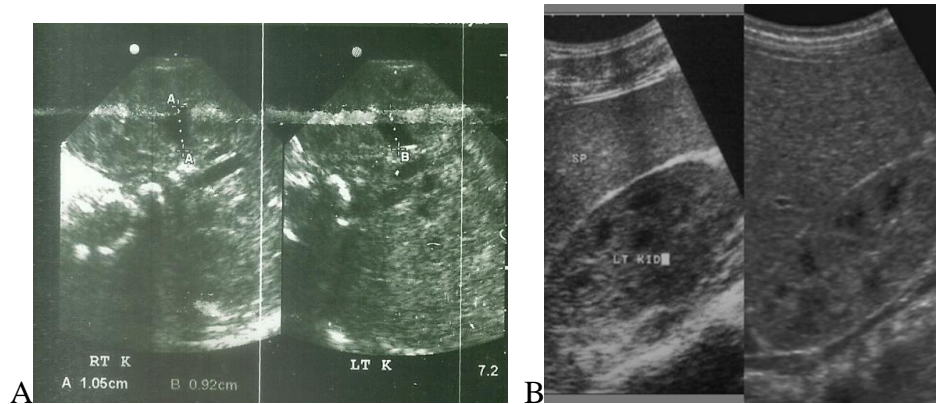| Count / Variables	No.	%
Mild hydronephrosis	5	38.4%
Moderate hydronephrosis	2	15.4%
Severe hydronephrosis	1	7.7%
Polycystic kidney	1	7.7%
Nephrocalcinosis	2	15.4%
Hypoplasia	1	7.7%
Renal agenesis and compensatory hypertrophy	1	7.7%
Total	13	100%

Figure (1): Ultrasound examination showed bilateral mild hydronephrosis, renal pelvic diameter of rt. Kidney was 10.5 mm and of lt. kidney was 92 mm (A). Follow up of the ultrasound one month later showed normal kidney and the case diagnosed as transient hydronephrosis (B).
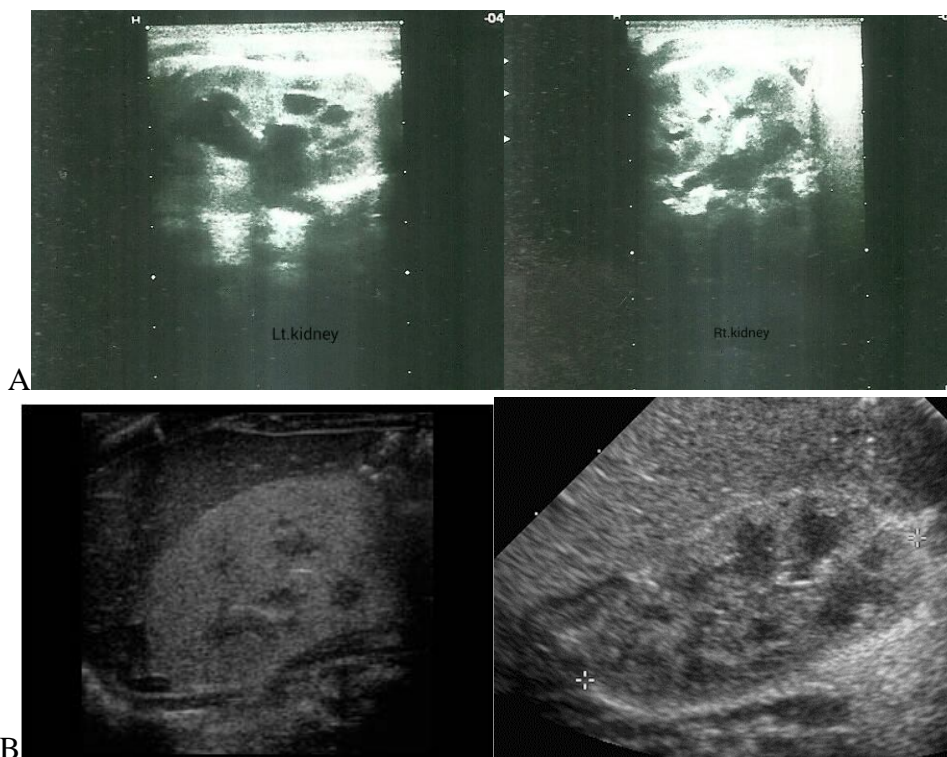

Figure (2): Ultrasound examination showed moderate hydronephrosis with dilatation of pelvicalyceal system(A). Follow up of the ultrasound 3 months later showed normal kidney and the case diagnosed as transient hydronephrosis (B).
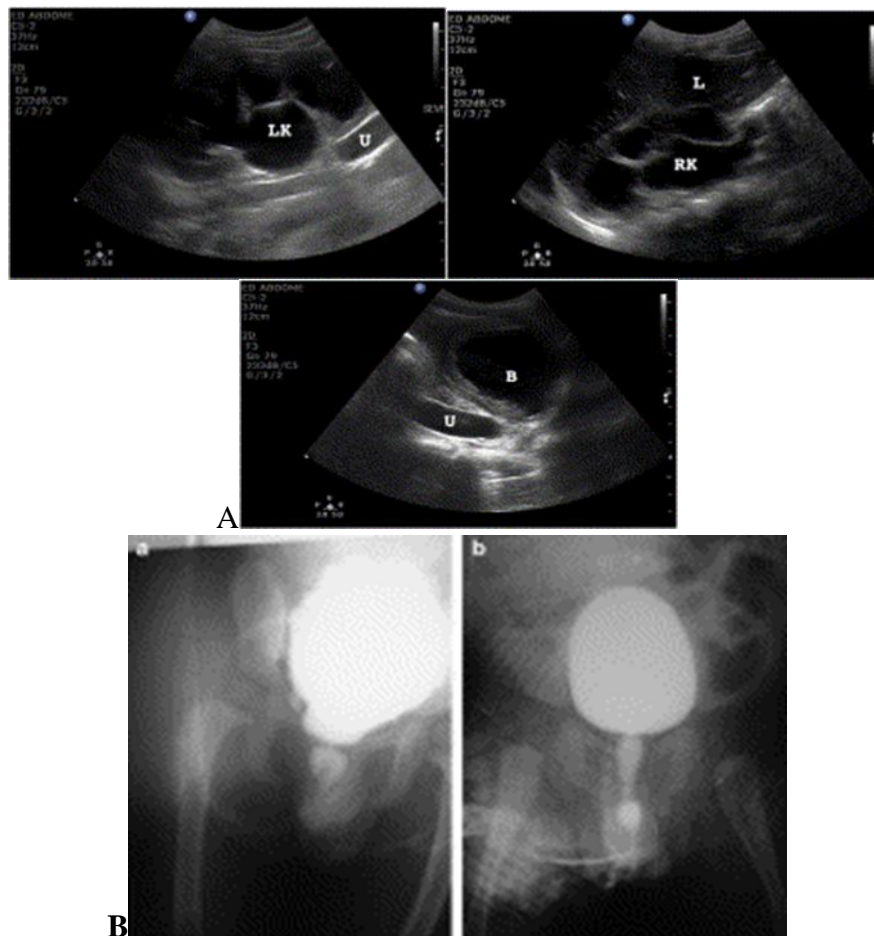
MOFTAH M. RABEEA *et al.*

Figure (3): Ultrasound examination showed bilateral moderate hydronephrosis and enlarged filled bladder (LK: left kidney, RK: right kidney, U: ureter B bladder, L: liver) (A). The case underwent at 1 month old an ascending cystourethrography showed that there was a congenital posterior urethral valve (B).
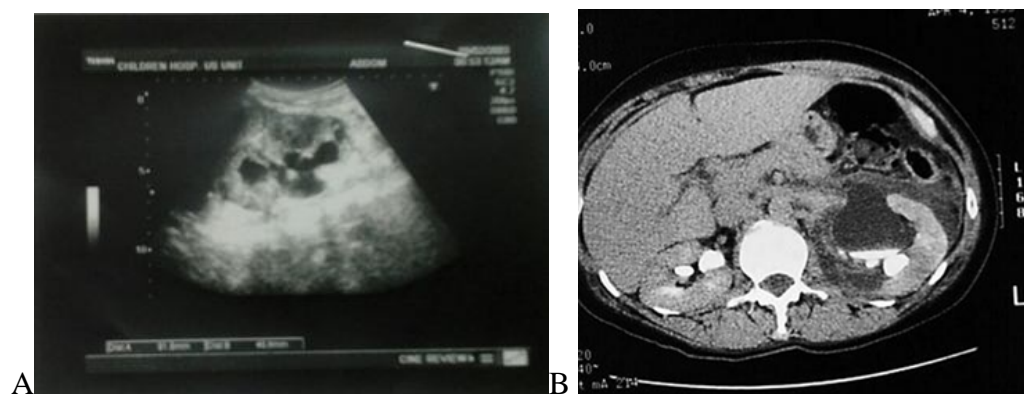

Figure (4): Ultrasound examination showed severe left hydronephrosis with dilatation of pelvicalyceal system and loss of corticomedullary differentiation (A). 3 months later, the case underwent computed tomography (CT) scan with intravenous urographin contrast medium showed that there is pelvi-ureteric junction obstruction (B).
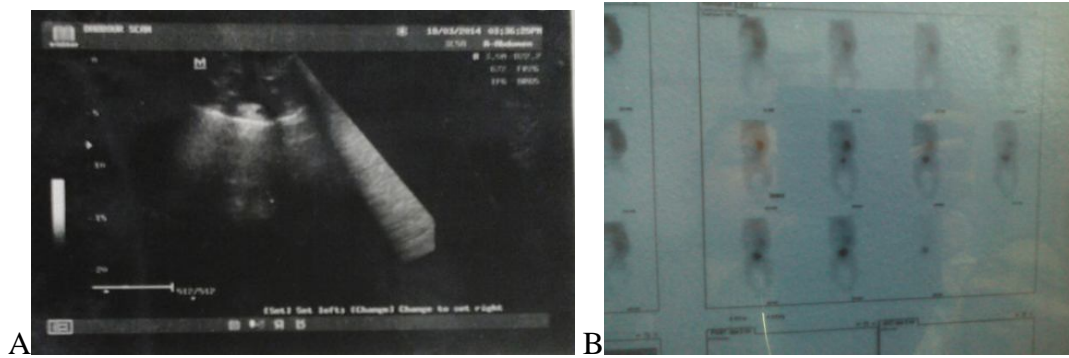
Figure (5): Ultrasound examination showed left enlarged polycystic kidney with marked thinning out of parenchyma (A). The case was subjected to TC 99m DTPA dynamic renal scan showed compensated overall renal function with markedly diminished left renal function (B).
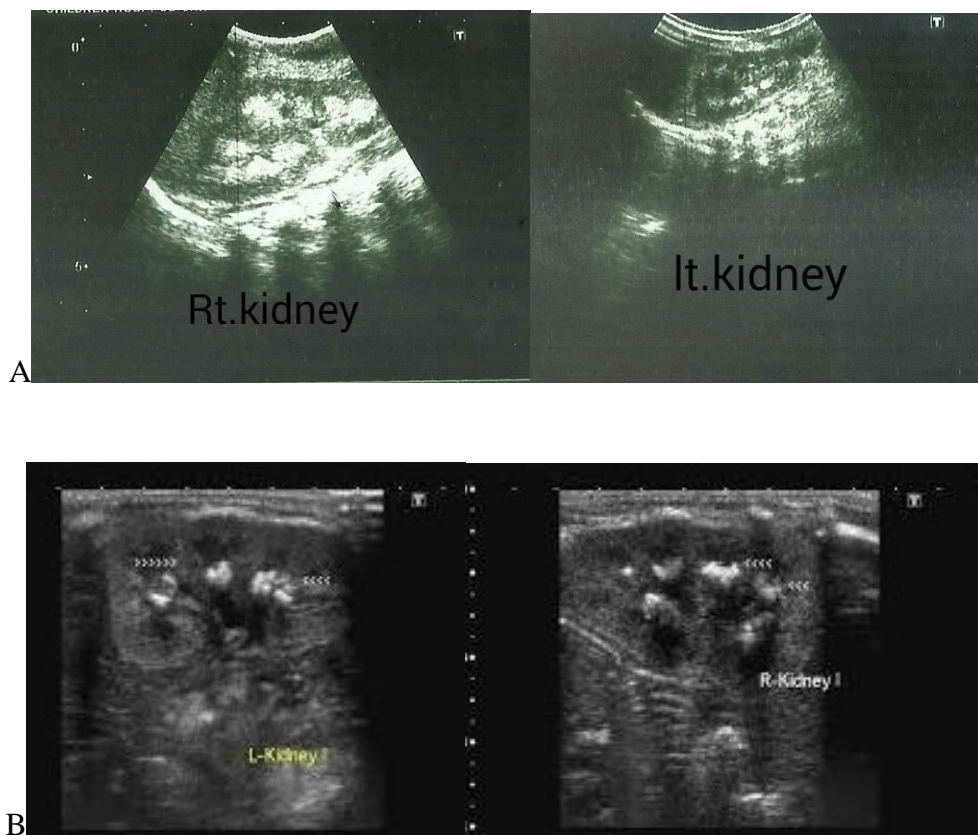

Figure (6): Ultrasound examination showed bilateral nephrocalcinosis of two cases (A) and (B).
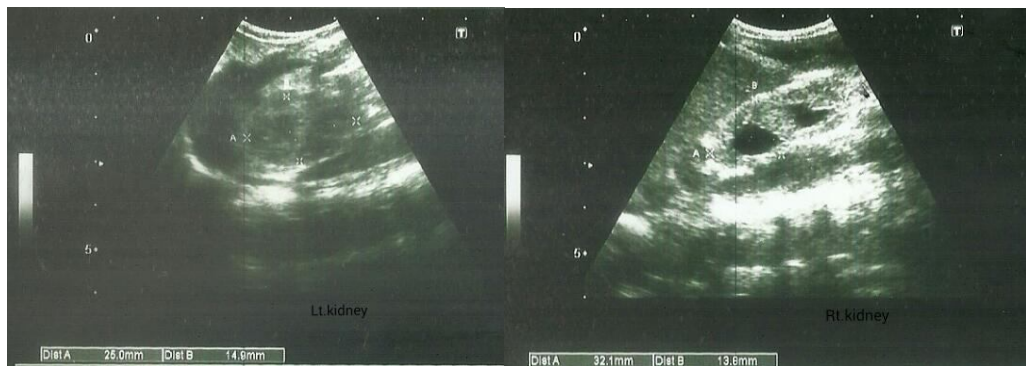
Figure (7): Ultrasound examination showed bilateral renal hypoplasia with longitudinal diameter of left kidney 25mm, and longitudinal diameter of right kidney 32mm.
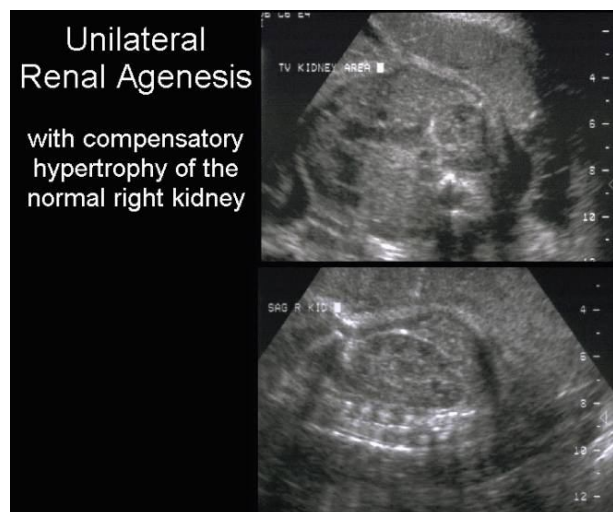

Figure (8): Ultrasound examination showed left renal agenesis with compensatory right renal hypertrophy.

Comparison between abnormal cases and normal neonates in relation to demographic data showed that there was no significant difference between both groups by using chi-square test and no significant relation to other variables (Table 4).

Table (4): Comparison between abnormal cases and normal neonates in relation to demographic data.

Count / Variables	Urological congenital anomaly No	Yes	P
Gestational age (weeks)			0.27
≤28	19(5%)	1(7.7%)	
29-32	56(14.9%)	2(15.4%)	
33-36	123(32.6%)	1(7.7%)	
37-42	179(47.5%)	9(69.2%)	
Body weight (kg)			0.76
≤1	15(4%)	0	
1-1.49	52(13.8%)	1(7.7%)	
1.5-2.49	111(29.4%)	3(23.1%)	
2.5-3.99	196(52%)	9(69.2%)	
≥4	3(0.8%)	0	
Post natal age (days)			0.77
≤7	239(63.4%)	8(61.5%)	
8-30	138(36.6%)	5(38.5%)	
Maternal age (years)			0.63
Less than 20	24(6.4%)	0	
20-35	280(74.3%)	10(76.9%)	
More than 35	73(19.4%)	3(23.1%)	

Comparison between abnormal cases and normal neonates in relation to mode of delivery showed that majority of cases with congenital anomaly group delivered vaginally with significant difference by using chi-square test, and no significant relation to other variables. Comparison between abnormal cases and normal neonates in relation to prenatal history showed that no statistically significant difference between both groups by using chi-square test. Comparison between abnormal cases and normal neonates in relation to family history of CAKUT showed that frequency of positive family history was more among positive group with statistically significant difference by using Fisher exact test. Comparison between abnormal cases and normal neonates in relation to serum creatinine level showed that positive group had higher creatinine level compared to negative with significant difference by using unpaired t-test (Table 5).

Table (5): Comparison between abnormal cases and normal neonates in relation to prenatal history, family history, mode of delivery and serum creatinine level.

Count / Variables	Urological congenital anomaly No	Urological congenital anomaly Yes	P
Mode of delivery			
Vaginal	122(32.6%)	8(61.5%)	0.04
CS	255(67.4%)	5(38.5%)	
Prenatal history			
Consanguinity	65(98.4%)	1(1.6%)	
Irrelevant	316(97.5%)	8(2.5%)	
DM	18(75.7%)	3(14.3%)	6.02
HTN	19(95%)	1(5%)	
RH	7(100%)	0	
Epilepsy	3(100%)	0	
Asthma	5(100%)	0	
Family history of CAKUT			
No	374(99.2%)	11(84.6%)	0.001
Yes	3(0.8%)	2(15.4%)	
serum creatinine level Mean +SD	n = 377 0.46+0.07	N =13 0.69+0.3	0.001

Comparison between abnormal cases and normal neonates in relation to different risk factors showed that Positive family history of renal anomalies together with family history of DM and maternal age above 35 were considered predictors for renal anomalies by binary logistic regression (Table 6).

Table (6): Comparison between abnormal cases and normal neonates in relation to different risk factors**.**

Variables	P	Odd's (95%CI)
Family history of renal congenital anomalies (+ve)	**0.04**	1.1(-0.4-16)
Mode of delivery (vaginal)	0.12	0.9(0.02-11)
Maternal history of DM	**0.08**	1.09(0.2-13.6)
Maternal age >35yrs	**0.09**	0.8(-0.3-12)

CI= Confidence interval

Prognosis of abnormal cases detected by ultrasound showed that the majority of abnormal cases had good prognosis, and only 24% for surgical intervention (Table7).

Table (7): Prognosis of abnormal cases.

Number	Prognosis	Percent
6 cases (5 cases with mild hydronephrosis and one case with moderate hydronephrosis)	Spontaneous improvement	46%
2 cases (one case with nephrocalcinosis of prematurity and other case with unilateral agenesis)	Follow up	15%
2 cases (one case with renal tubular acidosis and other case with bilateral renal hypoplasia and renal impairment)	Medical treatment	15%
3 cases (one case with severe hydronephrosis diagnosed by C.T. as pelviureteric junction obstruction and another with moderate hydronephrosis diagnosed by ascending cystourethrography as posterior urethral valve and a case with left poly cystic nonfunctioning kidney	Surgical intervention	24%

DISCUSSION

Our study showed that the overall incidence of neonates with congenital anomalies of kidney and urinary tract (CAKUT) was 3.3%,which was similar to **Richter et al. (2012)**.

The most prevalent anomaly was hydronephrosis which was differentiated in groups according to the degree. Grading systems of hydronephrosis have been devised to communicate the degree of upper collecting system dilation. The most common system used was originally designed for grading neonatal and infant hydronephrosis **(Keays et al., 2008)**. Our study showed that 38.4% of abnormal cases were mild hydronephrosis, moderate hydronephrosis represented 15.4%, and severe hydronephrosis represented 7.7%. So, cases with hydronephrosis represented 2% of all sample size. The follow up ultrasound revealed that all cases with mild hydronephrosis showed improve-ment, and also one case with moderate hydronephrosis. These cases were diagnosed as transient hydronephrosis and represented 46% of positive cases. The case with bilateral moderate hydro-nephrosis underwent ascending cysto-urethrography and showed posterior urethral valve. The case with severe hydronephrosis underwent computed tomography with contrast showed pelviureteric junction obstruction. The remaining cases were two cases with nephrocalcinosis represented 15.4%; one of them was nephrocalcinosis of prematurity, and the other was renal tubular acidosis. One case showed polycystic kidney represented 7.7%. One case with unilateral renal agenesis represented 7.7%, and one case with bilateral renal hypoplasia represented 7.7%. Results of our study were similar to **Susanne et al.(2012)** who stated that ultrasound screening of the kidneys and

urinary tract showed hydronephrosis representing about 1.5%.

Our study showed that transient hydronephrosis represented 46% of positive cases which was similar to **Nguyen et al. (2010)** who stated that transient hydronephrosis represents 41-88 % of detected prenatal hydronephrosis which is resolved at birth or in early infancy.

Comparison between abnormal cases and normal neonates in relation to demographic data as gestational age, maternal age and body weight showed no significant difference between both groups and no significant relation to other variables. These results were different from a study which showed that advanced maternal age associated with increased risk of CAKUT **(Margarett et al., 2011).** And different from a study which showed that there were significant differences between cases and controls with regard to average gestational age and average birth weight with increased risk with low birth weight and prematurity **(Nicola et al., 2011).** These differences from these studies can be explained by small sample size of our study.

In comparison between abnormal cases and normal neonates in relation to mode of delivery, our study showed majority of cases with in congenital anomaly group delivered vaginally with significant difference and no significant relation to other variables. These results were different from a study which showed that increased incidence of CAKUT with cesarean section and the reason for this finding is not clear because it is not related to prenatal diagnosis of the malformation **(Nicola et al., 2011).** These

differences from this study can be explained by small sample size of our study.

In relation to prenatal history, our study showed no statistically significant difference between both groups. These results were different from a study which showed that maternal DM is significantly associated with CAKUT **(Margarett et al., 2011).** This difference can be explained by small sample size of our study.

In relation to family history of renal anomalies, our study showed that frequency of positive family history was more among positive group with statistically significant difference which suggests a genetic predisposition. This resultwas similar to**Toka et al.(2010)** who stated that familial cases of CAKUT have been reported which suggests a genetic predisposition.

Serum creatinine level in our study showed that positive group had higher serum creatinine compared to negative with significant difference. The elevated value of creatinine in CAKUT group was related to the case with bilateral renal hypoplasia with high serum creatinine Level. This result was similar to **Lewis et al. (2008)** who stated that small kidneys (decreased amount of functional renal tissue) are the leading cause of renal replacement therapies in children and are much more common than congenital nephrotic syndromes or polycystic kidney disease.

Different risk factors in our study showed that positive family history of renal anomalies together with family history of diabetes mellitus and maternal age above 35 were considered predictors

for renal anomalies by binary logistic regression.

Follow up showed that five cases with mild hydronephrosis and one case with moderate hydronephrosis represented 46% of abnormal cases showed spontaneous improvement, and one case with nephrocalcinosis of prematurity and other case with unilateral agenesis for follow up represented 15%,and one case with renal tubular acidosis and other case with bilateral renal hypoplasia and renal impairment for medical treatment represented 15%,and one case with severe hydronephrosis diagnosed by C.T. as pelviureteric junction obstruction, and another case with moderate hydro-nephrosis diagnosed by ascending cystourethrography as posterior urethral valve, and a case with left poly- cystic nonfunctioning kidney. The three cases for surgical intervention represented 24%. These results were similar to a study which showed that most cases with hydronephrosis give spontaneous resolution except cases with larger initial APD, grade 4 hydronephrosis are independently associated with lower likelihood of resolution, and large initial APD has predictive value for surgical intervention **(Michelle et al., 2011).**

Quirino et al. (2012) stated that, after about 20 years of systematic approach to prenatally detected nephrouropathies, understanding of clinical course and natural history of CAKUT has clearly improved.

CONCLUSION

Patients with CAKUT must be followed until adulthood with strict control of BP and renal function, especially for the high-risk subgroup of infants with associated hydronephrosis at baseline. Prediction of the risk of CKD and hypertension in individual cases is difficult, and therefore, regular follow-up remains the only way of recognizing these subjects.

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MOFTAH M. RABEEA *et al.*

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مسح بالموجات فوق الصوتية لحديثى الولادة لإكتشاف التشوهات الخلقية فى الكلى والمسالك البولية

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خلفية البحث:التشوهات الخلقية في الكلى والمسالك البولية تمثل السبب الأكثر شيوعا للمراحل المتأخرة من أمراض كلى الأطفال، كما أن الإكتشاف المبكر لتلك التغيرات يتيح الوقت المناسب للتدخل المبكر وعمل الفحوصات اللازمة وبداية العلاج.

الهدف من البحث: تحديد نسبة حدوث التشوهات الخلقية في الكلى والمسالك البولية لحديثي الولادة، وكذلك تحديد الأطفال الأكثر قابلية لحدوث تلك التشوهات الخلقية.

المرضى وطرق البحث: أجريت هذه الدراسة على ٣٩٠ طفلاً من حديثي الولادة تتراوح أعمارهم بين ٣-٣٠ يوماً بقسم حديثي الولادة بمستشفى المطرية التعليمي ومستشفى الحسين الجامعي، وذلك في الفترة من يوليو ٢٠١٤ إلى يوليو ٢٠١٥، وقد تم ضم جميع الأطفال الموجودين بالقسم فيما عدا الأطفال الذين يعانون من تشوهات خلقية ظاهرية، أو يعانون من مشاكل جراحية طارئة، أو خلل بالتمثيل الغذائي وقد خضعت جميع الحالات بعد أخذ الموافقة من الأهل لأخذ التاريخ المرضى الكامل والفحص الإكلينيكي الشامل و فحص بالموجات فوق الصوتية وإخبار وظائف الكلى، كما خضعت بعض الحالات إلى فحوصات إضافية عبارة عن عمل أشعة مقطعية بالصبغة، وعمل تصوير بالنظائر الضوئية،وأشعة تصاعدية بالصبغة.

النتائج: أسفرت الدراسة عن اكتشاف ٣.٣% حالة إيجابية من العينة الخاضعة للدراسة، كما أسفرت الدراسة أن الأطفال الذين لديهم إستعداد أعلى للإصابة بتشوهات خلقية بالكلى والمسالك البولية هم من لديهم تاريخ عائلي للإصابة بتشوهات الكلى، ومن يزيد سن الأم لديهم عن ٣٥ عاماً، أو تكون الأم مصابه بالبول السكري.

الخلاصة: التشوهات الخلقية في الكلى والمسالك البولية تمثل مشكلة صحية رئيسية وهي السبب الرئيسي للمراحل المتأخرة من المرض الكلوي في الأطفال، كما أن التشخيص المبكر يتيح وقتا للمتابعة والتدخل المبكر لمنع أو على الأقل إبطاء التدهور.