Association of Autism Spectrum Disorder with Pediatric Kidney Disease

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ABSTRACT

Background; Neurodevelopment deficits have long been recognized as a major complication of pediatric chronic kidney disease (CKD). Some of this impairment has been attributed to the possible effects of kidney failure: uremia, anemia, hypertension and malnutrition,However, no published papers specifically examining the prevalence of ASD within the pediatric nephrology population.

Aim and objectives; this study designed to evaluate the association of autistic spectrum disorder with pediatric chronic kidney diseases.

Subjects and methods; This is an Observational Cross Sectional study that included One hundred children with chronic kidney disease not on dialysis recruited from the Pediatric nephrology Clinic, Pediatrics Department , Faculty of Medicine, Ain Shams University, Cairo, Egypt, during their follow up visits from February 2022 to august 2022 , randomly selected, all selected patient were subjected to detailed history ,full clinical examination and pediatric symptoms check list questionnaire.

Result; no autistic disorders were detected in our studied group but behaviour change was demonstrated in 9 percent of studied group

Conclusion; no correlation between chronic kidney diseases and autism but there is a positive correlation between CKD and behavioral problems .

Keywords; autism spectrum disorder, chronic kidney disease; pediatric.

Introduction

Autistic spectrum disorder is a heterogeneous early-onset and lifelong neurodevelopmental disorder which is highly heritable but with as yet no established biomarkers. Mental health, learning and physical co-morbidities are common***(Lord et al., 2018).***

Over the last 10 years, there has been an increase in the knowledge of genetic basis of kidney disease, with a highly significant overlap between pathogenic genetic copy number variants found in kidney disease (cystic kidney diseases, pyelo-calyceal dilatation, vesico ureteric reflux) and neurodevelopment disorders ***(Loirat et al., 2010).***

However, no published papers specifically examining the prevalence of ASD within the pediatric nephrology population. Kidney disease and ASD can be seen to co-exist in many multisystem genetic disorders ***(Gipson and Johnston, 2017)***.

Autism traits are often not apparent until a child is older, particularly in those with good intellectual ability. The presence of emotional and behavioral difficulties such as anxiety or hyperactivity might cause diagnostic overshadowing in these children which can be attributed to the medical condition ***(Clothier and Absoud, 2020).***

Ethical Considerations.

- Ethical approval will be taken from research Ethics Committee, Faculty of Medicine, Ain Shams University
- An informed written consent will be taken from the parents or care givers of the patients
- Patient data confidentiality were preserved during all study procedure
- The patient and parents have the right to withdraw any time
- There were no conflict of interest regarding the study or publication
- There is no financial support or sponsorship

Sample size:

Joanna Clotheir and Michael Absoud (2020) reported a prevalence of 10.7% (24.224). A sample size of at least 75 cases produces a two-sided 95% confidence interval with a width equal to 0.150 when the sample proportion is 0.10.

inclusion Criteria:

- Known children with CKD stage 1-4 patient
- Both sex
- aged 2-14
- Not on dialysis .

Exclusion Criteria:

- CKD patient on dialysis
- Known patient with other pediatric mental disorders,or Other chronic illness, genetic disorders, organic disease.

Study procedure:

This is an Observational Cross -Sectional study that included One hundred children with chronic kidney disease not on dialysis recruited from the Pediatric nephrology Clinic, Pediatrics Department , Faculty of Medicine, Ain Shams University, Cairo, Egypt, during their follow up visits during the period of February 2022 to August 2022 . all the studied children were subjected to all the following :

I- Full detailed history including :

- Demographic data
- detailed developmental history and family history of learning problems, psychiatric disorders and social disability.
- Antenatal , natal, and postnatal histories
- history of Renal disease (etiology, onset, duration, compliance to treatment)

II- thorough clinical examination with stress on :

- Dysmorphic features.
- Neurodevelopment findings of clinical syndromes associated with ASD .

III- Psychiatric evaluation based on the Clinical Interview For Children And their caregivers to Assess:

- Psychosocial function by using pediatric symptoms check list
- Diagnosis of ASD Using DSM-5 diagnostic criteria
- Assess the severity of autism using the Arabic version of the Childhood Autism Rating Scale (CARS)

Result

Our result will be demonstrated in the following tables:

Table 1: Demographic data distribution among study group

Demographic data	Total (n=100)
Age "years"	
Range	2-15
Mean±SD	8.14±2.33
Gender	
Female	39 (39.0%)
Male	61 (61.0%)
Consanguinity	
No	88 (88.0%)
Yes	12 (12.0%)

This table show demographic data among studied group

Table (2): chronic Kidney Disease distribution among study group

.Kidney Disease	No.	%
Minimal Change Nephrotic Syndrome	76	76.0%
Post Infection Glumerlunephritis	5	5.0%
Bartter Syndrome	3	3.0%
Ig A nephropathy	2	2.0%
Repeated UTI	2	2.0%
Focal Segmental Glomerulosclerosis	1	1.0%
Nephrotic Syndrome without biopsy	1	1.0%
Renal tubular acidosis	1	1.0%
Congenital	**9**	9.0%
Vesicoureteric reflux	*3*	3.0%
Neurogenic Bladder	*2*	2.0%
Posterior uretheral valve	*2*	2.0%
Ectopic Kidney	*1*	1.0%
Hypoplastic Kidney	*1*	1.0%

This table show that the most common chronic renal disease is nephrotic syndrome followed by congenital causes.

Table (3): distribution of significant behavior and emotional problems among studied group

	Total (n=100)
significant behavior and emotional problem	
Attention	*2 (2.0%)*
Anxiety and depression	*8 (8.0%)*
Behavioral interpersonal subscale	*4 (4.0%)*

This table show 9 case of behavior problem most of them 8 case suffer from depression and anxiety behavior changes .

Table (4): DSM5 for autism and CARS distribution among study group

	No.	**%**
DSM5 and CARS for autism		
Negative	100	100.0%
Positive	0	0.0%

This table show negative result for autism

Table (5): correlation between chronic kidney diseases and behavior and emotional problem .

Kidney Disease	**significant behavior and emotional problem**		**Test value**	**P-value**	**Sig**
	No (n=91)	**Yes (n=9)**			
Bartter Syndrome	3 (3.3%)	0 (0.0%)	0.303	0.582	NS
Ectopic Kidney	1 (1.1%)	0 (0.0%)	0.099	0.753	NS
Focal Segmental Glomerulosclerosis	0 (0.0%)	1 (11.1%)	10.101	0.002	S
Hypoplastic Kidney	1 (1.1%)	0 (0.0%)	0.099	0.753	NS
Ig A nephropathy	2 (2.2%)	0 (0.0%)	0.200	0.655	NS
Minimal Change Nephrotic Syndrome	69 (75.8%)	7 (77.8%)	0.018	0.894	NS
Nephrotic Syndrome without biopsy	1 (1.1%)	0 (0.0%)	0.099	0.753	NS
Neurogenic Bladder	2 (2.2%)	0 (0.0%)	0.200	0.655	NS
Post Infection Glumerlunephritis	4 (4.4%)	1 (11.1%)	0.766	0.382	NS
PUV	2 (2.2%)	0 (0.0%)	0.200	0.655	NS
Repeated UTI	2 (2.2%)	0 (0.0%)	0.200	0.655	NS
RTA	1 (1.1%)	0 (0.0%)	0.099	0.753	NS
VUR	3 (3.3%)	0 (0.0%)	0.303	0.582	NS

This table show significant correlation of focal segmental glomerulosclerosis and behaviour change

Discussion:

In this study 100 patients diagnosed as CKD were enrolled with mean age 8.14±2.33 years. Male to female ratio was 1.56:1. male predominance was reported by many other authors from different countries ***(Shi et al., 2021).***

This could be attributed to higher frequency of congenital abnormalities of the kidney and urinary tract (CAKUT) in males ***(Harambat et al., 2012***).

In this study pediatric symptoms check list applied to 100 case of CKD Patient searching for behavior change which reveal 9% percent of cases with positive behavior change most of them show depressive disorder which may be due to Chronic disease increases the risk of depression because it increases economic burden, reduces quality of life, and impairs activities of daily living***(Kim et al., 2022).***

this result go on with other study which shows that Depression seems to be more prevalent in the presence of a chronic disease. Even though survival rates of children with CKD are significantly higher than in the previous decades, issues associated with the disease itself may predispose them to develop depression. The exact prevalence of this psychiatric disorder in pediatric CKD patients varies (10–35%) depending on the progression of CKD (KTx, dialysis, or pre-ESRD) and the age of the child (young children or adolescents)***(Dryjańska et al., 2023).***

In study by ***Kogon et al, 2016*** showed that 7% of children and adolescents with CKD met the study criteria for depression and 5% reported elevated depressive symptoms***(Kogon et al., 2016).***

attention deficit had positive result in our study this go on with meta analysis study on Fifteen studies, with a total of 9304 participants, were included. Cognitive function broadly deteriorated from stage 1 to stage 5. Early stage CKD was associated with a drop in speed of processing, attention, response speed, and short-term memory abilities. Moderate stage CKD was associated with deficits in executive functioning, verbal fluency, logical memory, orientation and concentration***(Brodski et al., 2019)*** it may be due to vascular injury and uremic toxin***(Kim et al., 2022).***

Uremic toxins accumulate in the body fluids of patients with progressive CKD, and have a direct impact on the development of cerebrovascular disease. Recent studies have reported that uremic toxins cause cognitive impairment in patients with CKD. A recent review article established that uremic toxins, such as uric acid, indoxyl sulfate, p-cresyl sulfate, interleukin-1β (IL-1β), IL-6, tumor necrosis factor-α, and parathyroid hormone, are likely to have an impact on the CNS, although the underlying mechanisms have yet to be elucidated***(Watanabe et al., 2014).*** .

It is believed that consanguinity increases recessive gene expression and therefore autosomal recessive disorders by unmasking hidden traits. An autosomal recessive transmission is believed to be a possible genetic contributor to the development of autism spectrum disorder***(Chaste et al., 2012).***

Consanguinity was demonstrated in 12% of our studied patients yet no autistic patient among them it may be due to small study sample

Our study show negative result for autistic manifestation unlike other study which show Kidney disease and ASD can be seen to co-exist in many multisystem genetic disorders . Tuberous sclerosis, for example, is a multisystem disorder resulting from mutations in either the *TSC1* or *TSC2* genes, leading to abnormal signaling in the mammalian target of rapamycin (mTOR) pathway. The condition is commonly associated with autism in up to 61% of patients, with the presence of renal angiomyolipomata, cystic kidney disease and hypertension in 80% ***(Clothier and Absoud, 2021).***

Conclusion:
Patient with chronic kidney disease even not on dialysis has sign of significant behaviour change need to be more investigated
Recommendations:
Despite no positive result with autism in our study it should be investigated in large study group with mainly congenital anomalies of kidney disease
Follow up of patient with CKD on dialysis as well
Limitations
Our result may be explained by small group of congenital disorder involved
Refusal of caregiver to share in the study
Uncooperative patient according to DSM V quastionnaire

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