



Bayley- III Scores of Children with Congenital Anomalies of the Kidney and Urinary Tract

ORIGINAL
ARTICLE

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ABSTRACT

Objective: Congenital anomalies of the kidney and urinary tract (CAKUT) are the most common causes of chronic renal failure in children. Although data about the growth failure and cognitive impairment in children with end-stage renal disease are available, there are insufficient data about the developmental screening in infancy of children with CAKUT. The aim of this study is to evaluate the neurodevelopment of children with CAKUT using the Bayley Scales of Infant and Toddler Development Screening Test, Third Edition (Bayley-III).

Methods: The cognitive, language, receptive communication, expressive communication, global motor, gross motor, and fine motor scores of children aged 1–41 months diagnosed with CAKUT (n=30) were compared with healthy controls (n=32).

Results: There was no significant difference between groups with regard to the age, height, weight, head circumference, body mass index, mid-arm circumference, triceps skinfold thickness and the language, expressive communication, receptive communication, gross motor, fine motor, and global motor scores ($p>0.05$). Maternal age, the weight at birth, and the educational level of mothers were similar in both groups ($p>0.05$). There was no significant relationship between the educational level of mothers, iron deficiency anemia, and Bayley-III scores ($p>0.05$). Cognitive scores of children with CAKUT were significantly lower than scores of the control group ($p=0.04$). Cognitive scores of patients with recurrent urinary tract infection were lower than -1 standard deviation value.

Conclusion: This study demonstrated that children with CAKUT who have a recurrent urinary tract infection history have delayed cognitive developmental outcomes compared with healthy children, as assessed using Bayley-III. The neurodevelopment of these children should be closely followed up and supported in the early period.

Keywords: Child, congenital anomaly, kidney, Bayley-III

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INTRODUCTION

Congenital anomalies of the kidney and urinary tract (CAKUT) include the kidneys, collecting system, or both, and arise as the result of factors affecting nephrogenesis, such as maternal, placental, fetal, environmental, and genetic factors. CAKUT constitute approximately between 20% and 30% of all anomalies determined in the antenatal period, and the overall rate of CAKUT in live and stillborn infants is 0.3 to 1.6 per 1000 (1,2). CAKUT usually progress to chronic renal disease, and they are the most common cause of renal replacement therapy for end-stage renal disease (ESRD) in childhood (3). The ESRD leads to growth failure and developmental delay, cognitive impairment, severe psycho-social adaptation problems, multi-system complications, and an increased mortality and morbidity (4).

One of the commonly used reliable tests for the evaluation of developmental delay in children aged between 1 and 42 months is “Bayley Scales of Infant and Toddler Development Screening Test, Third Edition” (Bayley-III). This test was first described in 1969, revised in 1993, and standardized in 2006 by Bayley (5). Bayley-III assesses the cognitive, language, and motor development of infants and children. The language scale is assessed as receptive and expressive communication, and the motor scale is assessed as gross motor and fine motor subscales.

The ESRD is a risk factor for a low IQ and academic unsuccess in a schoolchild, leading to a neurocognitive developmental delay in the pre-school period when rapid neurologic maturation occurs. Renal disease in early infancy is one of the risk factors for delayed developmental outcomes (6). Differently from literature, we aimed to evaluate the neurodevelopment of children who had CAKUT without ESRD by using the Bayley-III test.

MATERIALS and METHODS

Data of 30 patients with CAKUT aged between 1 and 41 months and 32 healthy children were included in the study. The exclusion criteria were the presence of acquired urinary system anomalies, chronic neuro-muscular diseases, epilepsy, dysmorphic findings or genetic syndromes, hypoxic and/or premature birth history, neonatal hyperbilirubinemia, hypoglycemia history, and surgery history. The Mersin University Ethics Committee approved the study (MEU 2016-113).

The height, weight, head circumference, and mid-arm circumference were measured with standard anthropometric techniques. The left-arm triceps skinfold thickness was measured by using standard Lange calipers and anthropometric measurements recorded from patients' files. We calculated standard deviation scores for each measurement by using the standardized measures for Turkish children (7). Complete blood count, serum ferritin, and urinary anemia results were recorded from patients' files. Iron deficiency anemia was defined as the hemoglobin level <11 mg/dl and ferritin level <12 mcg/L, if these laboratory findings were not attributable to other causes (8). The urinary culture positivity ≥ 2 times was accepted as a recurrent urinary tract infection (UTI) in patients with CAKUT (9). The newborn hearing screening was recorded as normal in all cases.

Data of the cases whose cognitive, language, and motor scale scores had been evaluated with Bayley-III were studied retrospectively. The cognitive scale included thinking, learning, information processing, and problem-solving skills with plays and activities. The receptive communication subscale evaluated hearing, understanding, and responding abilities. The expressive communication subscale evaluated communication abilities using sounds, words, and body language. Coordination of motor skills, sensory and perceptual motor integration, and main locomotion stages were scored with fine and gross motor subtests. The composite test scores scaled as 40–160 were within the normal range of the Bayley-III, the mean value was identified as 100, and a standard deviation (SD) of 15. Infants who had cognitive, language, or global motor composite scores less than 85 were defined as developmentally delayed (5). An experienced specialist, blinded to the diagnosis (K.M.), performed the Bayley-III tests.

Statistical Analysis

In the statistical analysis of data, number (N) and percent (%) values were given as descriptive statistics for categorical socio-demographic variables. The association between the categorical variables was examined by the chi-square test. The normality distribution of continuous variables was tested by the Shapiro–Wilk test. The Student's t-test was used to test the difference between the averages. The analysis of variance was carried out in comparison of the mean values of independent groups. The results were considered to be statistically significant if P-values were less than 0.05.

RESULTS

Data of 62 children (30 patients, 32 controls) were included in the study. Characteristic features and anthropometric measurements were shown in Table 1. The patient and control groups were similar in regard to gender, age, birth weight, and maternal

Table 1. Characteristics and anthropometric measurements of patients and controls

	Patient (n=30)	Control (n=32)	p
Gender			
Female (%)	16 (53)	14 (43)	0.488
Age (month)	27.58±9.30	22.96±9.59	0.087
Birth weight (g)	3301.6±514.9	3211.5±371.5	0.476
Mother's age (years)	30.8±5.3	31.6±5.6	0.638
Weight (SDS)	-0.03±1.13	-0.11±0.79	0.775
Height (SDS)	0.03±1.11	0.07±0.71	0.881
HC (SDS)	-0.14±0.79	-0.02±0.81	0.592
BMI (SDS)	-0.04 ±1.08	0.07±0.79	0.655
MAC (SDS)	-0.50 ±0.69	-0.48±0.67	0.910
TSF (SDS)	-0.17±0.5	-0.02±0.53	0.349

HC; head circumference, BMI; body mass index, MAC; mid-arm circumference, TSF; triceps skinfold thickness, SDS; standard deviation score

Table 2. Diagnosis of the patients and the frequency of recurrent UTIs

Diagnosis	n (%)	Recurrent UTI
		n (%)
Renal parenchymal malformations	6 (20)	2 (16)
Polycystic kidney disease	1 (3)	-
Multicystic dysplasia	1 (3)	-
Renal agenesis	4 (13)	2 (16)
Anomalies of renal embryonic migration	5 (16)	1 (8)
Renal ectopia	3 (10)	-
Horseshoe kidney	2 (6)	1 (8)
Anomalies of the collecting system	19 (63)	9 (75)
Vesicoureteral reflux	6 (20)	4(33)
Ureteropelvic junction obstruction	11 (36)	4(33)
Double collecting systems	2 (6)	1 (8)

UTI; urinary tract infection

age ($p>0.05$). The mean values of the height, body weight, head circumference, body mass index (BMI, kg/m²), mid-arm circumference, and triceps skinfold thickness measurements were similar in both groups ($p>0.05$). Diagnoses of the patients and frequency of recurrent UTI are shown in Table 2. The mean cognitive, language, global motor scores, and mean receptive communication, expressive communication, fine motor, gross motor subscores are shown in Table 3. The mean cognitive score of the patient group was significantly lower than the control group's score ($p=0.04$). There was no significant difference between Bayley-III scores of the groups with or without iron deficiency anemia (Table 4). In the

patient group, Bayley-III scores were statistically similar between the patients who had and did not have a recurrent UTI history. The mean cognitive score of patients with a recurrent UTI was lower than -1 SD value (Table 4). The educational level of mothers, classified as the primary school, secondary school, high school, and university was similar between the patient and control groups ($p>0.05$), and there was not a significant difference between the Bayley-III scores of groups with regard to educational level of mothers ($p>0.05$).

DISCUSSION

Congenital anomalies of the kidney and urinary tract (CAKUT) are the underlying reason of ESRD in 30%-50% of children diagnosed

with it (3). Cognitive impairment and learning difficulties are common in children with ESRD compared to healthy peers. Attention deficit, memory and learning problems, and low IQ scores are observed particularly in dialysis patients. The onset of ESRD in childhood causes more occupational and marital problems in adulthood (10). Therefore, early management of CAKUT is important for preventing complications and unfavorable developmental outcomes.

Psychomotor development is affected by many genetic and environmental factors in childhood. We considered that recurrent UTIs, hospitalizations, or frequent outpatient clinic controls could cause the neuromotor retardation in children with CAKUT based on the influence of chronic diseases on neurocognitive development. In this retrospective study, we evaluated the neurodevelopment of normally growing children with CAKUT and without the onset of ESRD by using the Bayley-III test.

We found the Bayley-III scores to be similar in the language and motor scales. The mean cognitive score of children with CAKUT was significantly lower than the control groups' mean score. The mean cognitive score of patients with a recurrent UTI history was lower than -1 SD value. The febrile UTIs (UTI) incidence in children with CAKUT accompanied by severe hydronephrosis is the highest in the newborn period and the first months of life (11). This period is critical for neurodevelopment, so we consider that recurrent UTIs, frequent hospitalization, and parenteral treatments due to pyelonephritis could cause developmental delay, because hospitalizations change the environmental factors such as materials, settings, and social and physical needs that support child development. In this study, we found the highest frequency of recurrent UTIs in the collecting system anomaly group. We did not find a statistically significant difference between groups with or without

Table 3. Mean scores of Bayley-III in patients and controls

	Patient (n=30)	Control (n=32)	p
Cognitive	83.60±8.38	100.00±11.61	0.04
Language	99.92±8.88	106.00±13.91	0.07
Receptive communication	11.80±1.60	12.23±2.58	0.18
Expressive communication	9.08±1.73	9.73±2.70	0.31
Global motor	98.36±8.73	103.46±13.17	0.11
Gross motor	9.08±1.68	9.69±2.63	0.33
Fine motor	10.32±1.97	11.53±2.51	0.06

Bayley III, Bayley Scales of Infant and Toddler Development Screening Test, Third Edition

Table 4. Bayley-III scores with and without iron deficiency anemia and recurrent UTIs

		Cognitive	Language	Receptive Communication	Expressive Communication	Global Motor	Gross Motor	Fine Motor
Controls (n=32)	With IDA (n=10, %31)	102.50±15.58	102.38±13.08	11.75±3.19	9.12±1.80	104.25±18.01	9.87±3.48	12.00±2.72
	Without IDA (n=22,%68)	99.16±9.73	107.61±14.32	12.44±2.33	10.00±3.02	103.11±11.00	9.61±2.27	11.33±2.47
	p	0.51	0.38	0.53	0.45	0.84	0.81	0.54
Patients (n=30)	With IDA (n=10, %33)	83.66±9.35	99.22±8.25	11.00±1.65	8.66±1.87	96.11±7.67	9.00±1.00	9.66±2.12
	Without IDA (n=20,%66)	83.56±8.10	100.31±9.45	10.68±1.62	9.31±1.66	99.62±9.26	9.12±1.99	10.68±1.85
	p	0.97	0.77	0.65	0.38	0.34	0.86	0.22
	With RUTI (n=12, %40)	82.15±10.83	100.38±7.92	11.25±1.16	8.87±1.95	101.38±9.36	9.50±1.51	10.87±2.23
	Without RUTI (n=18, %60)	85.05±7.30	99.70±9.52	10.58±1.76	9.17±1.66	96.94±8.32	8.88±1.76	10.05±1.85
p	0.09	0.86	0.34	0.69	0.24	0.40	0.34	

IDA; iron deficiency anemia, RUTI; recurrent urinary tract infection

recurrent UTI with regard to the Bayley-III scores. However, we think that neurodevelopment of children especially with VUR or UPJ obstruction must be evaluated with larger serried studies.

The study of Demirci et al. (12) which included 1514 Turkish children demonstrated significant associations between the maternal and paternal educational background, socio-economic status, consanguineous marriage, and developmental delay in children. The elementary school or a lower educational level, low socio-economic status, and the presence of consanguineous marriage were associated with the high prevalence of developmental delay in children. Other studies also verify these findings (12-13). Not finding a significantly association between the Bayley-III scores and the maternal educational level could be explained with a small sample size in our study. The presence of consanguineous marriage, the paternal educational level, and the family's income level were not examined in our study due to a lack of data.

The presence of high quantities of iron in oligo-dendriocytes in a developing brain, the need for iron in the energy metabolism of glial cells, and the negative effect of iron deficiency anemia (IDA) on neuro-cognitive functions are known (14-15). Myelination, dopamine and nor-epinephrine metabolism, neuronal energy metabolism, and there by child development are negatively affected by iron deficiency (16). In our study, IDA was found in 10 patients (33%) and 10 controls (31%), and a significant relationship was not found between IDA and low Bayley-III scores. The CAKUT and IDA comorbidity and the influence of the anemia on child development should be investigated with the studies including a larger series of patients.

In't Wuod et al. (17) studied maternal risk factors for the CAKUT spectrum. Maternal obesity was related to an increased risk of a double-collecting system and VUR, gestational diabetes mellitus was related to an increased risk of posterior urethral valve, and assisted reproductive techniques were related to an increased risk of CAKUT in general. Torabi et al. (18) showed a significant relationship between the developmental delay in children aged between 4 and 60 months and a high maternal BMI and gestational diabetes mellitus. When these results are evaluated together, we may suggest that our study should be supported by new studies that investigate the development of children with CAKUT and their maternal risk factors.

A normal cognitive development depends on acquiring language and motor skills. In a study investigating the interrelationships between motor, cognitive, and language development, the Bayley-III test was used in 77 children with developmental delay, and a strong correlation was shown between the motor, cognitive, and language scales when compared with results of 130 normally developing children. In conclusion, the importance of the early medical applications supporting one development area was emphasized, and it should be remembered that these applications would also contribute other development areas (19). We also started the applications that would support development in the early period of our patients' lives, in whom we detected cognitive delayed outcomes.

CONCLUSION

Our study contributes to the literature, to the best of our knowledge, as the first case-control study that applied the Bayley-III test

in children with CAKUT, although it does not explain the direct effects of CAKUT on the neuromotor development. Neurologic maturation is a process affected by the environmental and genetic factors in pre-natal, peri-natal, and post-natal periods. CAKUT with recurrent UTIs may be one of the factors that negatively affects this process, and severe complications such as ESRD and dialysis may compromise developmental outcomes. Therefore, it would be right to prevent recurrent UTIs and follow up the neuromotor development of children with CAKUT by using developmental screening tests since early infancy.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Mersin University (MEU 2016-113).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

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Author Contributions: Conceived and designed the experiments or case: ÖT, KM. Performed the experiments or case: ÖT, KM. Analyzed the data: MT. Wrote the paper: ÖT, OH, AD. All authors have read and approved the final manuscript.

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