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Neurodevelopmental status in children with congenital hypothyroidism.

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ABSTRACT… Objectives: To determine the neurodevelopmental status in children with congenital hypothyroidism. **Study Design:** Cross Sectional Study. **Setting:** Department of Pediatric Endocrine and Developmental Pediatrics Outpatient at The Children's Hospital and The Institute of the Child Health (CHICH) Multan. **Period:** January to December 2019. **Material & Methods:** A total of 119 children, 1-5years of age having congenital hypothyroidism were included. Their socioeconomical status, age at which the diagnosis was made, duration of thyroxine intake was noted. Development in domains of personal-social, fine motor-adaptive, language and gross motor skills was assessed by using The Denver developmental screening test (DDST). Developmental quotient of each domain was measured and less than 70% was considered significant delayed. **Results:** Out of 119 patients, 47.8% were male, 61.3% were among the age group of 1-3 years and the mean age was 1.40 ± 0.489 years. Forty-five percent (45.4%) belonged to low and 47.1% to middle socioeconomical status. Only 46.2% children started taking thyroxine within 2 months of life. Significant delay in personal-social domain was detected in 73.9% (n=88) children while 80.7% (n=96), 80.7% (n=96) and 86.6% (n=103) patients had significant developmental delay in fine motor-adaptive, language and gross motor skills respectively. Developmental delay was significantly low in children started on thyroxine therapy within 2-months of age (p-value ≤ 0.05 for all domains of development. **Conclusion:** Children with congenital hypothyroidism suffer from delayed development, so these patients must be referred for developmental therapy along with medical therapy.

Key words: Congenital Hypothyroidism, Neurodevelopment, The Denver Developmental Screening Test.

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INTRODUCTION

Congenital hypothyroidism (CH) is one of the causes of delayed Development in children.[1] It occurs in 1/4000 births.[2] This can be prevented by early identification of hypothyroidism and timely treatment with thyroid hormones replacement.[3,4] New born screening is essential for the diagnosis of CH within 1st week of life before appearance of clinical manifestations, but in areas where no screening programs are available diagnosis and management may be delayed.[5] Some studies show that despite treatment, few patients show some impairment in developmental domains like cognition, speech, mathematical skills, fine motor skills, in later life. This deficit can be prevented by timely identification, early start of treatment and proper dosage of hormonal therapy.[6-9]

The Denver developmental screening test (DDST), covers broad range of ages. This test safes time & cost of the clinician as it uses single test for all children. It measures developmental age in terms of personal-social, Fine moto-adaptive, language and Gross motor skills.[10,11]

The aim of this study was to evaluate the neurodevelopmental status of children with CH at the CHICH Multan.

MATERIAL & METHODS

This study was conducted at The CHICH Multan. Patients on regular follow up of Pediatric Endocrine and Developmental Pediatric Outpatient clinics from January to December 2019 were included in this study. After approval from ethical committee

of the Hospital, 119 children of both gender, 1 to 5 years, with CH were enrolled.

Children having acquired hypothyroidism, premature delivery, history of birth asphyxia and inborn error of metabolism were excluded from the study.

Parents were detailed about the study and written consent was taken. CH was diagnosed on clinical features and hypothyroidism was defined as an elevated TSH levels together with decreased serum thyroid hormone level.[12] Duration of Thyroxine intake and socioeconomic status was noted. Patients were stratified into different groups to minimize the effect of different modalities like age, gender, socioeconomic status and duration of thyroxine intake. Age was divided into two groups, 1-3 years and >3-5years. Timing of making diagnosis of Hypothyroidism was grouped into two, 1st within 1-year of life and 2nd after 1-year of life. Regarding duration of therapy two groups were made, thyroxine intake within 2-months of life and after two months of life. Socioeconomic status was divided into low (monthly income <20,000 rupees), middle (monthly income 20000-50000 rupees) and upper (monthly income>50000rps) groups.

Developmental status of each child was measured by using Denver developmental screening test (DDST) in Developmental domains of personal-social, fine motor-adaptive, language and gross motor skills. Developmental quotient (DQ) of each domain was measured by applying formula. DQ= Developmental age/Chronological age 100. Developmental quotient (DQ) below 70% was considered significant developmental delay.[10,11,13]

SPSS software version 20 was used for data analysis and interpretation. Descriptive statistics were applied. Frequencies of variables and p value. were calculated.

RESULT

Out of 119 children 47.8% (n=57) were males. Amongst age group 1-3years were 61.3% (n=73) and in >3-5years group were 38.7% (n=46) with mean age of 1.4±0.49 years. In terms of socioeconomic status 45.4% (n=54) were in low, 47.1% (n=56) in middle and 7.6% (n=9) in upper status. Diagnosis of congenital hypothyroidism was made before 1-year of life in 61.3% (n=73) and 38.7% (n=46) after 1-year. Regarding duration of therapy 46.2% (n=55) started taking thyroxin within two months of life while 53.8% (n=64) started after two months of life (Table-I).

Developmental Quotient (DQ) of personal-social domain showed significant delay in 76.5% (n=78) patients while fine motor-adaptive, language and gross motor skills had delay in 73.1% (n=87), 68.9% (n=82) and 86.6% (n=103) patients respectively (Table-II).

The number of children starting thyroid replacement therapy within 2-months had lower frequency of significant developmental delay compared to those who started it after 2 months of life (gross motor delay p-value 0.000, fine motor delay p-value 0.008, language delay p-value-0.019 and for social-personal delay p-value - 0.052), (Table III).

Age (years), mean ± SD	**1.4 ± 0.489**
(N%)	
Age groups 1-3years >3to5years	 73-(61.3) 46-(38.7)
Sex Male Female	 57-(47.8) 62-(52.2)
Socioeconomic status Low Middle Upper	 54-(45.4) 56-(47.1) 09-(7.6)
Thyroxine intake Within 2 months After 2 months	 55-(46.2) 64-(53.8)
Diagnosis of Congenital Hypothyroidism Before 1 year of age After 1 year of age	 73 (61.3) 46 (38.7)

Table-I. Baseline characteristics of children with congenital hypothyroidism (N = 119).

Development Domain	Significant Delay	
	Yes	No
Personal-Social	78(65.5%)	41(34.5%)
Fine-motor adaptive	87(73.1%)	3226.9%)
Language	82(86.6%)	37(13.4%)
Gross-motor skills	103(86.6%)	16(13.4%)

Table-II. Distribution of developmental delay domains in children with congenital hypothyroidism (N=119).

Development Domain	Significant Delay	Thyroxin Intake Within 2-months		P-Value
		Yes	No	
Gross motor	Yes	49	54	< 0.001
Fine Motor	Yes	42	45	0.008
Language	Yes	39	43	0.019
Social	Yes	33	45	0.052

Table-III. Relationship between Developmental delay and timing of Thyroid replacement therapy.

DISCUSSION

CH is the most common preventable cause of intellectual disability and delayed development.[1] Early CH screening & hormonal replacement therapy with levothyroxine (L-T_4) has improved the intellectual outcome & growth in hypothyroid children.[14] However, some studies reported that even in patients with CH who receive early treatment, deficits in development (including cognitive performance, speech, learning, fine motor coordination) may be observed.[8,9]

During pregnancy maternal and fetal thyroid hormones are essential for the development of fetal brain. Brain development starts from intrauterine period but it continues till 2 to 3-years. So deficient thyroid levels affect the development in intrauterine period and first 6 months are also important for neurodevelopment in the presence of thyroid hormone. This study shows that children with CH are delay in gross motor, fine motor, language and social domains of development which is almost similar to other studies.[15-17] Oerbeck Bargagna et al detected in their observational study that neurological outcome is poor in children with severe CH as compared to the children with normal thyroid functioning.[18]

Hormone replacement therapy started within 2 weeks after birth can normalize intellectual development in children with congenital hypothyroidism.[2] This study also shows a greater number of patients with significant delay in development who started thyroxine replacement therapy after 2-months of life. Klein et al first reported the negative effect of 5points decrease in IQ level for every month delay in start of thyroxine replacement therapy from birth to 6 months of life.[1] According to another study neurological development is retarded despite of early and effective treatment in newborns with congenital hypothyroidism. This could be due to effect of thyroid hormones on neurodevelopment during intrauterine period.[19]

CONCLUSION

Children with Congenital hypothyroidism have delayed development, so should be screened at neonatal period for hypothyroidism for early detection, and must be referred for developmental therapy by multidisciplinary team as soon as possible along with hormonal replacement therapy.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Erum Afzal	Literature search, study design and concept, data acquisition, analysis and interpretation, final approval.	
2	Waqas Imran Khan	Data acquisition, analysis and intepretation, study design, final approval.	
3	Sajjad Hussain	Data acquisition study design, analysis and interpretation, final approval	