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FACTORS THAT AFFECT THE DEVELOPMENT OF FUNCTIONAL HEART DISORDERS IN CHILDREN WITH UNDIFFERENTIATED CONNECTIVE TISSUE DYSPLASIA

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ABSTRACT

Connective tissue dysplasia is a complex and rare ontogenetic developmental anomaly that remains one of the least studied problems in modern medicine. It serves as a morphological basis for functional changes in the heart. The study examined 79 preschool and school-age children with connective tissue dysplasia and minor heart developmental anomalies. It was found that external phenotypic markers of connective tissue dysplasia syndrome and stigmas of embryogenesis occur with high frequency.

Clinical manifestations of the disease were also recorded. Functional disorders of the heart associated with phenotypic features of connective tissue dysplasia and stigmas of dysembryogenesis were investigated. Additionally, the anamnestic data of mothers influencing the probability of developing connective tissue dysplasia in children were analyzed.

INTRODUCTION

In genetics and clinical medicine, the main attention is given to Connective Tissue Dysplasia Syndrome (CTDS) as it is the base of many genetic disorders. Connective tissue dysplasia (CTD) refers to a group of genetically determined disorders that affect the body's connective tissue. Protein matrix is an important component of connective tissue which takes role in supporting structural and physiological functions of numerous organs, including heart [1,2,3,4].

In recent years, the prevalence of undifferentiated connective tissue dysplasia (UCTD) has been increasing, which is associated with its rising occurrence in various somatic conditions [3,4]. The adverse environmental factors lead to an increase in mutagenic gene growth. Factors influencing the development of polygenic pathology originate from the moment of conception and underlie the course of all conditions arising during pregnancy and childbirth. They are also associated with intercurrent diseases in the pregnant woman, which lead to changes in the fetus. [3.2]. Functional heart disorders are one of the basic manifestations of

UCTD in children and adolescents. Dysplasia of connective tissue may lead to some pathological changes in the cardiovascular system, particularly cardiac malformations, valve's dysfunction, arrhythmias and etc. [3.7]. Marphan's phenotype is the most common manifestation of heart in group of children and adolescents with UCTD. Children with this phenotype have such characteristics as elongated limbs and joint hyper. These children may also have some changes in cardiac structure for example: abnormal extension of the aorta, arrhythmias, additional chords in the ventricles, the mitral and tricuspid valves' prolapse [3,7]. Possible causes of connective tissue dysplasia can be genetic mutations depending on gene expression and penetration, heredity or random genetic changes [6,7]. Often women in pregnancy with CTD can face different complications.

Materials and Methods

The study was conducted in polyclinics (No. 22,23,24,26,62) of Uchtepa district in Tashkent. The study was conducted among 167 children. In selection process specially-designed computer program (ASCTD-SSCC.exe) was used. Into this program children with 81 phenotypic features and 44 stigmas of disembryogenesis were included. In accordance with the set of identified features, the results were determined, the amount of which expressed the severity of UCTD [1]. Notably, the severity was estimated according to the algorithm below:

Purpose of the research

Observing functional features of heart in group of children with undifferentiated dysplasia of connective tissue in Uchtepa district of Tashkent. Assessment of CTD severity was done with the help of specific computer program ASCTD-SSCC (assessment of the severity of connective tissue dysplasia depending on the severity of symptom complexes in children)

If the patient scores **0-19 points** in Table 1 and **0-11 points** in Table 2, this corresponds to **Grade I CTD**, which is considered normal.

If the patient scores **20-39 points** in Table 1 and **12-22 points** in Table 2, this corresponds to **Grade I (mild) CTD**.

If the patient scores **40-59 points** in Table 1 and **23-34 points** in Table 2, this corresponds to **Grade II (moderate) CTD**.

If the patient scores **60-80 points** in Table 1 and **35-44 points** in Table 2, this corresponds to **Grade III (severe) CTD.**

Results

Assessment of the severity of connective tissue dysplasia in children was based on the expression of symptoms (ASCTD-SSCC.exe). Following tables and figures represent results of the research.

Severity Grades of CTD in Children Identified at Family Polyclinics No. 22, 23, 24, 26, and 62 in the Uchtepa District of Tashkent.

Table 1

Degree of severity	FP 22	FP 23	FP 24	FP 26	FP 62	Overall percentage %
Healthy	18	24	12	9	25	88 52,6%
Mild	13	11	8	5	19	56 33,5%
Moderate	4	6	3	1	7	21 12,6%
Severe	-	1	-	-	1	2 1,2%
Total	35	42	23	15	52	167 100%

A total of 167 children participated in the study, of whom 79 were diagnosed with CTD. In terms of severity, 88 children (52.7 %) were classified as grade 0 (healthy), 56 children (33.5 %) as grade I (mild), 21 children (12.6 %) as grade II (moderate), and 2 children (1.2 %) as grade III (severe).

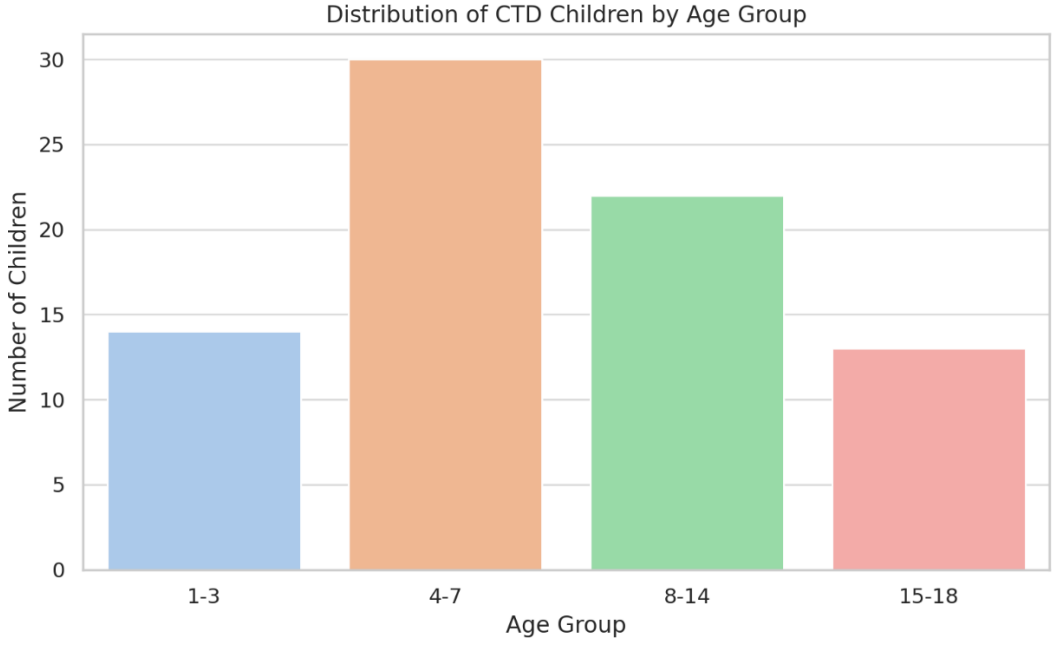

Figure 1 Children with CTD were identified in the following age groups: 14 children (17.7%) were between 1 and 3 years old, 30 children (37.8%) were between 4 and 7 years old, 22 children (27.8%) were between 8 and 14 years old, and 13 children (16.7%) were between 15 and 18 years old.

Distribution of Children by Gender

Table 2

№	Girls	Boys	Total quantity	Percentage%
1.	6 (7,5%)	8 (10,1%)	14	17,7%
2.	13(16,4%)	17(21,5)	30	37,9%
3.	9(11,3)	13(16,4%)	22	27,8%
4.	8 (10,1%)	5(6,3%)	13	16,7%
Total	36(45,5%)	43(54,4%)	79	100%

This table presents data on children with various degrees of UDCTD who exhibited phenotypic signs of mild, moderate, and severe severity. The total number of such children was 79, including 36 girls (45.5%) and 43 boys (54.4%).

Pregnancy Complications in Mothers of Children with UDCTD

Table 3

Pathologies	FP 22	FP 23	FP 24	FP 26	FP 62	Total quantity	Percentage%
Gestoses of various severity	17/5	18/7	11/4	6/2	27/13	31	39,2%
Rupture of uterus	-	-	-	-	1	1	1,2%
Early delivery	4	1	-	-	-	3	3,7%
High risk of arterial hypertension	5	2	1	1	5	12	19,9%
C-section	1	2	1	1	4	9	11,3%
Extension of aorta	-	1	-	-	2	3	3,7%

Table 3 presents data on the complications identified in mothers from the NDCT group during pregnancy. The study is based on data collected from five polyclinics in the Uchtepa district. The most frequently observed complications were gestoses of varying severity, accounting for 39.2% of all cases. The least common complication was uterine rupture, observed in 1.2% of cases. A full analysis is provided in the table above.

Functional Heart Disorders in Children and Adolescents

Table 4

	Pathologies	Boys 43 (54,4%)	Girls 35 (44,3%)
1.	Cardiovascular System Defects	2 (4,65%)	3 (8,57%)
2.	Abnormal Aortic Enlargement	1 (2,33%)	2 (5,71%)
3.	Additional Ventricular Chords	6 (13,95%)	4 (11,43%)
4.	Arrhythmias	7 (16,28%)	5 (14,29%)
5.	Mitral and Aortic Valve Prolapse	3 (6,98%)	3 (8,57%)
6.	Sinus Node Weakness Syndrome	2 (4,65%)	2 (5,71%)
7.	Aortic Stenosis	2 (4,65%)	1 (2,86%)

The table contains data on functional heart disorders in children and adolescents, grouped by sex: 43 boys and 35 girls.

DISCUSSION

The findings of this study emphasize the high prevalence and clinical relevance of undifferentiated connective tissue dysplasia (UCTD) among children in the Uchtepa district of Tashkent. Of 167 children screened, 79 (47.3%) were diagnosed with varying degrees of CTD, which aligns with global trends indicating increasing recognition of connective tissue disorders in pediatric populations.

A key outcome of the study was the clear association between phenotypic markers of CTD and functional heart disorders. Functional anomalies such as mitral and aortic valve prolapse, arrhythmias, and additional ventricular chords were frequent among affected children. These findings are consistent with previous literature describing the cardiac manifestations of CTD as consequences of structural and biochemical irregularities in connective tissue matrix proteins, particularly fibrillin and collagen [3,7].

Age-related trends also emerged, with children aged 4–7 comprising the largest subgroup (37.8%) diagnosed with CTD. This may be attributed to increased physiological stress during early school years that unmasks latent cardiovascular symptoms. Additionally, male children were slightly more affected (54.4%) than females (45.5%), although the sex difference was not pronounced enough to draw strong conclusions.

Another important contribution of this study is the identification of maternal pregnancy complications as possible contributors to the development of CTD in offspring. Nearly 40% of mothers of children with CTD had experienced gestosis, and 19.9% were noted to have high-risk arterial hypertension. These findings support the notion that intrauterine environmental factors, including placental insufficiency, oxidative stress, and maternal vascular dysfunction, may alter fetal gene expression and organ development, including the connective tissue system [8].

The application of the OSTDSTVSKD.exe diagnostic tool allowed for an objective and structured assessment of phenotypic signs and disembryogenesis stigmas, ensuring a more standardized evaluation of CTD severity. This approach holds promise for broader clinical application, particularly in settings where clinical suspicion of CTD may otherwise be overlooked due to its subtle or polymorphic presentation.

Nevertheless, the study has limitations. Being geographically limited to five polyclinics in a single district, generalization of findings should be approached with caution. Moreover, the study design was cross-sectional, preventing conclusions about the temporal sequence or causality between maternal factors and child outcomes. Longitudinal studies and genetic testing (e.g., NGS) would further elucidate the pathophysiological mechanisms involved.

CONCLUSION

This study highlights the need for early identification and monitoring of CTD in children, especially those with relevant family and prenatal histories. Early detection of functional heart disorders in such patients can enable timely interventions, reduce long-term complications, and improve quality of life. Further research in this field will allow for a more precise understanding of the mechanisms underlying the development of cardiac

pathologies in UCTD and will contribute to the development of new methods for their prevention and treatment.

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