

DENTITION CHANGES IN GENETIC DISEASES

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ABSTRACT

This paperwork aims to identify the dentition's changes in genetic diseases and to find solutions to solve them. Method: We studied 31 patients with different genetic diseases (Down syndrome, Turner syndrome, Prader-Willy syndrome, Bardet-Biel syndrome, Tourette syndrome, Pfeiffer syndrome, and schizophrenia). The patients were of school age (7-14 years old) and followed socialization programs within a foundation, the study taking place over 1 year). Conclusion: the most frequent cases were represented by dental malocclusion (98,16%), correlated with mental retardation and facial dysmorphism (74,2%), shape and structure anomalies (76,11%), mandibular hypoplasia (33,3%) and 6% pigmentation on the mucous membranes. Conclusions: We believe that the health education of parents with rare genetic diseases that affect skeletal development should be emphasized in order to ensure better oral health in this group. The health system should develop screening strategies and education and support services. Also, access to dental treatments for patients with rare genetic diseases should be supported through various programs.

Keywords: dental changes, genetic disease, child

INTRODUCTION

Genetic diseases have a prevalence of about 65 cases per 100,000 individuals. Regarding the 7000 existing rare diseases, most of them are genetic diseases, and only 700 diseases from them are characterized by craniofacial damage. It is considered that only 20% of the 700 cases with craniofacial damage have a genetic component [1]. Rare genetic diseases are usually debilitating chronic diseases about the phenotype. Most of the time these patients suffer from physical and mental problems that disturb their daily life.

In recent years, the efforts of the geneticists were focused on understanding the molecular and cellular mechanisms that determine the development of dentition, respectively dental pathology. Mouse embryos [2] and birds [3] were used as experimental materials to follow embryogenesis.

In the stage of embryonic development, the dental differentiation is the result of the

interaction at the molecular level between ectoderm and mesenchyme [4,5], a process in which about 200 genes are involved [6].

The Fibroblast growth factor (FGF) and the transforming growth factor (TGF) play an important role in morphogenesis. Practically, the dentition scheme is determined even before the moment of the visible eruption of the teeth.

The lack of one or even more teeth (dental agenesis) is the most common anomaly. Here we are faced with the variants of: hypodontia (missing 1-6 teeth, excluding the 3rd molar), oligodontia (missing more than 6 teeth), respectively anodontia with total lack of teeth. One such case was reported in an extended family from China and it seems to have an inherited autosomal transmission [7]. Hypodontia/oligodontia can be associated with various syndromes of genetic origin characterized by cleft lip or even palatal vault. Up to this point, only 4 non-syndromic

hypodontia/oligodontia genes have been evident. These are:

- MSX1 – NS hypodontia [8]
- PAX9 – NS oligodontia [9]
- AXIN2 – oligodontia associated with colon cancer [10]
- EDA1 – NS oligodontia [11].

In 2011, Kantaputra and Sripathomsawat described cases of non-syndromic hypodontia caused by the WNT10A gene mutation. This gene from the WNT family encodes certain proteins on the cell surface and is responsible for some syndromes (ectodermal dysplasia, mesomelic dysplasia), but also for non-syndromic cases of hypodontia.

MATERIALS AND METHODS

The study was developed within the Scholar Center for Inclusive Education in Tirgu Mures after obtaining the informed consent from all the parents whose children were included in this project as well as the agreement of the school management. The number of participants was 31, aged between 7-14 years who were suffering from the following conditions (Down syndrome – 14 patients, Turner syndrome - 6 patients, Bardet-Biedel syndrome - 1 patient, Pfeiffer syndrome - 1 patient, Tourette syndrome, and schizophrenia – 8 patients). The gender distribution was 16 boys and 15 girls, respectively 51.16% male patients and 48.84 % female patients.

For the patients diagnosed with schizophrenia, the genetic factor was taken into account as a criterion for inclusion, namely the presence of cases with mental disorders in the extended family.

In order to have a clearer picture, we compared the data obtained in this study with a group of patients without chronic diseases and having the same gender distribution, respectively age groups.

In this study, the behavior of the patients was monitored regarding the previous visits to the dentist (discussing with the parents), the dental treatments and prevention, the oral hygiene of the patients from the 2 study groups, the breastfeeding period that each benefited from, the dental anomalies and dental malocclusion.

RESULTS

1. The number of the patients participating in the study was 31, respectively 51,16% male and 48,84 % female patients.

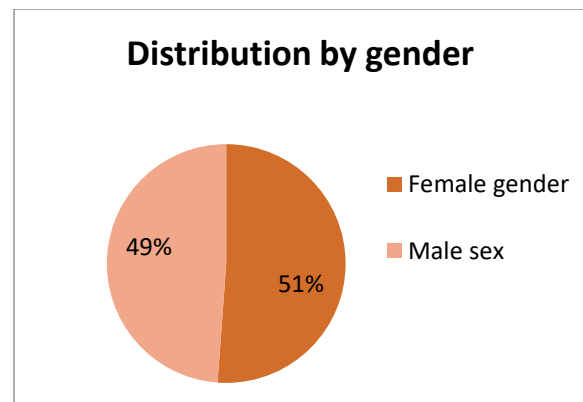


Figure 1 Distribution by gender.

2. The patients aged between 7-14 were divided into 2 age groups : the first group of 18 children between 7-10 (25,8 % boys and 32,25 % girls) and the second of 13 children (22,58 % boys and 16,12% girls).

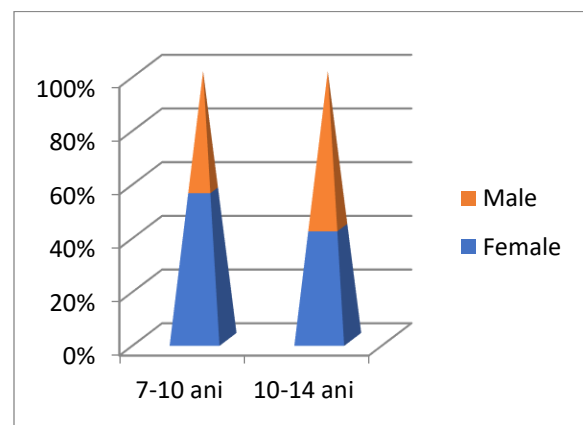


Figure 2 Distribution by gender and age groups.

3. From the total of 31 patients studied, the distribution by genetic diseases is as follows: Down syndrome – 14 patients (45,16 %), Turner syndrome - 6 patients (19,35 %), Bardet-Biedel syndrome - 1 patient (3,22 %), Pfeiffer syndrome - 1 patient (3,22 %), Tourette syndrome -1 patient (3,22%),schizophrenia –8 patients (25,80%).

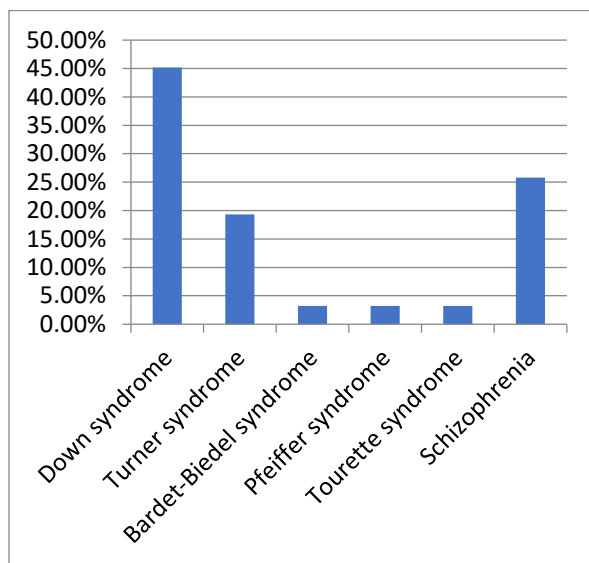


Figure 3 Distribution by genetic diseases.

4. The most frequent cases were represented by dental malocclusion (98,16 %) correlated with mental retardation and facial dysmorphism (74,2 %) , shape and structure anomalies (76,11%) , mandibular hypoplasia (33,3 %) and pigmentation on the mucous membranes (6%).

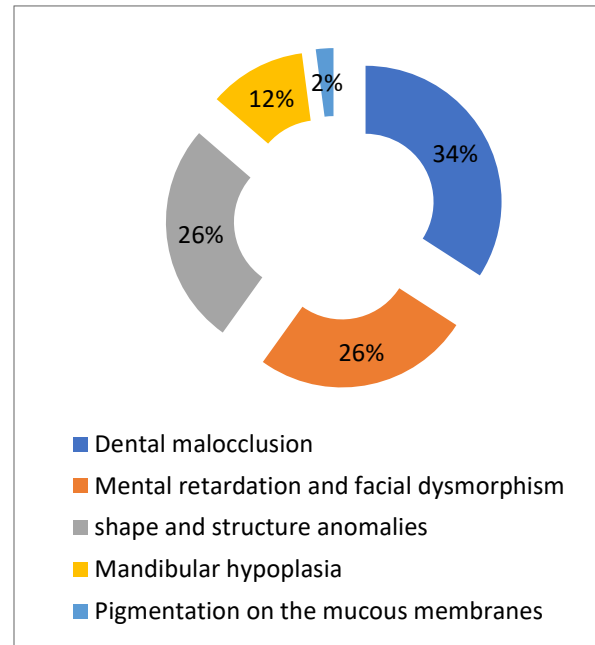


Figure 4 The main dental changes.

DISCUSSIONS

With a percentage of 46.42% of the total number of patients from the group of rare diseases, Down's syndrome stands out as the main genetic disease. The incidence of this syndrome is between 1:750 and 1:1000 births. Characteristic for this syndrome is the presence of an additional chromosome to chromosomal pair 21 (also called trisomy 21).

Down's syndrome is characterized by a series of features that refer to physical, mental and medical damage. It is characterized by mental disability (which increases over time) but also cardiac abnormalities as well as damages to the immune system, all of which affect the oral health [12].

Patients with Down syndrome have facial dysmorphism, narrowed palate, macroglossia, delays in tooth eruption, as well as malformations of the teeth morphology.



Figure 5 Changes in dental morphology typical for Down syndrome, girl 12 years old .

Figure 5 show the dentition of a 13 years old girl diagnosed with Down syndrome. We can observe inverse gears with lateral deviation of the median line, lack of lateral group contacts, dentomaxillary disharmony class 3 Angle, vertical incisor-canine level, lateral-frontal incisor-canine level, occlusal contacts being maintained only at the level of the last molars.

At the patients with Down syndrome, the normal development of the oral structure is altered, changes can be found in the shape of the crown, the size of the teeth, delays in tooth eruption, even hypodontia, all of which influence mastication, swallowing and even generate difficulties in expression [13].

Individual oral hygiene was evaluated in the case of patients with Down's syndrome using the simplified oral hygiene index of Green and Vermillion. We took into account the 2 components, the residual index (DI-S) and the calculus index, the evaluation being made on a number of 4 posterior teeth and 2 anterior teeth.

Considering the facial dysmorphism, narrowing of the palate, malformations in the morphology of the teeth, macroglossia and delayed tooth eruption, we can conclude that we will face a greater risk of facing periodontal diseases, malocclusion, respectively dental caries [14].

Another special case that we focused on was that of an 11 years old boy diagnosed with

Prader Willi syndrome, mental retardation and polymorphic dyslalia.

Prader Willi syndrome is a rare genetic disease with a prevalence of 1:12000 that can affect both sexes and races equally. The disease occurs as a result of the elimination of seven genes from the short arm of the paternal chromosome 15. The diagnosis of the disease is clinical, but currently it is possible to carry out genetic testing through the FISH technique, which highlights 97-98% of cases and is recommended for newborns with severe hypotonus syndrome [15].

The typical symptoms of the disease refer to an excessive food appetite (hyperphagia, obsession with food) - which can eventually lead to morbid obesity -, growth retardation, mental retardation, lack of sexual character development. In the long term, it can cause type 2 diabetes, heart problems and respiratory failure. If the diet is well controlled and there are no overweight problems, adults can have a life expectancy similar to the normal population [15]. Phenotypically speaking, patients with Prader Willi syndrome have a narrow forehead, almond-shaped eyes and a triangular mouth with a thinner upper lip and downward-pointing cheeks.

Prader Willi syndrome is associated with a reduced amount of saliva and an alteration of its quality. The increased proportion of ions and proteins and the reduced amount of saliva change the properties of the saliva, making it sticky.



Figure 6 Changes in dental morphology for S. Prader Willi, 11-year-old boy.

In this case, we observe a sagittal, transverse, vertical occlusion ratio when the mandible is in the maximum intercuspation position. Atypical pathological occlusion, reverse engagement, abnormal generating occlusal dysfunctions can be noticed. The inoclusion space is formed by the vestibular faces of the upper teeth and the lingual faces of the lower teeth or is absent.

Thus, a poor hygiene, the reduced amount of saliva and a diet rich in carbohydrates determine an increased risk for gingivitis and dental caries [15,16,17]. A change in the mucous membranes due to *Candida albicans* superinfection can be noted.



Figure 7 – Changes in the mucus membranes – infection with *Candida albicans*.

Another special case that raises a series of problems from the dental management's

point of view is that of a 12-year-old girl with dwarfism associated with malformative syndromes at the level of the head, chest, limbs, as well as moderate mental retardation. Dwarfism, in the form encountered by us (disproportionate dwarfism) refers to individuals with a height of less than 147 cm (on average 120 cm) with short limbs and trunk, reduced mobility at the elbows, deformations of the spine, compression of the spinal cord. In this case, the patient is also facing moderate mental retardation. The most common cause of dwarfism is achondroplasia (80%) among cases that refer to the form of disproportionate dwarfism (similar to the case studied by us).

Achondroplasia is caused by a genetic mutation that encodes a growth factor receptor FGFR3 (fibroblast growth factor receptor 3), a mutation that occurs on the 4th pair of chromosomes. The prevalence of achondroplasia is 1:25,000 births and the diagnosis can be established through genetic testing. In patients with achondroplasia, due to the FGFR3 mutation, normal bone development no longer occurs, which interferes with the normal development of the skeleton [18]. The oral examination revealed features associated with achondroplasia: short stature, severe hypoplasia in the middle of the face, closing the mouth can only be done by tensing the muscles, the chin is not prominent [19].



Figure 8 - Changes in dental morphology in disproportionate dwarfism.

In this case, we could observe lingual malposition, impacted teeth, migration of neighboring teeth, loss of arch length, external root resorption of impacted teeth, persistence of temporary teeth, bone deformities. Sagittal inoclusion occurs, lack of dental contacts, dysfunctional contacts.

CONCLUSIONS

Numerous genetic diseases (Down syndrome, Turner syndrome, Prader syndrome, dwarfism, etc.) are characterized by facial dysmorphism influencing mastication, swallowing, deglutition and even generating difficulties in expression.

Most of the time, physical weakness is accompanied to a greater or lesser extent by mental weakness, this aspect making it even more difficult to maintain oral health for these categories of patients.

We believe that the emphasis must be placed on the health education of parents whose children suffer from rare genetic diseases that affect skeletal development in order to ensure better oral health in this group.

The health system should develop both screening strategies and education and support programs. Likewise, access to dental treatments for patients with rare genetic diseases should be subsidized through various programs.

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