Orthodontic Aspects on the Chronological and Dental Age in Children with Down Syndrome

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Genetics is a key discipline in medicine, but also a clinical discipline with medical and social implications. The interest in reducing the number of genetic disorders and recognizing the risk of them repeating when a family confronts itself with a genetic anomaly becomes more and more important in the hierarchy of prophylactic emergencies. Presenting themselves as metabolic diseases (monogenic mutations) or malformations (polygenic and multifactorial heredity) because of their frequency, these disorders position themselves on an ascendant curve. They become difficult to deal with for the society, for the family and for the interested individual and cause emotional disorders. The Down syndrome is the most frequent type of genetic disorder. It is characterized by a specific set of signs and symptoms. People with Down syndrome require special medical care that, apart from the family, must include a team of doctors of various specializations and also a dentist. They are predisposed to hearing and sight disorders and thyroid problems as well. In 50% of the cases there are also anomalies of the heart, and the risk of leukaemia is 20 times higher. Some of them even develop an Alzheimer type dementia during their life. The people with Down syndrome can have an average IQ up to a moderate form of handicap. In particular, the studies on Down syndrome in dentistry are quite frequent, but they focus more on cavities, periodontal disease and hypodontia. In spite of this, the connection of Down syndrome and dental eruption is less studied. Consequently, the present study is intended to fill this missing part from the specialized literature, focusing on the relation between the Down syndrome and the chronological and dental ages in children. The health of the oral cavity is neglected in these patients, their parents focusing more on the treatment of the other systemic disorders of their children; the lack of interest is reflected in their poor oral hygiene.The trial group included 94 children with mixt dentition, aged between 6 and 12, divided as follows: 36 children with Down syndrome enrolled at the Educational Centre for Inclusive Education no. 1 of Tg. Mures and Alpha Transilvana Foundation. The chronology and the eruption sequences are subjected to certain variations and they are influenced by the presence of cavities, the premature loss or, on the contrary, the prolonged retention of deciduous teeth as well as dental anchylosis. Dental maturation is less subjected to variations, as it is a progressive, continuous and cumulative process. The presence of Down syndrome in children generates a delay in teeth eruption by 1.27 years compared to the data identified in the specialized literature and to the information obtained on the healthy children included in the study.

Keywords: chronological age, Down syndrome, psychological factors, genetics, dentistry

Mentioned by Esquirol in 1838, the Down syndrome was first described in 1946 when Sequin referred to it as *furfuraceous idiocy.* In the same period, Langdon Down studied the psychomotor delay, considering the disease a rewoken racial *tare* and named it *Mongolian idiocy.* The label of *Mongolian idiocy* is also explained by the fact that patients individualize themselves through a pseudo-Mongolian fetish that stands for one of the key elements in establishing a diagnosis. In 1959 Lejeune, Gautier and Turpin discovered the chromosomal aberration and the disorder became the *trisomy 21* or the Down syndrome.

Trisomy 21 (Down syndrome) is caused by the apparition of a third chromosome 21. If the human cell normally contains 23 pairs of chromosomes, in the Down syndrome (DS) the cell has 47 chromosomes. The excess of genetic material, as additional genes along chromosome 21, leads to the apparition of the Down syndrome.

The incidence of the disease is of 1:650-1:800 in living new born children, with a higher frequency in male children (3/2), the risk for the disease to appear increasing with the mother's age [1, 2].

The child's physical features directly related to the genes transmitted from the mother or the father explain the similarities so often noticed between parents and children.

The medical progress as well as the specialized educational programs designed especially for these children lead to the present day normalization and deinstitutionalization tendencies of these patients. Once the dentist is familiarized with the patient's medical history and he takes the necessary caution measures, these patients can be treated in a regular dental office.

The aspect of a child with Down syndrome is specific, the diagnose being based on the association of more modifications.

The specific morphological features are muscle weakness - hypotonia, statural hypotrophy, overweight, flat occiput, wide fontanel, flat profile, short neck, excessive skin on the back of the head, oblique eye lids, Brushfield spots, epicanthus, flat nasal base, small anteverted nostrils. There are also a number of ocular dysfunctions, of particular importance for the Down syndrome. Apart from lid infections and conjunctivitis, the most common and

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important infections are the ones that distort the image on the retina. Most of them are refraction errors, like myopia, hyperopia and astigmatism. The outer ear is significantly smaller, in inferior position, the ear lobe is hypoplastic or absent, the helix is bent, the child presenting various hearing disorders. The hands are short and wide, brachydactyly, clinodactyly of the little finger, simian crease and sandal gap [3- 6].

Congenital cardiac diseases appear in 40-50% of the patients with Down syndrome, being an important reference element for the survival rate. Various cardiac malformations can be associated with the Down syndrome, but the most communes are represented by atrioventricular defects, atrial and ventricular septal defects and the tetralogy of Fallot [7]. Thus, an electrocardiogram is recommended to all patients [8].

There is an association between thyroid dysfunctions and the Down syndrome, so that a routine check is recommended. Some of the thyroid dysfunctions identified in children with Down syndrome are congenital hypothyroidism, primary hypothyroidism, auto-immune thyroid or Hashimoto thyroid, compensated hypothyroidism and hyperparathyroidism [9].

Children with Down syndrome present a high risk of infections, in general infections of the upper respiratory tract characterized by pronounced severity and prolonged persistence of the disease [10]. Some of the anomalies associated to the Down syndrome are light and medium lymphopenia of T and B cells, deficiency in the proliferation of T lymphocytes and defective neutrophil chemotaxis. The suppression of the immune system leads to a higher risk to certain types of neoplasms, the most frequent one being acute leukaemia developed during childhood [11].

Children with Down syndrome can also present various gastrointestinal disorders as oesophageal reflux, diarrhoea, constipation, abdominal pain and discomfort. Nonetheless, they can also present structural and functional dysfunctions as intestinal atresia or gastrointestinal malformations [12]. Among them, atresia and oesophageal and duodenal stenosis are the most frequent along with the Hirschprung disease, ring-like pancreas and non-perforated anus [13].

Obstructive sleep apnea is frequent in children with Down syndrome, its prevalence ranging between 20-80% in children affected by the Down syndrome [14, 15], compared to 1-2% in regular paediatric population. The high incidence is caused by the anatomic and functional features of the syndrome (macroglossy, glossoptosis, lymphatic hypertrophy of nodules, hypoplasia of the middle part of the face, muscle weakness - hypotonia) [16]. Most children with this syndrome present dysfunctions of teguments, like palmoplantar hyperkeratosis, seborrheic dermatitis, cutaneous xerosis, geographic tongue or fissured tongue [9].

The affected people present a high risk of developing neoplasms. The risk of developing leukaemia is 10 to 20 times higher in their case, with a risk of 2% at the age of 2 years and up to 2.7% at the age of 30. They represent approximately 2% of the total number of lymphoblastic leukaemia (ALL) and approximately 10% of acute myeloid leukaemia in children and adolescents (AML) [16].

The cognitive development of patients with Down syndrome seems to be characterized by clear differences between the individuals [17]. The scarce cognitive activity, caused by intellectual issues, have a direct influence on the processing of information, leading to modifications in attention, memory, language acquisition and other developmental abilities [18, 19].

Children with Down syndrome present a distinct cognitive phenotype, characterized by a certain type of deficiencies, when compared to healthy children in process of development or to other children suffering from other types of cognitive disorders. In general, these children present a specific memory pattern and ability to process information, including weak working memory. Their implicit memory is intact but their long term memory for processing explicit information is short. At the same time, they tend to be slower in acquiring new competencies and present difficulties in assimilating them. Thus, the competences they demonstrate on certain occasions can be absent on other occasions. At the same time, they present linguistic deficiencies, their linguistic capacity being inferior to that characteristic to their mental age.

Children's attention is poor, accompanied by difficulties in staying focused, hyperactivity and impulsive behaviour. A study conducted by Sivan Ekstein and Benjamin Glick on a two year interval, showed that 43.9% of the children in a clinique in Istanbul presented a high risk of developing ADHD [15].

Because of their severity and high incidence, otorhinolaryngeal dysfunctions are a key element in the clinical picture of the syndrome as it contributes to the child's mental disability. Studies show that the loss of hearing, even mild loss of hearing (<15 dbhl) can have a negative effect on the perception of speaking, learning and even on language development. This is even more important in the case of Down syndrome where expressive language abilities are even less developed than cognitive abilities. Early treatment and diagnosis can improve linguistic abilities, increasing the productivity of live [20].

The frequent causes of hear loss in children with Down syndrome are the cerumen impaction, medium otitis or mechanic anomalies. Frequently, the internal ear hypoplasia was diagnosed with histological studies and imagistic methods using magnetic resonance. The collapse of the Eustachian tube, hypotonia, mucous and adenoidal hypertrophy, all of them reduce the organ's function and contribute at the insufficient ventilation of the middle ear. A narrow auditory canal accompanied by the presence of the cerumen impaction at an early age makes the process of establishing the diagnosis to be a difficult one or possibly leading to a wrong diagnosis. The global prevalence of hear loss in children with Down syndrome was estimated at 34-78% [21].

The most frequent disorders in these children are bad breath, macroglossy, open-bite, fissured lips and tongue, angular cheilitis, bruxism, microdontia, dental crowding, poor oral hygiene, delayed eruption and reduced incidence of cavities [22].

Microdontia is frequently identified in both temporary and permanent dentition. The clinical crown is conic, shorter and smaller. Apart from this, it is noticed the presence of hypoplastic and hypocalcified teeth. The tetracycline administered in the first part of life leads to certain characteristic spots. Apart from these, children present intrinsic colorations, located or generalized, slightly detectable with dental instruments. Hypoplastic defects are often the result of frequent illnesses and prolonged fevers. Anodontia is more frequent in children with Down syndrome but the distribution of anodontia is, in general, similar to that of unaffected people. Anodontia manifests itself mostly at molar 3, premolar 2, laterals included. The only teeth permanently present are the first molars.

Sometimes, the deciduous teeth can present a delayed resorption being present up to a more advanced age. Taurodontia influences mainly the second inferior molar.

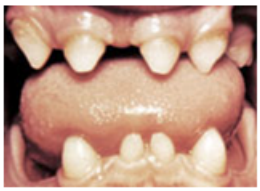


Fig. 1. Intraoral view

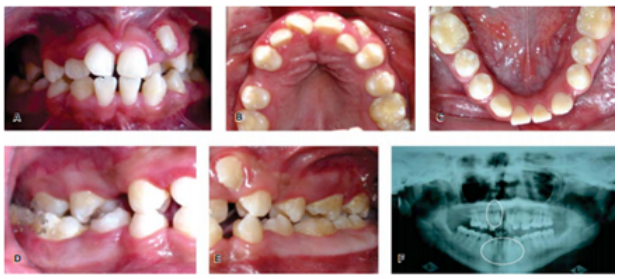


Fig. 2 Intraoral view: malocclusion, bacterial plaque, crowding, anodontia (Toledo M. B., Lopez P.)

They are characterized by a pulp chamber of exaggerated volume, with the tendency of getting wider towards the apex. The prevalence of cavities is reduced because of delayed eruption, reduced time exposure to cariogenic environment, anodontia, the presence of microdontia that favours the space between the teeth and the saliva with a high *p*H level and high bicarbonate level [23, 24].

The fissured tongue is the most frequent disorder that appears on soft tissues, with a prevalence ranging between 10 and 95%, its frequency being directly proportional with age. To this disorder is added angular cheilitis that appears because of muscle weakness - hypotonia, bad breath and protruded tongue. Macroglossia is significantly more obvious in children than in adults with Down syndrome. As a consequence of the above mentioned elements, the lips present various fissures [25, 26].

A study applied to a trial group of 47 children with Down syndrome shows that:

- the relationship between the maxillary and the base of the skull is normal, the maxillary developing in a sagittal plane according to the base of the skull;
- children present maxillary hypoplasia, especially in horizontal plane, but also in vertical plane;
- between 8 and 18 years the development of the maxillary is similar to that of the regular population, but it starts with a less developed bony mass;
- the development of the maxillary stops at an earlier age at those affected [27].

Malocclusions are frequent in children with Down syndrome influencing considerably their everyday life. Apart from the functional implications they confront themselves with (speech, mastication and swallowing deficiencies) they are also subjected to discrimination because of their physical aspect. The most frequent malocclusions are open-bite, anterior-posterior cross-bite and protrusion of frontal teeth [28]. The physical aspect is modified because of the brachycephalic facial profile, with flattened occiput and prominent fontanels. Some authors notice the presence of fontanels for a longer period of time. Given the insufficient level of development of the middle section of the face it appears a mandibular prognathism, the patients presenting quite often Angle class III malocclusion. From a study applied on 100 patients with Down syndrome, results that 33% of them present anterior cross bite, 31% posterior cross bite, and 21% open bite. The insufficient development of the middle segment of the face generates other modifications, as well. Sometimes, the palate can be characterized by atresia while other times there can be labial or palatal clefts or bifurcated uvula. The narrowing of the nasopharynx accompanied by hypertrophied tonsils leads to a specific posture of the lips. Consequently, it appears bad breath, labial incompetence accentuated by the presence of macroglossia. All of them generate the disequilibrium between labial and lingual forces, and the anterior open-bite becomes more pronounced [29].

Although children with Down syndrome present a lower incidence of cavities, they often confront themselves with *periodontal disorders*. The insufficient manual dexterity makes their brushing be performed incorrectly, resulting in high accumulation of dental plaque which favours gingivitis and periodontal disorders [30]. Although it is an important factor, the inappropriate hygiene is not the dominant factor in periodontal disease. The main bacteria identified in the subgingival plaque of adolescents with Down syndrome were Aggregatibacter actinomycetemcomitans, Capnocytophaga and Porphyromonas gingivalis. They have a weak immune system, with an inflammatory answer either weak or too intense, increasing significantly the alteration of the periodontal tissue. The responsibility for this goes to the poor neutrophil chemotaxis, the partial phagocytosis of leukocytes against the staphylococcus and the abnormal development of lymphocytes [31-33]. Personality disorders can cause difficulties during the dental treatment. The dentist must build a relation of confidence with the patient, the former's communication abilities being key factors in the success of the treatment as it is absolutely necessary for the treatment to be painless. Local anaesthesia must be used even to the slightest possible pain. When necessary, general anaesthesia is also used. Another thing that must be taken into consideration is that the vascular access is more difficult because of the patients' tendency towards obesity. To this is added the patients' enlarged tonsils, the diminished subglottic area, macroglossia which make aerial management be more difficult. Sedation is not recommended in those with poor ventilation. At the same time, the atlantoaxial instability must be taken into consideration. Thus, the exaggerated and uncontrolled extension of the head must be avoided. A cervical radiology is recommended for 3 years old patients which must be repeated before and after puberty. In patients with congenital anomalies, with antecedents of infectious endocarditis or artificial cardiac valves, as well as, heart transplant prior to any dental treatment that might imply a transitory bacteraemia it is necessary an antibiotic prophylaxis. Among the dentist's interventions we mention subgingival curettage, extractions, application of dental dam, orthodontic rings. The risk of developing viral infections is higher in these children. The B hepatitis virus is the most frequent in their case (40%). Consequently, immunization results essential, especially in pre-school children as they are the most susceptible to these infections.

Sometimes, patients with Down syndrome cam present gastro-oesophageal reflux (between 13.8% and 59% of cases), disorder that can remain unidentified in the absence of frequent episodes. This disorder, caused by the acidity level of the gastric juice, leads to dental erosion and, consequently, an anaesthetic aspect and dental sensitivity [34, 35].

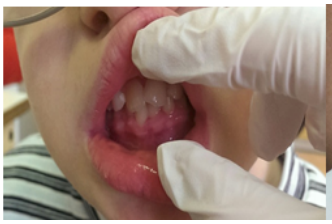
Experimental part

The trial group included 94 children with mixt dentition, aged between 6 and 12 years, divided as follows: 36 children with Down syndrome enrolled at the Educational Centre for Inclusive Education no. 1 of Tg. Mures and Alpha Transilvana Foundation, and the other trial group consisting

of 58 healthy children, without general disorders, enrolled at the Integrated Centre of Dental Medicine of the University of Medicine and Pharmacy of Tg. Mures, who attended regular controls or they were in different dental or orthodontic treatment stages. Clinical and radiological examinations were conducted and they were used to establish the correlation between dental and chronological age, eruption sequences as well as eruption disorders.

Results and discussions

The data obtained after the examination of the oral cavity were recorded in the dental chart of the patient with Down syndrome. For each subject included in the trial there were observed the following: the dental age, the eruption sequences of permanent teeth on the four quadrants of the oral cavity: UR (upper-right), UL (upper-left), LR (lower-right) and LL (lower-left) as well as eruption disorders.



C.D. 11 years – dental age, 10 years (conic teeth, dental crowding) (child with Down syndrome)

M.G. 12 years – dental age, 12 years (reverse occlusion, conic teeth) (child with Down syndrome)

Correlations between dental and chronological age

Table 1

GENDER DISTRIBUTION OF CHILDREN WITH DOWN SYNDROME

Age	Girls	Boys	Total
6-9	6	8	14
9-12	8	14	22

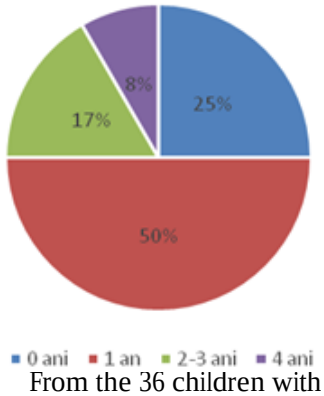


Fig. 3 Concordance between dental and chronological age in children with Down syndrome

From the 36 children with Down syndrome, 9 children (25%) presented concordance between dental and chronological age. In most children, 18 (50%) the age difference between the two ages was of 1 year. The most significant difference appeared at 3 years old children (8), the difference between the two ages being of 4 years. At the same time, another 6 children (16%) presented 3 years and 2 years difference, respectively, between dental and chronological age.

The group of children with Down syndrome was compared to a group of 58 children with no general disorders who came for check-up or control at the Integrated Centre of Dental Medicine of the University of Medicine and Pharmacy Tg. Mures [40].

After examining the oral cavity, it was noticed that at most children, 43 of them, dental and chronological ages were correlated. 6 children presented a 1 year delay in dental eruption and 4 children a 2 years delay. Early eruption was noticed in 5 children.

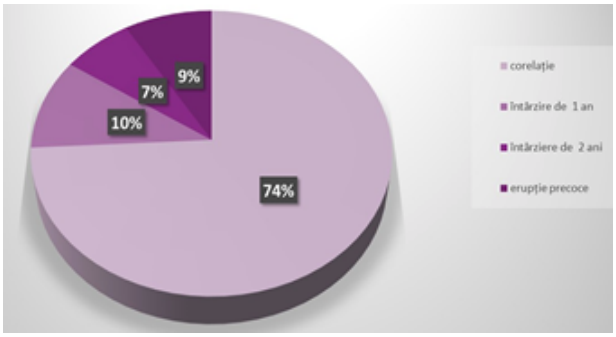


Fig. 4 Correlation between dental and chronological age in clinically healthy children (1,2 and 3 years delay)

In order to identify the statistical relation between the presence of Down syndrome in children and the delayed teeth eruption in relation to the patient's chronological age, various statistical calculations of correlation and regression were used.

The trial group included 36 children with Down syndrome and 58 healthy children.

First of all, it was analysed the correlation factor between the presence of the disease and the delay recorded in teeth eruption, identifying the value of the correlation coefficient of 0.609, value considered to be average to high when referring to the relations between the two variables. To make sure this relationship does not undergo any problems related to multicollinearity, the variation inflation factor was tested (VIF test). The results were significantly below the maximum admitted limit of 10, and thus the data were accepted without any multicollinearity problems.

Secondly, in order to analyse the statistical influence and meaning of the model used, it was used the simple regression model - OLS (Ordinary Least Squares). It allows the accurate measurement of the statistical relation between independent and dependent variables.

The statistical model relied on the pattern of fixed effects, suitable to the relation studied in the present paper. The statistical calculation of regression indicated the prediction value R^2 equal to 0.37 and the statistical appropriateness of the model of 99%. Referring to the direct relation between the presence of Down syndrome in children and the delayed eruption age of teeth compared to the chronological age, it was identified a statistically significant relationship with positive coefficient of 99%, with $p<0.001$.

Thus, we can confidently say that the presence of Down syndrome in children influences significantly the discrepancy between the moment of teeth eruption and the chronological age compared to children without this syndrome. The weighted average value of this difference in the trial group taken into consideration in this study is of 1.27 years. Thus, the presence of Down syndrome in children leads to 1.27 years delay in teeth eruption compared to the data identified in the specialized literature and the data obtained from the group of healthy children.

The results of this study, statistically significant are corroborated with the results obtained by other authors. S. Asokan, MS Muthu et al., in a study conducted on 41 children with Down syndrome, aged between 6 and 10 years old also obtained a statistically significant value, that indicated a delayed eruption of teeth in the trial group ($p<0.004$) [22].

A similar study was conducted by P. Diz and J. Limeres in 2010. They studied the differences between dental and chronological age in children with Down syndrome, brain paralysis and mental retard, respectively. The trial group of children with Down syndrome included 37 children, aged

Table 2
RESULTS OF THE STUDY

Total group **Control group** **Trial group**	**94** **58** **36**
Correlation coefficient between the presence of the disease and delayed eruption	0.609
Regression coefficient R^2	0.37
Average delay	1.27
P value	**<0.001**

between 3 and 17 years old. The results of the study were similar to the results of the present study, but only for the trial group of girls, where 3 of 10 patients presented a 2, 2 and a half and 3 years delay, respectively, with p=0.02 (95% reliability level). The trial group of boys did not provide statistically significant results, unlike the present study where no gender determined differences were noticed [41].

The possible differences of delay may be caused by various factors as regional differences, the different structure of the trial group, local and general factors.

The distribution of eruption patterns in children with Down syndrome

Referring to the eruption patterns, the following were noticed: analysing 144 quadrants there were observed 6 eruption patterns, four favourable and two unfavourable ones, for both arches, the resulting data being presented in table 2.

On the maxillary, there were the following favourable growth patterns 4-5-3 and 4-3-5. There weren't any unfavourable patterns on the maxillary arch.

On the mandible, there were the following favourable growth patterns 4-3-5 and 3-4-5. The unfavourable patterns were 5-4-3 and 3-5-4.

Table 3
DISTRIBUTION OF ERUPTION PATTERNS ON THE MAXILLARY AND THE MANDIBLE

Maxilary (UR, UL)	**Trial group** Sick children
Eruption pattern	No. of quadrants n=64
Favourable patterns 4-5-3 4-3-5	 n=35 (24%) n=29 (20%)
Unfavourable patterns **none**	

Mandible (LR, LL)	**Trial group** Sick children
Eruption pattern	No. of quadrants n=80
Favourable patterns 3-4-5 4-3-5	 n=14 (10%) n=20 (14%)
Unfavourable patterns **5-4-3** 3-5-4	 **n= 20 (14%)** n= 26 (18%)

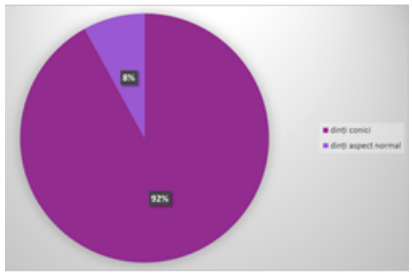


Fig. 5. The presence of conic teeth

Conic teeth
Normal teeth

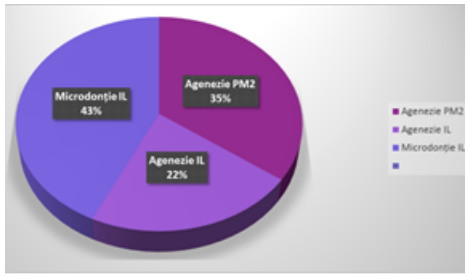


Fig. 6 Other dental anomalies

Microdontia
Agenesis

The presence of conic teeth was noticed at a considerable number of subjects, most of them presenting a conic short and small crown.

The chronology and the eruption sequences are subjected to various variations and also influenced by factors as the presence of cavities, the premature loss or prolonged retention of deciduous teeth and also dental anchylosis. Dental maturation is less subjected to variations as it is a progressive, constant and cumulative process [41].

The causes of delayed eruption in children with Down syndrome are unknown, because of the incomplete understanding of the factors involved in the normal eruption process. Nonetheless, it seems to be influenced by genetic factors. At individuals without disorders, there is a resorption of the bone which can be reduced in children with Down syndrome. There are suggestive evidences that the eruption rate is influenced by the periradicular vascularization of the conjunctive tissue. The insufficient peripheral circulation can be one of the factors that contribute at the delay of the eruption process. At the same time, it can also be caused by the delayed growth and development of the maxilla and the mandible, elements characteristic to this syndrome. Some authors correlate the low weight at birth with delayed eruption (Pindborg, Billewicz, Infante and Owen) [42]. Eruption is a physiological process that has a significant influence on the normal development of orofacial complexes.

The development of the dental-facial complex is a key indicator for the orthodontist and the maxillofacial surgeon. The evaluation of the level of development of dental structures can determine the best moment for the beginning of the orthodontic treatment which implies the use of extra oral forces or functional devices [43]. At the same time, these evaluations can help the dentist in deciding to remove or keep the deciduous teeth. In addition to the dental age, the orthodontist must also assess the skeletal age of the patient prior to deciding the treatment plan [41].

The delayed eruption can influence the accuracy of the diagnosis as well as the treatment plan. Thus, it can have a significant impact on the patient's state of health.

In conclusion, children with Down syndrome require long time monitoring to intercept any anomalies related to their teeth eruption period in order to increase their life quality and improve their state of health.

Conclusions

The presence of Down syndrome in children influences significantly the discrepancy between the teeth eruption and chronological age.

The presence of Down syndrome in children generates a delay of 1.27 years compared to the data found in the specialized literature and the one resulted from the group of healthy children.

The favourable eruption patterns noticed in the study on the maxillary were 4-5-3, 4-3-5 in proportion of 24% and 20% respectively, not being noticed any unfavourable patterns. On the mandible, the favourable patterns were 3-4-5- and 4-3-5, in proportion of 10% and 14% respectively. The unfavourable patterns were 5-4-3 and 3-5-4, noticed in 14% and 18%, respectively.

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