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Research Report

The role of cervical vertebrae maturation in defining the chronological age of Down syndrome children

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ABSTRACT

Background: *The difficulty of determining chronological age is increased in individuals with conditions that may affect normal development. Some systemic conditions in children, for example Down syndrome, may cause abnormal physiological maturation. Skeletal and dental age are considered the most apt physiological age indicators in determining chronological age.* ***Purpose:*** *This study aimed to compare and analyze the relationship between two developmental parameters (dental history and skeletal age) as indicators of the chronological age of children with Down syndrome.* ***Methods:*** *The study design was cross-sectional with a paired t-test to analyze the differences in chronological and dental age of the samples. The radiograph selection was based on purposive sampling. The study material consisted of 30 panoramic radiographs and lateral cephalometrics of 6-14 years old children with Down syndrome and those experiencing normal development (control group) divided into two groups of 15 subjects who attended the Pediatric Dentistry Polyclinic, RSGM, Universitas Padjadjaran. Statistical analysis employed a t-test to determine the difference between chronological and dental age, while a Spearman rank correlation was used to evaluate the correlation between dental and skeletal age.* ***Results:*** *The results showed there to be no statistical difference between chronological and dental age, where $p > 0.05$, but a significant relationship between dental and skeletal age in children diagnosed with Down syndrome, where $p = 0.05$.* ***Conclusion:*** *It is concluded that dental age identified by means of the Nolla method is closer to chronological age than skeletal age using the cervical vertebrae maturation method.*

Keywords: *Down syndrome; dental age; skeletal age; CVM; chronological age*

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INTRODUCTION

Chronological age has many applications in areas as varied as: pediatrics, orthopedics, orthodontics, forensic medicine, anthropological, social and legal contexts such as criminal cases, kidnapping, employment, marriage, premature birth, adoption, illegal immigration, lack of a birth certificate or document-based fraud.[1-4] Chronological age is defined as the length of time that has elapsed since an individual's birth[5,6] and can be used to identify the specific stage of child development. However, it is a weak predictor of growth, rendering physiological age more reliable for evaluating the developmental period. Physiological age is determined by the level of functional development (maturation) of various body tissue systems measured by a range of parameters including: somatic maturation, sexual, skeletal and dental age.[3,7-9]

Somatic maturation can be assessed by analyzing a child's increasing height and weight during the growth period, while sexual maturation is associated with secondary sexual characteristics in boys and girls. Quantification of age by skeletal maturation can be undertaken through reference to changes in bone ossification, one of which is cervical vertebrae maturation (CVM), which are monitored by radiograph. Meanwhile, dental age is established based on the timing of the emergence of teeth and the stage of

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dental formation (calcification) which can also be observed radiographically.[1,3,7,8,10] The assessment of dental age based on tooth calcification using the Nolla method is more reliable than results obtained by other means, such as the Demirjian method. This is because the latter method uses two decimal fractions in the calcification stage, more than 90% researchers approved this method due to the more accurate result.[11]

Skeletal age can be determined through hand and wrist analysis by means of CVM method, of which the most widely-used variety is cervical vertebrae maturation stage (CVMS) analysis. Various studies on CVM have been performed.[12-14] In 1972, Lamparski *et al*. as cited in Bacetti *et al*.,[13] suggested a method for the evaluation of skeletal maturation based on morphological changes in the cervical vertebrae. The original Lamparski method was modified by Baccetti *et al*.,[8,13] and has proven to be sufficiently reliable and valid to replace palm and wrist analysis.

Certain systemic conditions may cause abnormal physiological maturation with the result that skeletal age is more delayed than dental age.[1] Systemic delayed eruption is associated with numerous genetic conditions including: cleidocranial dysplasia, hemifacial atrophy, mucopolysaccharidosis, Turner syndrome and Down syndrome.[15] The latter is a genetic disorder afflicting more than 5.8 million people that has become the most common genetic disorder resulting in intellectual disability. The clinical condition of Down syndrome, first diagnosed by John Langdon Down in the mid-nineteenth century (1866), is characterized by a central growth deficiency resulting in impaired mental development that ranges in severity from mild to moderate. The growth of individuals suffering from the condition is delayed in almost every aspect, including the development of teeth.[16–19]

de Moraes *et al*.[20] studied the chronology of dental mineralization in Down syndrome children and found the dental age of two-thirds of subjects of either gender to be generally more advanced, while that of one-third was delayed, meaning that the majority of patients had normal development. Other studies by de Moraes *et al*.[18] into the chronological analysis of mineralization using Nolla's method concluded that the dental age of Down syndrome individuals is similar to that in normal individuals.

The correlation between the stage of dental calcification and skeletal maturation that has been reported found there to be a correlation between dental age and skeletal analysis of the palms and wrists.[10] Research by Carinhena *et al*.,[21] into skeletal age comparing the CVM method and analysis of the palms and wrists in the pubertal growth spurt curve of Down's individual syndrome confirmed that both analyzes produce similar results.

Few studies are known to link dental age assessment through the stage of dental calcification with skeletal age determined by CVM. Therefore, the authors were interested in conducting research that aimed to compare dental and skeletal age, while linking both with chronological age. Taking the fact that both the panoramic radiograph and lateral cephalometry constitute dental diagnostics frequently performed by the dentist into account, the authors wished to examine further the comparison between dental age established by the Nolla method and skeletal age through CVM in Down syndrome children who were based in Bandung.

MATERIALS AND METHODS

The research material of this study was secondary data obtained from the results of the panoramic radiographic images and lateral sefalometri of 6–14 years old children with Down syndrome who attended the Oral and Dental Hospital, Universitas Padjadjaran. The control group was composed of healthy children of the same age and the sampling undertaken was purposive in nature. The study sample was divided into two groups, namely: Down syndrome children as the test group using primary data, and normal children as the control group using secondary data. Group membership satisfied the following inclusion criteria: the test group included Down syndrome children of all types aged 6–14 years, while membership of the control group was based on the panoramic radiographs and lateral cephalometric tests of normal children aged 6–14 years who underwent dental and mouth care at Oral and Dental Hospital, Universitas Padjadjaran. The results of a panoramic radiographic and lateral cephalometry test confirmed well-defiined detail, contrast and density and did not experience any distortion resulting from a radiologist's assessment.

The research samples meeting the inclusion criteria consisted of 15 children with Down syndrome as the test group and 15 normal children as the control/comparison group. The grouping of samples according to age shows the results of chronological, dental, and skeletal age calculations for those subjects with Down syndrome and their normal/control counterparts. The research was conducted using a cross-sectional study design with parametric and non-parametric statistical tests in order to compare two developmental parameters (dental and skeletal age) as chronological age images in Down syndrome children and to assess the relationship between dental and skeletal ages based on chronological age in children with this condition.

The study was conducted by assessing the results of the panoramic radiographs and lateral cephalometry tests in the form of analysis of ten radiographs completed on one day and repeated once at an interval of one week. Assessment and calculation of dental age based on the results of the panoramic radiographs followed the Nolla method. Assessment of skeletal age based on the radiographic results of lateral cephalometry in the determination of CVM level adhered to the methodology recommended by Baccetti *et al*.[22] Assessment and calculation of dental age using the results of the panoramic radiograph was based on the Nolla method, including the following

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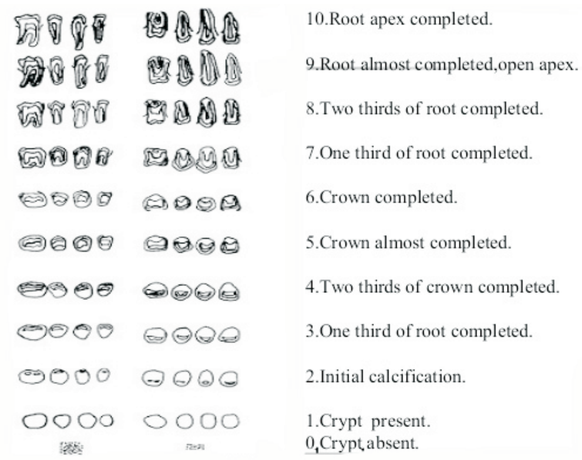

Figure 1. Stages of tooth classification.[4]

steps: identification of ten stages of maxillary tooth and mandible verification, the first column (right) assesses the growth stage of the central and lateral incisors, the second column - the canine teeth, the third column - the premolars and the fourth column - the molars (Figure 1).

Each stage was scored, with the score of each stage then being totaled. If one-third of the crown had been formed when the observation was conducted a value of 3.0 was assigned, whereas if one third of the roots had been formed a value of 7.0 was recorded. If the tooth was between the appropriate class of illustrations, the decimal fractional values of 0.2, 0.5 or 0.7 were registered as recommended by Nolla. If the radiographs were seen between two stages, a value of 0.5 was assigned. For example, if the radiograph reading was between one-third and two-thirds of the roots that had been formed, it was rated 7.5. If the radiographs showed a slightly larger step than the illustration class, but not as much as halfway between that stage and the next, a value of 0.2 was recorded. For example, if a radiographic reading was taken indicating that slightly more than two-thirds of the crown had been formed, it was rated 4.2. If the radiographs confirmed fewer stages than the illustrated class indication, a value of 0.7 was alloted. For example, if the stage is in the class of crowns that are two-thirds completed, the value was 3.7. The number of scores obtained for each tooth (maxillary and mandible) was recorded. This figure was then matched with the corresponding one within the age table of maxillary and mandibular teeth of both genders to translate the developmental value into a dental age.

Assessment of skeletal age by radiographic results of lateral cephalometry in the determination of CVM level was based on the findings of Baccetti *et al*. The stages of CVM classification according to the method of Baccetti *et al*. (Figure 2) are as follows: CVM 1 - the lower limit of the entire cervical vertebrae (C2-C4) was flat, the cervical vertebrae 3 and 4 (C3 and C4) bodies exhibited a trapezoidal shape (the superior vertebrae of the vertebrae body decreased from posterior to anterior/tappered). CVM 2 – the presence of concavity at the lower limit of cervical

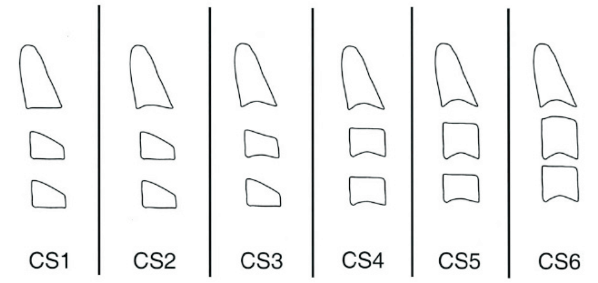

Figure 2. Stages of cervical vertebrae development according to Baccetti.[22]

vertebrae 2 (C2) (depth of basin equal to 0.8 mm), lower limit of cervical vertebrae 3 and 4 (C3 and C4) flat and body C3 and C4 still trapezoidal. CVM 3 – the presence of concavity at the lower limit of cervical vertebrae 2 and 3 (C2 and C3), the cervical vertebrae bodies 3 and 4 (C3 and C4) display a shape between the trapezoid or rectangle without substantial changes. CVM 4 - presence of concavity at the lower limit of cervical vertebrae 2, 3 and 4 (C2, C3 and C4). The cervical vertebrae bodies 3 and 4 (C3 and C4) show a horizontal rectangular shape. CVM 5 - presence of concavity at all lower boundaries of cervical vertebrae 2, 3 and 4 (C2, C3 and C4). At least one of the cervical vertebrae 3 and 4 (C3 and C4) shows a square shape, or one of which is still a horizontal rectangle. CVM 6 - the presence of clear concavity on the entire lower border of cervical vertebrae 2, 3 and 4 (C2, C3 and C4). At least one of the cervical vertebrae 3 and 4 (C3 and C4) is a vertical rectangle (vertical border becomes longer than the horizontal) or one of them is still square.

The statistical tests used in this study constituted the following: a paired t-test to analyze chronological age difference and dental age in Down syndrome children, a Rank Spearman correlation test to analyze the correlation between dental age with skeletal age, a Wilcoxon analysis test to analyze comparison of chronological age to childhood Down syndrome skeletal age, an unpaired t-test to know the difference in dental age between Down syndrome and control children and a Wilcoxon's analysis test to determine the skeletal age difference between Down syndrome and control children.

RESULTS

Down syndrome children constituted a test group of 15 people, with a highest chronological age of 178 months and a lowest of 85 months. The highest dental age was 144 months, while the lowest was 84. The mean age of skeletal childhood Down syndrome was in CVS2. The normal children acting as a control group amounted to 15 individuals, with a highest age of 164 months and a lowest of 98 months. The highest dental age was one of 156 months, while the lowest was 84 months. The average skeletal age of a normal child was in CVS2.

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Grouping of chronological age based on skeletal age in Down syndrome children was completed in order to compare chronological age with skeletal age as shown in Table 1. This shows a comparison of chronological age at CVS 2 and CVS 3 levels. A Wilcoxon analysis test obtained a p-value of 0.0050 < 0.05 and it can be concluded that there is a statistically significant chronological age difference between the CVS 2 and CVS 3 groups.

Table 1 shows a comparison of chronological age at CVS 2 and CVS 3 levels. A Wilcoxon analysis test obtained a p-value of 0.0050 < 0.05, thereby supporting the conclusion that there is a statistically significant chronological age difference between the CVS 2 and CVS 3 groups. Table 1 descriptively shows that the chronological age ratio at CVS 2 and CVS 3 levels is different. The Wilcoxon analysis test obtained a p-value of 0.0050 < 0.05, supporting the conclusion that there is a statistically significant chronological age difference between the CVS 2 and CVS 3 groups. The CVS 4 group (n = 1) was not included in the Wilcoxon analysis test because only one sample was found in patients with a chronological age of 178 months.

The dental age of children with Down syndrome was then compared with their chronological age to enable a comparison of the two ages as shown in Table 2, which descriptively shows that the mean of the chronological age in Down syndrome children is higher than that of their dental age. The difference between the mean chronological and dental age was 8.2 months, indicating that the dental age of a Down syndrome child was 8.2 months lower than his/her chronological age. Statistical analysis of paired t-tests was applied to identify the chronological and dental age differences in children with Down syndrome. This was not statistically significant (p-value = 0.2377 > 0.05). Therefore, it can be concluded that there is no chronological and dental age difference among Down syndrome children. An insignificant result is possible because of the small number of samples

In order to identify the relationship between dental and skeletal age in children with Down syndrome, a Spearman correlation analysis was completed and confirmed the existence of a statistically significant relationship between dental and skeletal age in children with Down syndrome with a value of 0.783. The test results obtained t value = 4.539. The coefficient of determination of the calculation results obtained was 61.3%.

The unpaired t-test was used to establish whether any difference in dental age between the children with Down syndrome and those in the control group existed. The result of the analysis confirmed a difference in dental age between those children with Down syndrome and the control group, although a significant test result (p-value = 0.0636 > 0.05) was absent. Consequently, it can be concluded that there is no difference in dental age between Down children and normal/control children. The average dental age of the Down syndrome children was 108.80 months, whereas in the control group it was 121.60 months. This suggests that the dental age of the Down syndrome child in the 6-14 years chronological age range was 12.80 months or 1 year 8 months lower than in the control group.

The Wilcoxon analysis test for skeletal age differences between the children with Down syndrome and the control group members shows that the majority of individuals with Down syndrome and normal children have a skeletal age in CVS 2. Down syndrome sufferers register a higher percentage (73.4%) when compared with that of normal children (46.7%). Wilcoxon test results obtained a p-value of 0.0763 > 0.05 indicating that there is no significant difference in skeletal age between children with Down syndrome and those in the control group based on chronological age.

DISCUSSION

Within this study, the chronological age of subjects was calculated from differences between radiographic exposure and date of birth, such as in the study conducted by Leonelli de Moraes et al.[18] The research sample consisted of a Down syndrome children group and control group of children in the 6-14 years age range. This age-based retrieval is based on the cervical vertebrae ossification process commencing when the fetus is in the womb and continuing until childhood. Therefore, changes in cervical

Table 1. Results of chronological age comparison test for skeletal age of Down syndrome children

Variable	n	Sum of Ranks	SD	Z	p-value
Chronological age-CVS 2	11	66			
Chronological age-CVS 3	3	39	6.41	-2.57	0.0050*)
Total	14	105			

Description: p-value = (< 0.05); *) = significant

Table 2. Differences test of chronological and dental age in children with Down syndrome

Chronological age average (months)	Dental age average (month)	Differential average between chronological and dental age (month)	n	SD	t-test	p-value
115.8	108.8	8.2	15	9.49	0.723	0.2377

Description: n = Sample, SD = Standard Deviation, *p-value* = (< 0,05)

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vertebrae maturation can be observed during the growth period,[37] in addition to the time of permanent dental eruption (excluding the third molar) between the ages of 6–13 years. Calcification of the permanent teeth begins at the end of the gestation period and continues to average until around the age of 16.[23] This represents a good time for dental age assessment based on tooth formation (dental calcification) and radiographic features.

Children with Down syndrome are at the CVS2 level, confirming that the majority experience delays in development when compared to their chronological age. This result is consistent with the finding of Leonelli de Moraes *et al*. that the skeletal age of children with Down syndrome is delayed during the ages of 7 to 15. Generally, the growth and development of children with Down syndrome experiences delays. Excess chromosomes in children with Down syndrome will alter the genetic balance of the body and result in changes in physical characteristics and intellectual abilities, as well as impairments to the body's physiological functions.[24]

The difference between chronological and dental age in Down syndrome children falling within the 6–14 years age range indicates that there is a delay in the growth and development of teeth in such individuals. The dental age of Down syndrome children lags 8.2 months behind their chronological age – a difference falling within the medium category. The division of dental age categories into "slightly, "moderately", or "notably" in terms of their contrast with chronological age is a classification previously used by other authors who consider a difference of approximately three months between dental and chronological ages as falling within the "normal" category.[2,20]

Sachan *et al*. evaluated the relationship between skeletal and palmar skeletal maturation indicators and CVM indicators with canine calcification based on the Nolla method in a Lucknow-India population. They concluded that there was a strong correlation in both male (r = 0.849) and female (r = 0.932) subjects and that canine calcification stages can be used in assessing skeletal maturation. However, regardless of the substantial correlations reported in the study, clinical significance may be limited to the individual level.[7]

The same results in this study showed there to be a statistically significant relationship between dental and skeletal age in Down syndrome children, with a coefficient of determination amounting to 61.3%. This provides insight into the fact that skeletal age is influenced by dental age in 61.3% of cases, while the remaining 38.7% represents the impact of variables other than dental age, such as: genetic, hormonal, nutritional, socio-economic, climatic, seasonal and factors including pharmacological biochemicals which can delay or accelerate aging because of certain abnormalities. Down syndrome is one of the most common causes of skeletal retardation.[21]

In their research, AbouHala *et al*.[1] show that there is a closer value and a smaller difference between dental and chronological age compared to skeletal and chronological age in Down syndrome individuals. It can therefore be said that establishing age by means of the Nolla method is more accurate than using the Greulich and Pyle method in determining skeletal and chronological age. AbouHala *et al*.[1] support these results. In this study, there was a statistically significant correlation between dental age and skeletal age with a t-count of 4,539. This correlation showed that establishing age by means of the Nolla method produces a result closer to a subject's chronological age than does skeletal age using the CVM method. This is because the Nolla method advocates analysis of two degrees of mineralization from the crown, thereby providing a more detailed value for the stage of dental calcification. It may be that dental age correlates more with chronological age. It is concluded that the dental age as determined by the Nolla method is closer to the chronological age than the skeletal age established by means of the CVM method.

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