

Skeletal Maturation Pattern among Down Syndrome Individuals in Benin, City. Nigeria.

*Osaronse Anthony **AGHIMIEN**, **Emmanuel Olubusayo **AJAYI**, **Idia Nibokun, **IZE-IYAMU**
[*Orthodontic unit, Dental Surgery Department, Federal Medical Centre, Keffi. Nasarawa State
**Department of Preventive Dentistry, University of Benin Teaching Hospital, Benin City, Edo State Nigeria]

Correspondence

Dr. Osaronse Anthony Aghimien
Orthodontic unit, Dental Surgery Department,
Federal Medical Centre, Keffi. Nasarawa State
Email: osaronse@yahoo.com

ABSTRACT

Background: The assessment of skeletal maturity is important in the timing of orthodontic treatment especially in the modification of dento-facial growth. The use of cervical vertebrae as a method of assessment of skeletal maturity has rarely been used among Down Syndrome.

Objective: To assess skeletal maturity among individuals with Down Syndrome using the cervical vertebrae maturation stages.

Methods: The study was conducted among 21 Down Syndrome with mean ages of 11.70 ± 1.83 years (males) and 13.64 ± 1.75 years (female); and 21 control individuals with mean ages of 12.00 ± 2.00 years (male), and 13.50 ± 1.90 years (female). The independent t-test and chi-square test were used to determine significant differences among the continuous (age) and categorical variables (cervical vertebrae maturation stages) respectively when matched with gender and chronological age. Fischer exact test was used when an expected frequency presentation was <5 . A p -value of < 0.05 was set as statistically significant.

Results: Down Syndrome males had delayed maturation at 11 years but accelerated at 12 with early attainment of maturity at 15 years. Down Syndrome female had a delay tendency in skeletal maturation from 11–15 years of age. Overall, Down Syndrome had a 1.242 probability of either having a delay or advancement in skeletal maturation which was not statistically significant. Conclusively, the skeletal maturation pattern between Down syndrome patients and normal individuals was not statistically different.

Conclusion: The average timing for commencement of orthodontic treatment especially growth modification for normal individuals can be applied for individuals with Down Syndrome as this present study did not show any statistically significant difference in their overall skeletal maturation.

Keywords: Skeletal maturity, Cervical Vertebrae Maturation, Down syndrome.

Osaronse A. Aghimien
<https://orcid.org/0002-6737-7959>

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Introduction

Down Syndrome (DS) is the most common chromosomal disorder. ¹ It was first described by John Langdon Down.² Chromosomal imbalance and the gene-dosage effect are responsible for the disorder.³ Incidence and prevalence rate varies among various populations.⁴⁻⁶ Adeyokunnu reported a 1 in 865 incidence rate of Down Syndrome among Nigerians.⁶

Skeletal maturation among Down syndrome has been commonly assessed using various methods ranging from hand wrist radiograph, dental calcification stages, insulin-like growth factor 1 (IGF-1).⁷⁻⁹ However, various observations have been made by different authors on the skeletal maturation of Down Syndrome individuals as being delayed, average or advanced in relation to their chronological ages.¹⁰⁻¹⁵

Cervical vertebrae maturation has rarely been used to assess the skeletal maturation of Down Syndrome individuals as most of the studies have been limited to the hand wrist radiographs.⁷

A high prevalence of malocclusion especially Angle's class III jaw relationship, anterior crossbite, posterior crossbite and anterior open bite have been reported among Down Syndrome individuals.¹⁶⁻¹⁹ Timely orthodontic intervention will address these occlusal disharmonies.²⁰ Therefore, understanding the pattern of skeletal maturation has become necessary to be able to implement appropriate treatment protocol in the management of Down Syndrome individuals.

The objectives of this study were to evaluate the pattern of skeletal maturation among Down syndrome using the cervical vertebrae maturation stages and also to determine if there was any significant difference in the pattern of skeletal maturity between individuals with Down syndrome and normal individuals in relation to gender and chronological age.

Material and Methods

This was a descriptive cross-sectional study. Lateral cephalometric radiographs of twenty-one (21) Down Syndrome (DS) individuals were compared with those of twenty-one (21) controlled individuals within the age range of 10 to 15 years (table 1). Down syndrome individuals were recruited from schools of special need individuals within the Benin City metropolis using the convenient sampling method

due to the rarity of the condition. The Down Syndrome (DS) individuals recruited for this study were initially clinically classified (by the investigator) using the Fried diagnostic index.²¹ According to Fried diagnostic index, an individual was said to be Down Syndrome Positive (DSP) if he had 6 to 8 clinical diagnostic features. All the participants in this study had between 6 to 8 clinical features. They were further confirmed to be trisomy 21 using cytogenetic analysis. The 21 controlled individuals matched for age and gender, were recruited using the systematic random sampling from the pool of pre-orthodontic patients attending orthodontic clinic at University of Benin Teaching Hospital. The lateral cephalographs of the study participants were taken using the Planmeca Proline XC cephalostat manufactured by Planmeca OY (Helsinki, Finland) 2006 model with a magnification factor of 1.08-1.13. Cervical vertebrae maturations (CVM) were staged using the method described by Baccetti et al.,²² (figure 1). The Cervical vertebrae maturations (CVM) stages were thereafter correlated with gender and chronological age.

Ethical approval for this research protocol before the data were collected was obtained from University of Benin Teaching Hospital Health Research Ethics Committee (ADM/E 22/A/VOL VII/1236). Written informed consent was obtained from the guardians of the Down Syndrome individuals before they were recruited for the study.

The cervical vertebrae maturation (CVM) of the participants was manually analyzed on a 0.003inch matte acetate paper using a pointed 0.5mm thick HB pencil under a light box. The posterior and anterior borders of the vertebrae were measured using a plastic millimeter rule. The landmarks proposed by Hellsing,²³ (figure 2) was used to analyze the morphology of the bodies of the second to fourth vertebrae (C2-C4). Concavity of the lower border of the cervical vertebrae has been proposed to be the most reliable parameter of maturation and is said to be present when the depth was greater than 1 mm.²⁴

Evaluations of the CVM on the lateral cephalographs were done at two different sections at intervals of 2 weeks for intraclass reliability assessment of the investigator using the Cohen's Kappa statistics (0.79).

The data were analyzed using the International Business Machine (IBM) SPSS version 20. The independent t-test and chi-square test were used to

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determine significant differences among the continuous and categorical variables respectively when matched with gender and chronological age. A *p*-value of less than 0.05 was set as statistically significant.

Inclusion Criteria for Down Syndrome individuals

1. Chronological age ranging from 10-15 years old (as at last birthday).
2. Individuals with scores of between 6-8 clinical features according to Fried's Diagnostic Rating (FDR).²¹
3. Individuals confirmed to be Down Syndrome using chromosomal karyotyping.

Exclusion Criteria for Down Syndrome individuals

1. Down syndrome individuals with unclear/distorted lateral cephalographs.
2. Down syndrome individuals with difficulty in neck stability.
3. History of trauma to the face and/or cervical vertebrae.
4. Individuals outside the age range of this study.

Inclusion Criteria for controlled individuals

1. Normal overall growth and development with no co-morbidities on review of their documentations.
2. Chronological age ranging from 10-15 years.

Exclusion criteria for controlled individuals

1. Individuals with unclear/distorted lateral cephalographs.
2. Individuals who did not give informed consent.

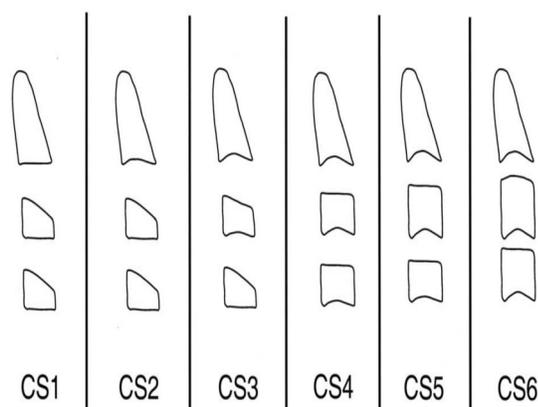


Figure 1: Cervical vertebrae maturation stages as described by Baccetti²²

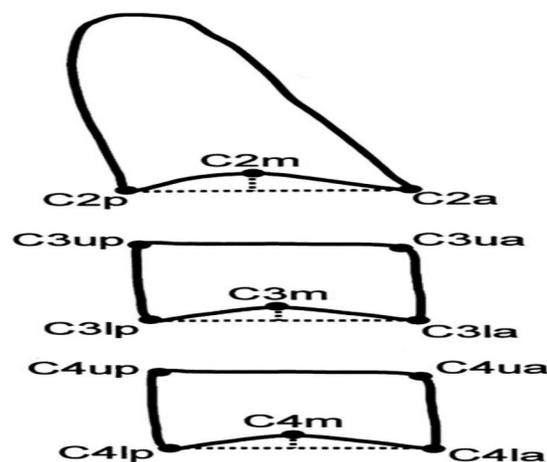


Figure 2. Helling's²³ cephalometric landmarks for C2-C4 evaluation.

Definition of Cephalometric evaluation

- C2p, C2m, C2a: the most posterior, the deepest and the most anterior points on the lower border of the body of C2.
- C3up, C3ua: the most superior points of the posterior and anterior borders of the body of C3.
- C3lp, C3m, C3la: the most posterior, the deepest and the most anterior points on the lower border of the body of C3.
- C4up, C4ua: the most superior points of the posterior and anterior borders of the body of C4.
- C4lp, C4m, C4la: the most posterior, the deepest and the most anterior points on the lower border of the body of C4.
- C2Conc: a measurement of the concavity depth at the lower border of C2 (distance from the line connecting C2p and C2a to the deepest point on the lower border of the vertebra, C2m).
- C3Conc: a measurement of the concavity depth at the lower border of C3 (distance from the line connecting C3lp and C3la to the deepest point on the lower border of the vertebra, C3m).
- C4Conc: a measurement of the concavity depth at the lower border of C4 (distance from the line connecting C4lp and C4la to the deepest point on the lower border of the vertebra, C4m).
- C3BAR: ratio between the length of the base (distance C3lp-C3la) and the anterior height (distance C3ua- C3la) of the body of C3.
- C3PAR: ratio between the posterior (distance C3up-C3lp) and anterior (distance C3ua-C3la) heights of the body of C3.

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- C₄BAR: ratio between the length of the base (distance C₄lp-C₄la) and the anterior height (distance C₄ua-C₄la) of the body of C₄.
- C₄PAR: ratio between the posterior (distance C₄up-C₄lp) and anterior (distance C₄ua-C₄la) heights of the body of C₄.

Stages of Cervical Vertebrae Maturation

Cervical stage 2 (CS₂). A concavity is present at the lower border of C₂. The bodies of both C₃ and C₄ are still trapezoid in shape. The peak in mandibular growth will occur on an average of one year after this stage.

Cervical stage 3 (CS₃). Concavities at the lower borders of both C₂ and C₃ are present. The bodies of C₃ and C₄ may be either trapezoid or rectangular horizontal in shape. This is the onset of the peak of the pubertal growth spurt.

Cervical stage 4 (CS₄). Concavities at the lower borders of C₂, C₃, and C₄ are now present. The bodies of both C₃ and C₄ are rectangular horizontal in shape. The peak in mandibular growth has occurred within one or two years before this stage.

Cervical stage 5 (CS₅). The concavities at the lower borders of C₂, C₃, and C₄ are still present. At least one of the bodies of C₃ and C₄ is square in shape. If not squared, the body of the other cervical vertebra is still rectangular horizontal. The peak in mandibular growth has ended at least one year before this stage.

Cervical stage 6 (CS₆). The concavities at the lower borders of C₂, C₃, and C₄ are still evident. At least one of the bodies of C₃ and C₄ is rectangular vertical in shape. If not rectangular vertical, the body of the other cervical vertebra is square. The peak in mandibular growth has ended at least two years before this stage.

RESULTS

Cervical Vertebrae Maturation (CVM) stages 1 and 3 were mostly represented among Down Syndrome while CVM 4 occurred most among the controlled. Cervical vertebrae maturation stage 5 was least represented among Down Syndrome while Cervical vertebrae maturation stages 2 and 5 were least represented among control individuals, as shown in figure 2.

Table 3 showed the distribution of the Cervical vertebrae maturation (CVM) stages in relation to gender. Male Down Syndrome participant were mainly represented at CVM stage 3 with 40% while male control participants were mostly categorized as

Cervical stage 1 (CS₁). The lower borders of all the three vertebrae (C₂-C₄) are flat. The bodies of both C₃ and C₄ are trapezoid in shape (the superior border of the vertebral body is tapered from posterior to anterior). The peak in mandibular growth will occur on an average of two years after this stage.

CVM 1 (27.3%) and CVM 3 (27.3%). Female Down Syndrome and control participants were mostly at CVM stage 4 with 36.4% and 30% representation respectively.

Among male participants (see table 4) at 11 years of age, 100% of the male Down Syndrome were at CVM₁ which appeared delayed as all the controls were at CVM₃. However, at age 12, there appeared to be an increase in the maturation process with 100% of the DS males now represented at CVM₃ when 50% of the control were at CVM₁ and another 50% of the control at CVM₃. This spurt in growth was maintained up till 13 and 14 years as male Down Syndrome continued to be at CVM₃ when the controls were already at CVM₄ at 13 years of age. This was suggestive of delay in skeletal maturation at age 13. By 15 years of age all the Down syndrome individuals were at CVM₅, while 50% of the control male were still at CVM₄. This implied that Down syndrome male individuals in this study attained skeletal maturity earlier than the control male.

Among the female individuals (table 5), at age 11, all the female Down Syndrome individuals were at CVM₁ while the female the control individuals were observed to be at CVM₃. The delay tendency among the Down syndrome female individuals continued till 13 and 14 years of age. At 13 years of age Down syndrome individuals were now at CVM₂ while the controls were at CVM₄. At age 14, all the control female individuals (100%) were at CVM₅, while 50% of the female Down syndrome was still at CVM₃. It was also observed that at age 15, about 40% of the female control individuals had completed the maturation process (CVM₆) when majority (80%) of the Down Syndrome were only decelerating (CVM₄) in their maturation process. It was concluded that female control individuals attained maturity earlier than female DS individuals.

Down syndrome individuals (irrespective of gender) only had a 1.242 greater probability of having either delay or advancement in skeletal maturation (P value= 0.306), as shown in table 6.

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Figure 3 showed a positive Spearman correlation between Down syndrome and control individuals. Some data points had both the square and round shapes in red and blue respectively. These points

showed areas of clusters of both the Down syndrome and control individuals, further showing the close relationship in their skeletal maturation processes

Table 1: Mean age distribution of study population

Variable	Down syndrome (Mean ± SD)	Control (Mean ± SD)	p value
	Male	11.70 ± 1.83	
Female	13.64 ± 1.75	13.50 ± 1.90	0.866
Total	12.71 ± 2.00	12.71 ± 2.00	1.000

Table 2. Overall distribution of cervical vertebrae maturation stages among Down syndrome (DS) and control (CON) study individuals

CMV stages	DS N (%)	CON N (%)
CVM1	5 (23.8)	4 (19.0)
CVM2	4 (19.0)	3 (14.3)
CVM3	5 (23.8)	4 (19.0)
CVM4	4 (19.0)	5 (23.8)
CVM5	3 (14.3)	3 (14.3)
CVM6	-	2 (9.5)
TOTAL	21 (100)	21 (100)
P value	0.178	0.437

P > 0.05

Table 3: Distribution of cervical vertebrae maturation stages according to gender between Down syndrome (DS) and Control (CON) study individuals

	MALE			FEMALE		
	DS n (%)	CON n (%)	Total	DS n (%)	CON n (%)	Total
CVM1	3(30.0)	3(27.3)	6(28.6)	2(18.2)	1(10.0)	3(14.3)
CVM2	2(20.0)	2(18.2)	4(19.1)	2(18.2)	1(10.0)	3(14.3)
CVM3	4(40.0)	3(27.3)	7(33.3)	1(9.0)	1(10.0)	2(9.5)
CVM4	-	2(18.2)	2(9.5)	4(36.4)	3(30.0)	7(33.3)
CVM5	1(10.0)	1(9.1)	2(9.5)	2(18.2)	2(20.0)	4((19.1)
CVM6	-	-	-	-	2(20.0)	2(9.5)
TOTAL (FE, P- Value)	10(100.0)	11(100.0)	21(100.0) 0.717	11(100.0)	10(100.0)	21(100.0) 0.736

FE- Fisher exact test

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Table 4. Comparative evaluation between the cervical vertebrae maturation (CVM) stages and chronological age between Down syndrome (DS) and Control (CON) males study individuals.

CA (YRS)	CVM ₁		CVM ₂		CVM ₃		CVM ₄		CVM ₅		FE	P Value	TOTAL
	DS n(%)	CON n(%)											
10	2(50)	2(50)	2(50)	2(50)	-	-	-	-	-	-	0.001	1.000	8(38.1)
11	1(100)	-	-	-	-	1(100)	-	-	-	-	2.000	0.157	2(9.5)
12	-	1(50)	-	-	2(100)	1(50)	-	-	-	-	1.333	0.248	4(19.0)
13	-	-	-	-	1(100)	-	-	1(100)	-	-	2.000	0.157	2(9.5)
14	-	-	-	-	1(100)	1(100)	-	-	-	-	-	-	2(9.5)
15	-	-	-	-	-	-	-	1(50)	1(100)	1(50)	-	-	3(14.3)
TOTAL	3	3	2	2	4	3	-	2	1	1			21(100)

DS= Down syndrome; CON= Control, $p > 0.05$, FE-- Fisher exact.

Table 5: Comparative evaluation between the Cervical Vertebrae Maturation (CVM) and chronological age among Down Syndrome (DS) and Control (CON) female study individuals.

CA (yrs)	CVM ₁		CVM ₂		CVM ₃		CVM ₄		CVM ₅		CVM ₆		FE	P-value	Total
	DS n(%)	CON n(%)													
10	1(100)	1(100)	-	-	-	-	-	-	-	-	-	-	-	-	2(9.5)
11	1(100)	-	-	-	-	1(100)	-	-	-	-	-	-	2.00	0.157	2(9.5)
12	-	-	-	1(100)	-	-	-	-	-	-	-	-	-	-	1(4.8)
13	-	-	2(100)	-	-	-	-	1(100)	-	-	-	-	3.00	0.083	3(14.3)
14	-	-	-	-	1(50)	-	-	-	1(50)	1(100)	-	-	0.75	0.386	3(14.3)
15	-	-	-	-	-	-	4(80)	2(40)	1(20)	1(20)	-	2(40)	2.66	0.264	10(47.6)
Total	2	1	2	1	1	1	4	3	2	2	-	2			21(100)

DS= Down syndrome; CON= Control, $p > 0.05$, FE-- Fisher exact.

Table 6: Estimation of the probability of Cervical Vertebrae Maturation (CVM) outcome between Down Syndrome and non-Down Syndrome Control (CON) female participants with the binary logistic model

Group	p value	Odds Ratio	95% CI
Down syndrome vs Control	0.233	1.448	0.788 – 2.660

$P > 0.05$

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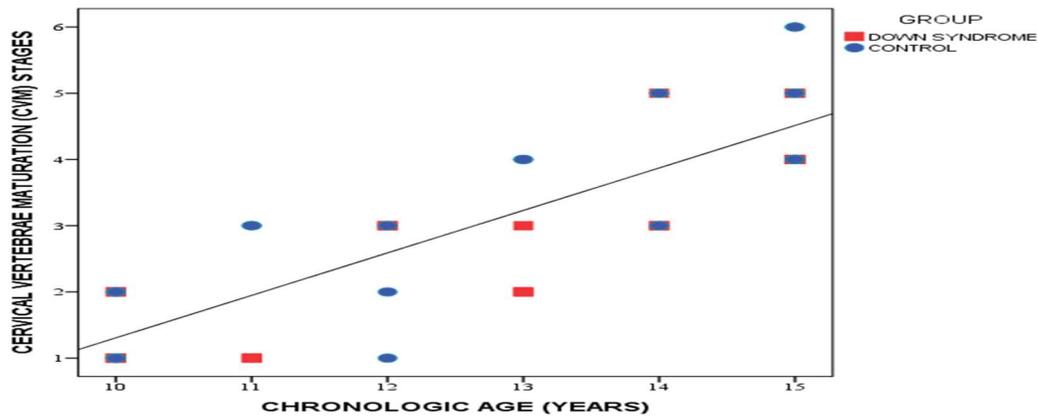


Figure 3: Overall correlation between Down Syndrome and control individuals: Spearman correlation (r_s) = 0.862, p-value = 0.0001.

Discussion

The evaluation of skeletal maturation is an important aspect of orthodontic treatment planning especially with regards to the jaw growth. Further investigation of skeletal maturation among Down syndrome individuals has become necessary as various authors have reported different rate of maturation in these individuals.^{9,10-15,25-28}

The acceleration in the rate of growth at 12 years of age and early attainment of maturity at 15 years of age as observed in this present study is suggestive of a short period of active growth among Down syndrome male individuals, and this corroborates the findings of De Moraes et al.⁹

Orthodontic treatment for these individuals should therefore be properly timed to avoid missing the short window of active skeletal growth among Down syndrome male individuals. Also, advanced skeletal maturation observed among male Down syndrome individuals at 15 in this current study is similar to the findings reported by Sannomiya et al.⁸ among 81 Portuguese Down syndrome individuals.

A delay in skeletal maturation was observed among a group of Brazilian Down syndrome population by Santos et al.²⁹ using the Eklof and Ringertz method of hand-wrist bone assessment, which is consistent with the observations made among the female Down syndrome individuals in this present study. When two other methods (Greulich-Pyle and Tanner-Whitehouse) were used by the same author,²⁹ the skeletal maturation of the same study population were observed to be advanced. This only agrees with observation made among 15-year-old male Down

syndrome individuals but at variance with the majority of the observations made among all other Down syndrome individuals in this present study. Apart from racial differences and the age ranges between this present study and the study conducted by Santos et al.²⁹ among 5-15 years old Brazilian population, the different methods used and individual differences may have accounted for the variations observed. This is suggestive of problems of validity or reliability with Eklo & Ringertz, Greulich & Pyle and also the Tanner & Whitehouse methods of hand-wrist bone assessment.

The outcomes of this present study further emphasized the influence of assessment techniques on the outcome of skeletal maturation determination. Variation in skeletal maturation even among similar population is also reported in the observation made by other authors.^{13,14}

Pozsony et al.¹³ reported advanced skeletal maturation among 100 individuals from the Caucasian Canadian population who were between 10-15 years of age. The findings¹³ are at variance with the observations made among majority of males and female Down syndrome individuals in this present study but in agreement with results from the study conducted by De Moraes and colleagues⁹ and among 6-15 years old female individuals, 6-10 year and 13-15 years old male individuals in another study.⁸ The finding by Pozsony et al.¹³ is however at variance with another study conducted among the Caucasian Canadian population.¹⁴ The differences observed between the authors^{13,14} further re-emphasized

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individual variations even though the study was among a similar population.

Significant positive correlation between dental calcification and the skeletal maturation process have been documented.³⁰⁻³² Although this present study also observed a tendency to exhibit delay in skeletal maturation among Down syndrome individuals, the differences observed in this present study were however not significant as against the significant delay in the dental calcification stages observed in the studies conducted by other authors.^{25,28} The different methodology and sample population in the studies^{25,28} and this present study could have accounted for the differences observed.

On the overall, this present study showed that Down syndrome individuals only had a 1.242 chance of having a delay or advancement in their skeletal maturation process when compared to the controls. It therefore suggests that skeletal maturation among Down syndrome individuals is generally within a normal range. These present findings support earlier researches which reported that majority of Down syndrome individuals are within normal development.^{10,11}

CONCLUSION

1. Down syndrome male individuals had a tendency to experience a delay in skeletal maturation at 11 years of age with accelerated growth rate to CVM₃ at age 12, and attainment of skeletal maturity (CVM₅) occurred at 15 years of age.

2. Down syndrome female individuals had a tendency to experience delay in skeletal maturation from 11 – 15 years when compared with the non-DS individuals. The result also showed that most of the female non-DS (40%) attained skeletal maturity (CVM₅) at 15 years which was earlier than Down syndrome female individuals, though not statistically significant.

3. Down syndrome individuals only had a 1.242 probability of experiencing a delay or advancement in skeletal maturity when compared with the non-DS individuals.

4. The average time for commencement of orthodontic treatment (especially growth modification) for normal individuals can be applied for individuals with Down syndrome as this present study did not show any statistically significant difference in their overall skeletal maturation.

However, individual variations should be strongly considered.

Conflict of interest.

Nil.

Sponsorship

None declared

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