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ORIGINAL ARTICLE



Evaluating the Effect of Dental Fluorosis on the Excessive Ginigval Display in the regional populatuion of Gurugram- An Observational Study

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ABSTRACT

Excessive Gingival display (EGD) plays an important role in altering the aesthetic appearance of an individual. This results into loss of confidence and self-esteem. There are many reasons behind this. However, dental fluorosis has never been considered as a factor that can cause the change in the display. Hence the aim of this pilot study is to evaluate the effect of dental fluorosis over the causes of excessive gingival display and to find its association. Over 223 subjects with dental fluorosis were examined for bony maxillary excess, gingival enlargement, maxillary lip length and excessive mobility of maxillary lip. The results were obtained after applying chi-square test at significance level of p < 0.05. The result showed no strong association of dental fluorosis with excessive gingival display. However some association was seen with respect to lip hypermobility. With the limitation of the study, it is recommended to consider the possibility of the relationship between the fluorosis and EGD and but no definite statement could be made. Further investigations are required to confirm the statement.

Key Words: Excessive Gingival display, dental fluorosis, lip hypermobility, lip length

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INTRODUCTION

The entertainment industry and television have established higher esthetic requirements for visitors through exposing them to awe inspiring faces with remarkable smiles. An attractive well-balanced smile can be a personal asset. There are a lot of factors that determine an esthetic smile, along with the colour, size, shape, symmetry, gingival display also plays an important role. Proper gingival display adds a great value to a perfectly aligned tooth. People who have excessive gingival display (EGD) while smiling are concerned about their looks. A lot them seek their dentist and wants them to find a solution [1]

Fluoride is one important nutrient which is essential for development and growth [2]Dental fluorosis is a result of excessive fluoride ingestion during the developmental years, before the tooth gets mineralised. It's effects ranges from chalky white patches to pitting of enamel and brownish discoloration, making it look unesthetic [3]. After the great work done by Dean and his co-workers, by establishing a relationship between fluoride and the developmental disturbances it causes along with its anti-cariogenic properties, it has always been an integral part of all the programs which focused on control and prevention of dental caries by using this unique anti cariogenic property of fluoride. Its injudicious use led to a certain prevalence and increase in the severity of the dental fluorosis [4]

In the literature, there have been no direct relationship of excessive gingival display and dental fluorosis till date but, the effects of chronic fluoride exposure have been linked to effects on soft tissues, bones and other systems as well. Fluoride is readily incorporated and accumulates in the bone. According to past histomorphological studies of bone, fluoride's effect on the increase in the bone mass is mostly due to higher rate of bone formation rather than decreased bone resorption. The bone formation is stimulated by theincrease in the osteoblast count. The mitotic effect of fluoride on bone cells has been confirmed in several laboratories. Also, there has been studies that proved fluoride also effects the precursor cells of osteoblast thus increasing bone formation [5]

It has been found that long term high exposure to fluoride increases the risk of skeletal fluorosis. It involves increased bone density. But skeletal fluorosis is seen when fluoride is more than 5000 parts per million (ppm). Also, quite a few changes in the mucosal cells have been reported. It has been seen that inhibition of enzymes involved in the pentose pathway, antioxidant defence system, the myosin ATPase

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pathway and collagen synthesis [6-7]. Therefore, with these facts, this was an initial study conducted to determine the effect of dental fluorosis over the excessive gingival display in the population of Gurugram district.

MATERIAL AND METHODS

This observational study was conducted in outpatient department at SGT Dental Hospital, Gurugram. Informed consent was obtained from the patients and participants who fulfilled the inclusion criteria were included in the study. The study was approved by ethical committee of Institutional review board before its commencement. The inclusion criteria were presence of dental fluorosis, born and bought up in Gurugram district, people who belonged to the age group 12-55 years and without systemic illness. The exclusion criteria were pregnant females, patient with any systemic illness that can influence the cause of excessive gingival display, patients who have developmental stains other than dental fluorosis.

Participants

This study included 223 patients (males and females) belonging to the age group 12-55 years. Further, the patients were also grouped based upon age: (1) Group I: 12-19 years; (2) Group II: 20-27 years; (3) Group III: 28-35 years; (4) Group IV: 36-43; (5) Group V: 44-51 years; (6) Group VI: 52 and above. However, for this study no patients were enrolled for the VI age group, hence the age group of 52 years and above was dropped for the study

Clinical Examination

Patients who fulfilled inclusion criteria were included in the study. First, dental fluorosis was recorded using Modified Dean's Fluorosis Index and oral examination was performed using basic diagnostic mirror set

Then, gingival display was evaluated under following causes of EGD:-

- 1) Bony maxillary excess
- 2) Gingival enlargement
- 3) Maxillary lip length
- 4) Excessive mobility of maxillary lip

Bony maxillary excess-

Bony maxillary excess is calculated by dividing the face into vertical thirds, and measuring each of them. If the middle third is longer than the rest, it is said to be maxillary excess. Excessive gingival display here is due to placement of teeth far away from the skeletal maxillary base. Further, depending upon the amount of display it is divided into three sub categories, degree 1: 2-4mm; degree 2: 4-8mm and degree 3: >8 mm of gingival display.(Figure 1).Further, depending upon the amount of display it is divided into three equal divisions.

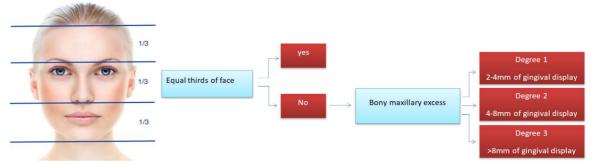


Figure 1: Determination and evaluation of bony maxillary excess

Gingival Enlargement-

Gingival enlargement is a multifactorial condition. It also leads to excessive gingival display as it begins to covers the crown portion Glickman's classification [7] was used to identify the presence or absence of gingival enlargement. (Figure 2).

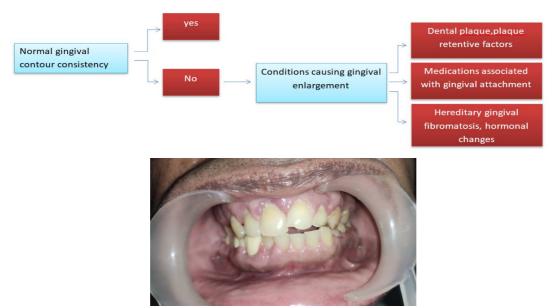


Figure 2: Determination and evaluation of gingival enlargement

Deficient Maxillary lip-

For measuring the length of maxillary lip, distance between subnasale to the inferior border of the upper lip is recorded. The average maxillary lip length measured was 23.4 ± 3.42 mm for men and 20.02 ± 2.89 mm for women in India. (Figure 3)

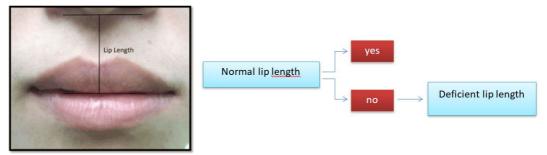


Figure 3: Determination and evaluation of upper lip length

Excessive mobility of maxillary lip-

Excessive lip mobility is usually the result of hyperfunctioning elevator muscles and leads to excessive gingival display. The maxillary lip, in a dynamic smile usually moves up by 6-8mm which is normal but the values can even be doubled if the muscles are hyperactive. To measure the excessive mobility of the lip, the gingival display is recorded from the zenith to the inferior border if the maxillary lip in a full dynamic smile. (Figure 4)

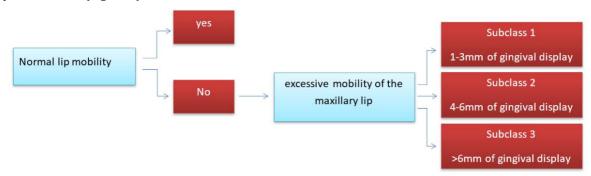




Figure 4: Determination and evaluation of lip mobility

STATISTICAL ANALYSIS

The observed data was deposited on a Microsoft Office Excel 2010spreadsheet. SPSS software version 22(USA) was used for the analysis of the collected data. Chi-square test was used with p value < 0.05 being significant for inter and intra group comparison between the etiology of excessive gingival display and demographic data along with dental fluorosis score.

RESULTS AND DISCUSSION

A total of 223 dental patients visiting dental hospital in Gurugram were taken into the final study. Out of which 102 (45.7%) were males and 121 (54.3%) were females of age 12 to 51. The demographic data of the population with the level of dental fluorosis among the population is depicted in Table 1.The association between gender and categories doesn't show any statistical significance (p value > 0.05) among bony maxillary excess and gingival enlargement. However, a significant relationship (<0.05) was associated with maxillary lip deficiency and highly significant with hyper lip mobility. In case of maxillary lip deficiency, the result suggests that out of 102 males, majority (70.6%) has shown lip length between 16-20 mm and minimum (12.7%) have lip length between 11-15mm. Similarly in females, maximum (71.9%) has lip length between 16-20mm and minimum (6.6%) have lip length between 21-25mm. (Table 2) In lip hypermobility, the males showed, 37.3% with no gingival display during dynamic smile, 47.1% showed 1-3mm of gingiva, 13.7% showed 4-6mm of gingiva and 2% (2) showed more than or equal to 7mm of gingival display during dynamic smile. Similarly in females, 16.5% (20) subjects showed no gingival display during dynamic smile, 55.4% (67) showed 1-3mm of gingiva, 24.8% (30) showed 4-6mm gingival display and in 3.3% (4) more than or equal to 7mm of gingival display was present during dynamic smile. The statistical analysis showed a significant correlation between hyper lip mobility and gender status in the given population (p = -0.003).

The statistical analysis showed that there were no age-related changes seen with any of the 4 categories and was accounted as non-significant p value as depicted in Table 3. With respect to dental fluorosis, only category with hyper mobility of lip showed statistically significant result, with lowest value seen in lip length equal to or more than 7 with dean's grade 4 and highest value seen in lip mobility 1-3 mm with dean's grade 1. (Table 4)No other category showed any significant (p <0.05) association with dental fluorosis.

Table 1 Relationship between Fluorosis and Gender

Gender	Fluorosis n (%)				Total		
	Questionable	Very Mild	Mild	Moderate	Severe		P Value
Male	23 (22.5)	27 (26.5)	21 (20.6)	15 (14.7)	16 (15.7)	102 (45.7)	
Female	35 (28.9)	33 (27.3)	20 (16.5)	19 (15.7)	14 (11.6)	121 (54.2)	
Total	58 (26.0)	60 (26.9)	41 (18.4)	34 (15.2)	30 (13.5)	223	0.71 (NS)

Chi-square test, *p-value < 0.05 is Significant (S), p-value > 0.05 is Non Significant (NS)

Table 2 Relationship between AGE AND various CATEGORIES of Excessive gingival display

Category		Age					
							Value
		1	2	3	4	5	
Vertical	No bony excess	46	60	38 (88.4)	23 (85.2)	21 (91.3)	
maxillary		(83.6%)	(80%)				0.64
excess	Bony excess present	9 (16.4)	15 (20)	5 (11.6)	4 (14.8)	2 (8.7)	
Gingival	Present	6 (10.9)	6 (8)	4 (9.3)	0 (0)	1 (4.3)	
enlargement	Absent	49 (89.1)	69 (92)	39 (90.7)	27 (100)	22 (95.7)	0.46
Upper lip	11-15 mm	12	16	4	5	2 (8.7%)	
length		(21.8%)	(21.3%)	(19.3%)	(18.5%)		
	16-20mm	39	54	32	18	16	0.28
		(70.9%)	(72%)	(74.4%)	(66.7%)	(69.9%)	
	21-25mm	4 (7.3%)	5 (6.7%)	7	4	5	
				(16.3%)	(14.8%)	(21.7%)	
Hyper lip	0 mm	10	22	11	7	8	0.39
mobility		(18.2%)	(29.3%)	(25.6%)	(25.9%)	(34.8%)	
	1-3 mm	29	35	22	18	11	
		(52.7%)	(46.7%)	(51.2%)	(66.7%)	(47.8%)	
	4-6mm	12	17 ()	9	2 (7.4%)	4	1
		(21.8%)		(20.9%)		(17.4%)	
	Equal and more than 7	4 (7.3%)	1 (2.3%)	1 (2.3%)	0 (0%)	0 (0%)	

Chi-square test, *p-value < 0.05 is Significant (S), p-value > 0.05 is Non Significant (NS)

Table 3 Relationship between GENDER AND CATEGORIES of excessive gingival display

Category	GENDER	P-Value		
		1	2	
Vertical maxillary excess	No bony excess	84 (82.4%)	104 (86%)	0.46
	Bony excess present	18 (17.6%)	17 (14%)	
Gingival enlargement	Absent	6 (5.9%)	11 (91%)	0.36
	Present	96 (94.1%)	110 (90.9%)	(NS)
Upper lip length 11-15 mm		13 (12.7%)	26 (21.5%)	0.02*
	16-20mm	72 (70.6%)	87 (71.9%)	(S)
	21-25mm	17 (16.7%)	8 (6.6%)	
Hyper lip mobility	0 mm	38 (37.3%)	20 (16.5%)	-0.003
	1-3 mm	48 (47.1%)	67 (55.4%)	
	4-6mm	14 (13.7%)	30 (24.8%)	
	Equal and more than 7	2 (2%)	4 (3.3%)	

Chi-square test, *p-value < 0.05 is Significant (S), p-value > 0.05 is Non Significant (NS)

DISCUSSION

This study was conducted to evaluate the relationship between the causes of excessive gingival display and dental fluorosis in the current population of Gurugram district. A total of 223 subjects were evaluated for a time period of upto 6 months. The main reason behind this cross sectional study was to focus on the relationship of dental fluorosis to that of the causes of excessive gingival display like Vertical maxillary excess, gingival overgrowth, maxillary lip deficiency and mobility of the maxillary lip. The present dental literature is insufficient to enlighten over this issue, hence this is the first study as per the current literature search. Sahil *et al* conducted a study in Gurugram district which revealed 46% of the population had dental fluorosis of which 9.6% and 11.23% reported to have severe degree and moderate degree of fluorosis respectively[8-9]

Our gingiva plays an important role in determining the esthetics of the smile. Sharma et al.[10] While smiling, the gingival exposure between the gingival edge of upper central incisor and lower edge of maxillary lip is considered normal. An exposure of 2-4mm of maxillary incisal edge when the lips are at rest state and exposure of 0-2mm are considered to be acceptable. And show od gingiva more than 2mm when a person smiles is referred to as Gummy smile[11].irregular tooth eruption, decrease upper lip length, excessive protruded maxilla or increased vertical growth of the maxilla, and hypermobility of levator muscles and the maxillary lip common causes of gummy smile[12]

Wolford et al explained Maxillary vertical excess as an excessive vertical growth of the bony maxilla If the lower vertical third of the face is longer than the other two-thirds, there is a vertical overexposure of the

maxilla and overexposure of the gums. Vertical Maxillary excess is considered to be more in females (+2.13 mm) than males (+1.03 mm) as concluded by Wu et al and Bhola *et al.* [13-14]. According to Peck *et al.*[15] and Mackley[16] anterior vertical maxillary excess (about 2-3 mm) is one of the most important cause of gummy smile.

Table 4 Relationship between FLUOROSIS AND CATEGORIES of excessive gingival display

Category	ationomp betti com	FLUOROSIS AND CATEGORIES OF excessive gingival dispi					P-
Category		FLUURUSIS					Value
		Questionable	Very Mild	Mild	Moderate	Severe	varac
Vertical maxillary	No bony excess	50 (86.2%)	51 (85.0%)	38 (92.7%)	24 (70.6%)	25 (83.3%)	0.12
excess	Bony excess present	8 (13.8%)	9 (15.0%)	3 (7.3%)	10 (29.4%)	5 (16.7%)	
Gingival enlargement	Absent	6 (10.3%)	1 (1.7%)	4 (9.8%)	3 (8.8%)	3 (10.0%)	0.37
	Present	52 (89.7%)	59 (98.3%)	37 (90.2%)	31 (91.2%)	27 (90.0%)	
Upper lip length	11-15 mm	10 (17.2%)	9 (15%)	8 (19.5%)	7 (20.6%)	5 (16.5%)	0.99
	16-20mm	42 (72.4%)	44 (73.3%)	28 (68.3%)	23 (67.7%)	22 (73.3%)	
	21-25mm	6 (10.3%)	7 (11.7%)	5 (12.2%)	4 (11.8%)	3 (10.0%)	
Hyper lip mobility	0 mm	17 (29.3%)	14 (23.3%)	11 (26.8%)	8 (23.5%)	8 (26.7%)	0.05
	1-3 mm	24 (41.4%)	32 (53.3%)	25 (61.0%)	24 (70.6%)	10 (33.3%)	
	4-6mm	14 (24.1%)	13 (21.7%)	5 (12.2%)	1 (2.9%)	11 (36.7%)	
	Equal and more than 7	3 (5.2%)	1 (1.7%)	0 (0%)	1 (2.9%)	(3.3%)	

Chi-square test, *p-value < 0.05 is Significant (S), p-value > 0.05 is Non Significant (NS)

In the present study, An Increase in size of gingiva results into gingival overgrowth that may cause gummy smile. Inflammatory gingival enlargement is the most common form that is clinically presented. Drug-induced gingival overgrowth is seen with certain systemic drugs, but is now less commonly observed. Inflammatory hypertrophy can be caused by long-standing bacterial plaques that cause constant irritation leading to chronic hypertrophy. According to a study byKalaviani et al. Studies show that the prevalence of inflammatory overgrowth is higher than the drug-induced overgrowth[17]

However, our study didn't show any statistically significant association between age group and gender or dental fluorosis with gingival overgrowth suggesting that dental fluorosis may not have any effect on the gingival growth of inflamed origin.

If the facial height, gingival height, lip length, and central incisor length of a patient with excessive gingival symptoms are normal, a possible cause could be hypermobile maxillary lip.Peck and Peck [18] reported that the lip length measured during a full smile was 22.3 mm and the average lip movement was 5.2 mm (23%). In addition, in a study assessing spontaneous smiles by Tarantili et al.[19] identified a decrease of 28% the length of the upper lip. According to Roe et al.[20], overall means of mobility of lips for females with normal lip length were 5.8 ± 1.7 mm, females with short lip length is 5.0 ± 1.3 mm, males with normal lip length is 6.7 ± 1.5 and males with short lip length is 5.7 ± 1.1 mm. Robbins[21] reported that the upper lip normally rises about 6-8 mm from the resting position to the position reached in a dynamic smile.

In-vitro evidences from the study where myotubes when treated for 72hrs with NaF at 1.5 ppmafter differentiation showed a noteworthy increase in their size. The diameter and fusion index increased, but the length of the myotube decreased compared to 1 ppm NaFand untreated controls. In addition, at 96 hours, the length of the myotube decreased further, but the diameter and fusion index increased. Following myotubal hypertrophy, muscle nuclei accumulate in the center of the myotube, which is characteristic of hypertrophy[22]This possibility could explain the reason behind the lip hypermobility detected in fluorosis cases in the study. However the association shown is weak.

It was seen that the NaF stimulated the pre-embryonic mesenchyme to differentiate into osteoblasts and deposition of bone matrix was present. Thus, NaF along with stimulating ongoing osteogenesis from differentiated osteoblasts, can also enable initiation of osteoblastic processes embryonic mesenchyme by substituting for the normal bone inducer[23]. NaF leads to increased formation of bone, resulting in a net increased bone mass (as does not increase resorption at the same time). The newly formed bones are mainly osteoids unless given calcium supplements to enhance mineralisation [24-25]

Fluoride may represent overstated physiological response but it's has therapeutic effect is selective on bone. It has been seen that the skeletal tissues respond to supplemental NaF by an increase in bone formation rate and increase in number of osteoblasts or osteogenic cells.

However, our study showed no significant finding in association with dental fluorosis and EGD. This study is a primitive study, hence the data collected is on small population. Therefore the results couldn't be generalised the entire population. Also, biochemical parameter of fluoride determination is lagging to give definitive conclusion of the relationship between dental fluorosis and EGD. An intensive and elaborative data set needs to be accumulated for further conclusion, use of molecular techniques to determine the underlying mechanism of the study relationship is required.

CONCLUSION

Being the first of its kind, the available data suggests that there might be a relationship of dental fluorosis with lip length or hyper lip mobility. However, with the limitation of the study, it is recommended to consider the possibility of the relationship and not a definite statement could be made. Further studies with the large data and more comprehensive study design is advised.

REFERENCES

- 1. Cheng HC, Cheng PC. (2017). Factors affecting smile esthetics in adults with different types of anterior overjet malocclusion. Korean | Orthod.;47(1):31-38.
- 2. Horowitz HS. (1989). Fluoride and enamel defects. Adv Dent Res.; 3(2):143-146.
- 3. Everett ET. (2011). Fluoride's effects on the formation of teeth and bones, and the influence of genetics. J Dent Res.;90(5):552-60.
- 4. Kumar N, Gauba K, Goyal A, Kapur A. (2018). Comparative evaluation of three different recording criteria of dental fluorosis in a known endemic fluoride area of Haryana. Indian J Med Res. 147(6):567-572
- 5. Lau KH, Baylink DJ. (1998). Molecular mechanism of action of fluoride on bone cells. J Bone Miner Res. 13(11):1660-7.
- 6. Park S, Ajtai K, Burghardt TP.(1999). Inhibition of myosin ATPase by metal fluoride complexes. BiochimBiophys Acta.1430(1):127-40.
- 7. Glickman I.(1950); A basic classification of "gingival enlargement". J Periodontol . 1950;21(3):131-139
- 8. Brizuela M, Ines D. (2020). Excessive Gingival Display. In: Stat Pearls [Internet]. Treasure Island (FL): StatPearls Publishing; Available from: https://www.ncbi.nlm.nih.gov/books/NBK470437/
- 9. Handa S, Prasad S, Rajashekharappa CB, Garg, Ryana HK, Khurana C. (2016). Oral Health Status of Rural and Urban Population of Gurgaon Block, Gurgaon District Using WHO Assessment Form through Multistage Sampling Technique. JClin of Diagn Res. 10(5):ZC43-ZC51.
- 10. Izraelewicz-Djebali E, Chabre C. (2015). Gummy smile: orthodontic or surgical treatment? Dentofacial Anom Orthod;18:102
- 11. Pausch NC, Katsoulis D. (2017). Gender-specific evaluation of variation of maxillary exposure when smiling. J Craniomaxillofac Surg;45:913-20.
- 12. Wu H, Lin J, Zhou L, Bai D. (2010). Classification and craniofacial features of gummy smile in adolescents. J CraniofacSurg;21:1474-9.
- 13. Wolford LM, Karras SC, MehraP. (2001). Considerations for orthograthic surgery during growth, part 2: maxillary deformities. Am J Orthod Dentofacial Orthop;119:102-5.
- 14. Bhola M, Fairbairn PJ, Kolhatkar S, Chu SJ, Morris T, de Campos M. LipStaT: (2015). The Lip Stabilization Technique- Indications and Guidelines for Case Selection and Classification of Excessive Gingival Display. Int J Periodontics Restorative Dent;35: 549-59.
- 15. Peck S, Peck L, Kataja M. (1992). The gingival smile line. Angle Orthod;62:91-100.
- 16. Mackley RJ.(1993). An evaluation of smiles before and after orthodontic treatment. Angle Orthod;63:183-90.
- 17. Kalaivani, N. (2020). "Estimation of prevalence of gingival enlargement a population-based study." The Journal of Contemporary Issues in Business and Government 26: 309-315.18.
- 18. McNamara JA. Jr, Brust EW, Riolo ML. (1993). Soft tissue evaluation of individuals with an ideal occlusion and a well-balanced face. In: McNamara JA Jr. (Ed.) Esthetics and the Treatment of Facial Form. Monograph 28.Craniofacial Growth Series. Center for Human Growth and Development, Ann Arbor pp98.
- 19. Tarantili VV, Halazonetis DJ, Spyropoulos MN. (2005). The spontaneous smile in dynamic motion. Am J Orthod Dentofacial Orthop;128:8-15.
- 20. Roe P, Rungcharassaeng K, Kan JYK, Patel RD, Campagni WV, Brudvik JS. (2012). The Influence of Upper Lip Length and Lip Mobility on Maxillary Incisal Exposure. Am J Esthet Dent;2:116-125.

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- 21. Robbins JW. (1999). Differential diagnosis and treatment of excess gingival display. Pract Periodontics Aesthet Dent;11:265-72.
- 22. Sudheer Shenoy P, UtsavSen, SakethKapoor, Anu V. Ranade, Chitta R. Chowdhury, Bipasha Bose. (2019). "Sodium fluoride induced skeletal muscle changes: Degradation of proteins and signaling mechanism", Environmental Pollution, 20-28
- 23. Hall B.K. "Sodium fluoride as an initiator of osteogenesis from embryonic mesenchyme in vitro", Bone, 1987
- 24. Marie P.J. and Hott M.(1986). Short-term effects of fluoride and strontium on bone formation and resorptionIn the mouse. Metab. C/in. Exp. 35:547-551.
- 25. Riggs B.L. (1983). Treatment of osteoporosis with sodium fluorrde: An appraisal. In: Bone and Mineral Research Annual 2. W.A. Peck, ed Elsevier, Amsterdam. pp. 363-393.

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