Journal of Coastal Life Medicine

Hormonal Fingerprints: A Potential Biomarker for Periodontal Disease

[1]Gautami S. Penmetsa, *[2]B. Anusha, [3]Praveen Gadde, [4]Joshna Itha, [5]Bhavya Manchala, [6]Manisha Beldhi

[1]Professor And Head, Department Of Periodontics And Implantology, Vishnu Dental College, Bhimavaram, India.. E-Mail: gautamipenmetsa@gmail.Com

[2]Assistant Professor, Department Of Periodontics And Implantology, Vishnu Dental College, Bhimavaram, India. E-Mail: anushab@vdc.edu.in

[3]Assosiate Professor, Department Of Public Heath dentistry,Vishnu Dental College, Bhimavaram, India. E-Mail: anushab@vdc.edu.in

[4]Post Graduate, Department Of Periodontics And Implantology, Vishnu Dental College, Bhimavaram, India. E-Mail: ithajoshna@gmail.com

[5]Post Graduate, Department Of Periodontics And Implantology, Vishnu Dental College, Bhimavaram, India. E-Mail: bhavyamanchala19@gmail.com

[6]Post Graduate, Department Of Periodontics And Implantology, Vishnu Dental College, Bhimavaram, India. E-Mail: beldhimanisha98@gmail.com

*Corrosponding author - B Anusha. E-Mail: anushab@vdc.edu.in

Abstract

Background: Hormonal fingerprints/ 2D:4D ratio of an induvidual was offlate considered as a potential biomarker in many medical diseases and conditions. However in dentistry, this 2D:4D ratio has not been substantiated for its role of dental conditions yet. As the role of steroid hormones in periodontal health has well been documented in the literature and 2D:4D ratio is a result of prenatal androgen exposure. Our aim is to evaluate its role in the periodontal status of the individuals.

Materials and Methods: A study proves 150 were evaluated for periodontal status using Russell's Periodontal index and 2D:4D ratio was measured using digital vernier callipers. 't' test, chi square test and binary regression analysis were the statistical tests implied in the results.

Results: A higher prevalence of low 2D:4D ratio was evidenced in males compared to females. However females evidenced good periodontal health than males. This increased incidence of periodontitis in males can be attributed to the environmental and psychosocial factors.

Conclusion: The role of 2D:4D ration in periodontitis appears obscure as although the prenatal androgen exposure seems to be higher in males which in turn exhibits beneficial effect on periodontal tissues. Our study demonstrated poor periodontal health compared to females.

1. Introduction

Biomarker also termed as a biological marker is referred to as a character which is an objective measurement that is evaluated as an indicator of not only the biological process but also related to processes that are involved pathologically and pharmacologically towards therapeutic intervention 2D:4D [1,2,3]. The second digit:fourth digit ratio which are the hormonal fingerprints are such

Journal of Coastal Life Medicine

biomarkers that displays sexual dimorphism thereby eliciting diverse phenotypic traits in humans thereby influencing the genetic make up of an individual.[4,5]

Hormones that are steroid in nature regulate and modulate not only growth and maintenance but also pay a key role in reproduction.These steroid sex hormones that are derivative of cholesterol have also been believed inplaying a crucial role in the maintenance of skeletal integrity of the alveolar bone. Testosterone is one such key regulatory hormone besides progesterone and dihydrotestosterone that is not only associated with bone metabolism, but also plays a vital role in the maintenance of bone mass.[6,7] The 2nd to 4th digit ratio of a hand is a sexually dimorphic trait and refers to the relative length of the fourth digit compared to the second digit and has been

noticeably a consistent feature of an individual that is stable and reproducible.[8]This 2D:4D ratio has grabbed enormous attraction in the recent times from the researchers point of view. This unique biomarker has been unravelled to envisage various medical diseases at a very early stage of life.It is also interesting to know that this biomarker has not been explored in dentistry to the extent to it had been in the medical field although a couple of studies have limited to only the correlation of 2D : 4D ratio to that of to early caries prognostic detection(1) and it's incidence in malocclusion.[9]Literature till date exist on its implications to periodontal disease. Hence this unique attempt that is the first of its kind has been done in implicating the 2D:4D ratio in the diagnosis of periodontal status of an individual.

2. Methodology

The study was conducted in the 150 patients attending the outpatient department. This study was approved by the human subjects ethics boardand was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013. A written informed and signed consent was ensured from all the patients prior to participation. Individualsabove 18 years of age and who are systemically healthy are included in the study.

Right hand of all the participants was taken for the digit ratio measurement as a means of standardization. Russell's periodontal index was taken into consideration for assessing the periodontal status of the individuals.

A digital vernier calliper was used to measure the midpoint of the basal crease till the tip of the digit and palm side of the hand was taken into account for measuring 2D:4D ratio. The obtained values were categorised as low digit ratio <1 and high digit ratio >1 after 2D:4D ratio was divided.(Figure 1)

Periodontal status (Russell's Periodontal index) was recorded under sunlight, using a mouth mirror and William's periodontal probe. A score from 0.1 to 0.2. correlated to clinically normal supportive tissues, ascore from 0.3 to 0.9 correlated to Simple gingivitis, a score from 1to 1.9 correlated to beginning destructive periodontal disease, ascore from 2to 4.9. correlated to established destructive periodontal disease and ascore from 5.0 to 8.0, correlated to terminal disease.

t-test, Chi-square test and binary regression analysiswere used for statistical analysis of the obtained results that were tabulated.

3. Result

Based on the obtained calculations 2D:4D ratiothan 1 and ≥1 were generalized for the entire study population. Out of 150 participants 92.1% were males and 78.4% were females with 2D:4D less than 1, 7.9% males and 21.6% females with 2D:4D ≥1. Male population showed higher prevalence in the low 2D:4D ratio. The results were statistically significant (p-value= 0.018)[Table 1]. When the digit ratio of males and females were compared, males had a lower 2D:4D ratio than females. Statistical significance was not evident in the results (p-value= 0.103) [Table 2].

Different age groups were compared to low and high 2D : 4D ratio. Statistical significance was not observed between different age groups.[Table 3].The different age groups were assessed to the 2D:4D ratio. The mean 2D:4D ratio did not show any significance between the different age groups. [Table 4]

The association between periodontal status and digit ratio was assessed and it was noted that 20.3% with a low digit ratio and 18.2% patients with a high digit ratio exhibited having clinically normal supportive tissues. 25.8% with a low digit ratio and 22.7% patients with a high digit ratio demonstrated simple gingivitis. 28.1% with a low digit ratio and 36.4% patients with a high digit ratio

Journal of Coastal Life Medicine

evidenced beginning of destructive periodontal disease. 19.5% with a low digit ratio and 13.6% patients with a high digit ratio showcased established destructive periodontal disease. 6.2% with a low digit ratio and 9.1% patients with a high digit ratio exhibited terminal disease.[Table 5]

The association between periodontal status and the gender was assessed.8.7% males and 11.3% and 10% females had clinically normal supportive tissues, 10% males and 15.3% females had Simple gingivitis, 18% males and 11.3% females had Beginning destructive periodontal disease, 11.3% males and 7.3 % females had Established destructive periodontal disease and 2.7% males and 6% females had terminal disease. Statistical significance was observed. The Pearson's correlation test showed that 2D:4D has no correlation with the periodontal status of the individual [Table 6].

BinaryLogistic Regression analysis showed females had 3.613 times high 2D:4D ratio compared to males which was statistically significant whereas its correlation with age and Russell's periodontal index did not show any statistical significance.[Table 7]

4. Discussion

The 2D:4D ratio that is established during the intrauterine period in the 13th week of pregnancy, is one of the modes of assessing prenatal androgen exposure.[5,10,11] This morphological indicator of sexual dimorphism is considered to be a put forth marker of intrauterine sex hormone levels because of its consistency throughout adulthood. This ratio varies considerably in either of the sexes as the second finger is smaller than the fourth finger in males and whereas they are of equal length in females or a longer second digit.[12,13]Literature review suggest that the 2D:4D in males is usually smaller than in females. A clear evidence of dimorphic tendency is evident in the right hand compared to the left and the reason behind of which remains unclear. Accordingly a higher fetaltestosterone and low oestrogen levels are associated with a low 2D:4D ratio and a high2D:4D ratio association was in synchronous with increased fetal oestrogen and low testosterone levels.Literature projected a probable impact of 2D:4D ratio on psychological illness such as stress,alcohol dependence,autism,cancers etc.[5,14,15]

Oral health which is the mirror of general health plays an important role in overall being of an individual. Dental caries and periodontal diseases are the two common diseases affecting the mankind. The association between dental caries and hormonal finger printing has been validated in the studies conducted byAkansha Rajawat etal andPriyanka et al.[1,9]As hormonal fingerprint is identified to be one potential biomarker that is reproducible and constant throughout the life this was by all mean implicated in our study to evaluate itsassociation to the periodontal status of the individual.

In our study when males and females were analysed for their 2D:4D ratio, it was found that a statistically significance was evident. On the other hand when the mean 2D:4D ratios were evaluated there was no statistical significance. The above results were in correlation with the studies conducted by Akanksha Rajawat etal wherein association of hormonal fingerprints in dental caries was evaluated in about 200 individuals.[1]Also in another study by Priya Verma etal hormonal fingerprints were investigated for their role in early detection of caries, 2D:4D ratio was statistically significant.[10]The association of hormonal fingerprints as risk implications were analysed for not only dental caries but also for malocclusion in a study by Priyanka et al and the findings were similar to that of our study.[9]

In our study the association of age groups was evaluated for, wherein no association with age and hormonal fingerprints were evident as already proven in the literature which coincides along with the fact that 2D: 4D ratio is stable and is associated with prenatal androgen exposure.(Manning et al. 1998; Williams et al. 2003).[4,16]

In our study Russell's Periodontal index score to 2D:4D ratio was analysed for and the findings revealed a low 2D:4D ratio and depicted an increased periodontal scores although not statistically significant. These findings are unique to our study as this is the first study of its kind.When Russell's Periodontal Index was looked in for its association with gender in our study, males showed an increased scores of the index depicting more periodontal diseases. A similar correlation with studies on gender and it's association to caries was depicted by Akanksha Rajawat etal, Priyaetal,Lakshmi etal. [1,10,17]

Journal of Coastal Life Medicine

The increased incidence of periodontitis in males in our studies appears mysterious and should be given a second thought as amongst the various steroid sex hormones that were elicited to have their influence on periodontal disease pathogenesis progesterone, testosterone and dihydrotestosterone has substantiated their effects on bone mineral metabolism.[18] However, testosterone secretion that is responsible for masculinisation and is produced by the adrenal cortex is regulated by ACTH and by pituitary adrenal androgen stimulating hormone. Literature evidences an accelerating matrix synthesis by periodontal fibroblasts and osteoblasts under testosterone influence playing a crucial role in the bone mass maintainence. [19,20]It was also proven in the literature that androgens decelarated IL6 production and prostaglandins secretion during inflammation.[21]

However our findings documented an inverse relationship to periodontitis in men which can be attributed to the following reasons. As stated by various authors Nazir etal,Ioannidouetal(2017) in the literature, higher prevalence of periodontal disease was documented in men than women revealing the crucial role of gender in the risk of developing periodontal disease. [22,23] The increased incidence of periodontal disease in males may probably be attributed to thebehavioural and environmental factors such as poor oral hygiene and tobacco smoking.(Ahamedetal).[24]Thiswas supported by studies by AntinaSchulzeetalwhich concluded increased periodontal disease that wasattributed to poor oral hygiene in males.[25] Also

in another study recently conducted by Lipsky it was put forth that due to improper oral hygiene habits and less positive attitude towards oral hygiene,men exhibited poor periodontal health thereby revealing the fact that men need to be more motivated than women.[26]

Environmental habits such as tobacco smoking which is higher in males also contribute to the deterioration of periodontal health as evident in recent studies that are documented in the literature by Goel and de AraujoNobreetal.[27,28] It's also of considerable interest to note that the psychosocial measures of stress associated factors in males like financial strain and distress are the significant risk indicators for periodontal disease.(Gencoetal)[29]

Thus it can be identified that 2D:4D ratio elicited positive results in periodontitis even as in dental caries and a low 2D:4D ratio demonstrated higher prevalence of periodontitis

5. Conclusion

Hormonal fingerprints that are sexually differentiated in males and females are a result of exposure to prenatal androgens. These can be utilised as potential screening tools not only to identify and depict their association to various medical conditions but also to correlate their relation to dental conditions. However our study was conducted with 150 patients to investigate the role of hormonal fingerprints. More studies in future can be conducted to reveal their association in not only periodontitis but in various other dental conditions as well thereby utilising the role of potential biomarker.

References

[1] Rajawat A, Majeti C, Podugu UK, Kaushik M, Nagamaheshwari X, Mehra N. Association of hormonal fingerprints and dental caries: A pilot study. J Conserv Dent 2020;23:337-40.

[2] Biomarkers Definitions Working Group, Atkinson Jr AJ, Colburn WA, DeGruttola VG, DeMets DL, Downing GJ, Hoth DF, Oates JA, Peck CC, Schooley RT, Spilker BA. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. ClinPharmacolTher 2001;69:89-95.

[3] Mayeux R. Biomarkers: Potential uses and limitations. NeuroRx 2004;1:182-8.

[4] Manning JT, Scutt D, Wilson J, Lewis-Jones DI. The ratio of 2nd to 4th digit length: A predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. Hum Reprod 1998;13:3000-4.

[5] Putza DA, Gaulin SJ, Sporter RJ, McBurney DH. Sex hormones and finger length. What does 2D:4D indicate? Evol Hum Behav 2004;25:182-99.

[6] Bhardwaj A, Bhardwaj SV. Effect of Androgens, Estrogens and Progesterone on Periodontal Tissues. J Orofac Res 2012;2:165-170.

[7] KatzIA, EpsteinS. Bone mineral metabolism at the menopause: Determinants and markers. In: Piero P Foa, editor, Humoral factors in the

Journal of Coastal Life Medicine

regulation of tissue growth. 1st ed. New York: Springer-Verlag 1993:211-23.

[8] Jeevanandam S, Muthu PK. 2D: 4D ratio and its implications in medicine. Journal of clinical and diagnostic research: J Clin Diagn Res. 2016;10:CM01–03.

[9] Priyanka GN, Prasad MG, Radhakrishna AN, Ramakrishna J, Jyothi V. The hormonal fingerprints and BMI: Implications for risk factors in dental caries and malocclusion. J Clin Diagn Res 2016;10: ZC06-9.

[10] Verma P, Hegde AM. Digit Ratio and Dental Caries: A Sexually Dimorphic Trait. Int J Clin Pediatr Dent 2018;11:1-6.

[11] Issrani R, Aljohani F, Prabhu N, Alam MK. Assessment of 2D: 4D ratio for the early diagnosis of caries and malocclusion in 7-15-year-old children. Bang J Med Sci. 2021;20:154-8.

[12] George R. Human finger types. Anat Rec 1930;46:199-204.

[13] Brown W, Hines, M, Fane, B, Breedlove, S. Masculinized finger length patterns in human males and females with congenital adrenal hyperplasia. Horm Behav. 2002;42: 380-86.

[14] Agnihotri AK, Purwar B, Jeebun N, Agnihotri S. Determination of sex by hand dimensions. Internet J Forensic Sci 2006;1:12–24.

[15] Kanchan T, Rastogi P. Sex determination from hand dimension of North and South Indians. J Forensic Sci 2009;54:546–50.

[16] Williams JHG, Greenhalgh KD, Manning JT. Second to fourth finger ratio and possible precursors of developmental psychopathy in preschool children. Early Hum Dev. 2003;72:57–65.

[17] Lakshmi CR, Radhika D, Prabhat M, Bhavana S mulk, Sai Madhavi N. Association between genetic taste sensitivity, 2D:4D ratio, dental caries prevalence, and salivary flow rate in 6-14-year-old children: a cross- sectional study. J Dent Res, Dental Clinics, Dental Prospects. 2016;10:142-7.

[18] Guncu GN, Tozum TF, Caglayan FE. Effects of endogenous sex hormones on the periodontium—Review of literature. Aus Dent J. 2005;50:138-45.

[19] Wilson JD, Gloyna RE. The intranuclear metabolism of testosterone in the accessory organs of reproduction. Recent Prog Horm Res 1970;26:309-36.

[20] Bhardwaj A, Bhardwaj SV. Effect of androgens, estrogens and progesterone on periodontal tissues. J Orofac Res. 2012:165-70.

[21] Nirola A, Batra P, Kaur J. Ascendancy of sex hormones on periodontium during reproductive life cycle of women. J Int Clin Dent Res Organ 2018;10:3-11.

[22] Nazir MA. Prevalence of periodontal disease, its association with systemic diseases and prevention. Int J Health Sci. 2017;11:72–80.

[23] Ioannidou E. The sex and gender intersection in chronic periodontitis. Front Public Health. 2017;5:189.

[24] Ahamed TS, Rajasekar A, Mathew M G Prevalence of Periodontal Disease among Individuals between 18-30 Years of Age: A Retrospective Study. Ann Med Health Sci Res.2021;11:198-204.

[25] Schulze A, Busse M. Gender Differences in Periodontal Status and Oral Hygiene of Non-Diabetic and Type 2 Diabetic Patients. Open Dent J. 2016 9;10:287-97.

[26] Lipsky MS, Su S, Crespo CJ, Hung M. Men and Oral Health: A Review of Sex and Gender Differences. Am J Mens Health. 2021;15:1-8.

[27] Goel K, Sharma S, Baral DD, Agrawal SK. Current status of periodontitis and its association with tobacco use amongst adult population of Sunsari district, in Nepal. BMC oral health. 2021;21:1-9.

[28] de AraujoNobre M, Malo P. Prevalence of periodontitis, dental caries, and peri-implant pathology and their relation with systemic status and smoking habits: Results of an open-cohort study with 22009 patients in a private rehabilitation center. J Dent. 2017;67:36-42.

[29] Genco RJ, Ho AW, Grossi SG, Dunford RG, Tedesco LA. Relationship of stress, distress and inadequate coping behaviors to periodontal disease. J Periodontol. 1999;70:711-23.

Journal of Coastal Life Medicine

TABLES

Table 1: Distribution of males and females in 2D:4D <1 or >1

SEX	2D:4D RATIO <1		2D:4D RATIO >1		P VALUE
	N	%	N	%	0.018
MALE	70	92%	6	7.9%	
FEMALE	58	78.4%	16	21.6%	
TOTAL	128	85.3%	22	14.7%	

(P Value <0.05 Is Considered To Be Significant)

TABLE 2: Comparison of 2D : 4D ratio among males and females

GENDER	N	MEAN ± SD	t value	P VALUE
Male	76	0.9486 ± 0.04146	-1.641	0.103
female	74	0.9843 ± 0.18535		

(P Value <0.05 Is Considered To Be Significant)

Table 3: Association of Age Groups to 2D:4D ratio

2D:4D RATIO	<20yrs		21-30yrs		31-40yrs		41-50yrs		51-60yrs		>60yrs		P VALUE
	N	%	N	%	N	%	N	%	N	%	N	%	0.554
Low	5	3.3	43	28.7	24	16	32	21.3	14	9.3	10	6.7	
High	3	2	6	4	3	2	6	4	2	1.3	2	1.3	

(P Value <0.05 Is Considered To Be Significant

Table 4: Comparison of Age Groups to 2D:4D ratio

Age Groups	N	MEAN ± SD	P VALUE
<20yrs	8	0.9713 ± 0.04486	0.162
21-30yrs	49	0.9469 ± 0.04930	
31-40yrs	27	0.9593 ± 0.04132	
41-50yrs	38	0.9666 ± 0.04069	
51-60yrs	16	0.9581 ± 0.05154	
>60yrs	12	1.0667 ± .45394	

(P Value <0.05 Is Considered To Be Significant)

Journal of Coastal Life Medicine

Table 5: Association of Russell's Periodontal Index score to low and high 2D:4D ratio

2D:4D RATIO	Russell's Periodontal Index Score					P VALUE
	0-0.2	0.3-0.9	1-1.9	2-4.9	5-8	0.891
Low	20.3%	25.8%	28.1%	19.5%	6.2%	
High	2.7%	3.3%	5.3%	2.0%	1.3%	

(P Value <0.05 Is Considered To Be Significant)

Table 6: Association of Russell's Periodontal Index score and Gender and Pearson Co Relation

| Gender	Russell's Periodontal Index Score					P VALUE
	0-0.2	0.3-0.9	1-1.9	2-4.9	5-8	0.188
Male	8.7%	10.0%	18.0%	11.3%	2.7%	
Female	11.3%	15.3%	11.3%	7.3%	4.0%	
Pearson Co Relation : 0.079						

(P Value <0.05 Is Considered To Be Significant)

Table 7: Binary Logistic Regression Analysis of variables

Variables	Sig.	Exp(B)	95% C.I.for EXP(B)	
			Lower	Upper
Gender	.017	3.613	1.261	10.352
Age Group	.520			
21-30yrs	.068	.182	.029	1.132
31-40yrs	.063	.134	.016	1.111
41-50yrs	.106	.191	.026	1.423
51-60yrs	.097	.131	.012	1.440
>60yrs	.226	.206	.016	2.662
Russell's Periodontal Index Score	.602			
0.3-0.9	.838	1.174	.252	5.463
1-1.9	.174	3.001	.614	14.661
2-4.9	.663	1.519	.231	9.979
5-8	.462	2.383	.235	24.151

Journal of Coastal Life Medicine

Fig. 1: Measurement Of 2D:4D ratio in males and females using digital Vernier Calipers
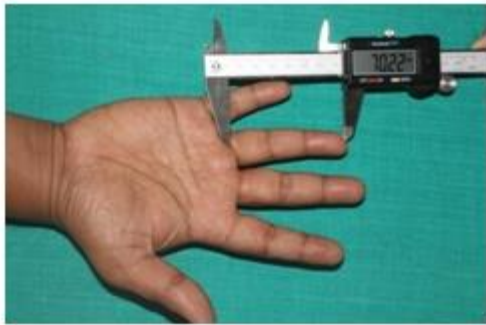
2D   4D

Measurement Of 2D:4D ratio in Males using digital Vernier caliper

2D   4D

Measurement Of 2D:4D ratio in Females using digital Vernier caliper

FIGURE 1