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KNOWLEDGE AND AWARENESS AMONG DENTAL STUDENTS REGARDING SCREENING TECHNIQUES FOR DOWN SYNDROME DURING GESTATION

Type of manuscript: Survey

Running Title: Questionnaire based study among dental students regarding their knowledge on prenatal screening of Down syndrome.

Janhvi Manohar[1], Dhanraj Ganapathy[2], Kiran Kumar Pandurangan[3], Ashok Velayudhan[4]

ABSTRACT*: Down syndrome is one of the most important causes of mental retardation in the world population. The purpose of prenatal screening is to identify those women at the increased risk for an affected pregnancy and to maximize the options available to these women. Second trimester serum screening for chromosomal aneuploidies involves combining the maternal age-specific risk for an affected pregnancy with the risks associated with the concentrations of maternal serum alpha-fetoprotein (MSAFP), unconjugated estriol (uE3), and human chorionic gonadotropin (hCG) (triple testing). A fourth analyte, inhibin-A (INH-A), is increasingly being utilized (quadruple testing). These techniques when employed with ultrasound soft markers scanning gives a true positive rate of 88% and significantly reduces the false positives. A questionnaire-based study was conducted among dental students of third, fourth year students and interns at a private dental college in Chennai, Tamilnadu, India to assess their knowledge and awareness of prenatal screening techniques for Down syndrome. A multiple-choice questionnaire was presented to 106 subjects and their responses were noted, tabulated and statistical analysis was performed using SPSS by IBM by performing Chi-square test. Among 106 subjects, 40 (37.7%) were interns, 33 (31.13%) were third year students and the remaining 33 were fourth year students. Interns and third year students had more knowledge and awareness regarding the prenatal screening techniques employed to diagnose Down syndrome of fetuses with a significant p value < 0.05.*

Keywords: *Down syndrome; ultrasounds; maternal serum tests; hCG; soft markers; nuchal translucency*

1. INTRODUCTION:

Chromosomal diseases are the leading cause of perinatal mortality and developmental abnormalities. In 1866, Langdon Down described for the first time the syndrome that today bears his name, in reference to individuals affected by the trisomy of chromosome 21, the most common chromosomal aneuploidy in humans (0.12% or 1 in 800 births).

[1]*Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India*
[2]*Professor and H.O.D, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-600077*
[3]*Senior Lecturer, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-600077.*
[4]*Professor and Head, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai-600077*
Corresponding author: Dhanraj Ganapathy
Professor and H.O.D, Department of Prosthodontics, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, No. 162, PH Road,
Chennai - 600077, Tamilnadu, India, Contact No: +91 9841504523

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(Fonseca et al., 2014) Down syndrome is the set of physical, mental, and functional abnormalities that result from trisomy 21, the presence in the genome of three rather than the normal two chromosomes 21.

The physical abnormalities that together give rise to the distinctive facial appearance associated with this condition include up slanting palpebral fissures with inner epicanthal folds, flatness of the bridge of the nose, midfacial hypoplasia, and a tendency to protrude the tongue, especially when very young. Many other functionally inconsequential minor abnormalities of the ears, hands, and feet may also be present, and stature is generally reduced. Approximately 40% of affected individuals are born with congenital heart disease, with endocardial cushion and related septal defects frequently being present. Obstruction of the intestinal tract also occasionally occurs during development. Although trisomy 21 is the autosomal trisomy most compatible with survival through the period of gestation, only about a third of affected embryos and fetuses are actually liveborn. (Epstein, 1989)

The diagnosis of aneuploidies depends on invasive procedures that are associated with risks of gestational loss. The total fetal loss for chorionic villus sampling and amniocentesis ranges from 1.5 to 2.0%. (Niederstrasser et al., 2017) In an attempt to indicate these tests only to patients considered to be at high risk, several screening strategies have been developed. Therefore, prenatal genetic counseling is necessary. In addition, several gynecology and obstetrics societies around the world recommend prenatal screening for aneuploidies in all pregnant women however many of the other countries are strictly against this practice. (of Obstetricians et al., n.d.) Screening has been defined as 'the structured application of a test or inquiry, to identify individuals at sufficient risk of a specific disorder to benefit from further investigation or direct preventative action,among persons who have not sought medical attention on account of symptoms of the disorder' (Wald, 1994). Criteria for worthwhile screening programs have been specified (Pergament, 2001). These include a well-defined medically important disorder with known prevalence and tests that are cost-effective, safe, accessible, and have well defined performance. Identification of women who are at high risk for fetal Down syndrome is consistent with this definition and the measures of utility. Patients who are screen positive are generally offered ultrasound evaluations of the fetus, genetic counseling, and definitive diagnosis through cytogenetic analysis of either chorionic villi in the first trimester or amniotic fluid cells in the second trimester. Women with a Down syndrome affected fetus frequently choose to terminate their pregnancy (Verp et al., 1988). However, this is not the goal of prenatal screening and diagnosis. The goal has been clearly defined by Peter Rowley (Rowley, 1984) who notes that 'the aim of genetic screening programs and prenatal diagnosis should be to maximize the options available to families rather than to reduce the prevalence of the disease'.

There have been an advent of a number of prenatal screening techniques which can be employed at different stages of trimesters. First-trimester screening allows early diagnosis of aneuploidy. There are many strategies that are available for chromosomal abnormality screening. The first-trimester combined test was introduced by Wald and Hackshaw (1997)4 and is one of the most popular and useful strategies. In this screening strategy, the risk is calculated based on the sonographic findings and maternal serum levels of free beta human chorionic gonadotropin (β-hCG) and pregnancy associated plasma protein A (PAPP-A).(Wald and Hackshaw, 1997) The screening performance of the combined test has been reported to range from 82 to 95% detection rate, with a 5 to 7% false positive rate. (Kagan et al., 2008; Nicolaides et al., 2005; Spencer et al., 2000, 2003; n.d.; Wald et al., 2005) However, it may vary between different ethnicities as well as by age group. (Li et al., 2015; Pan et al., 2015; Park et al., 2016)

Usually in the second trimester, serum marker assay tests can be performed to screen for Down syndrome which can be double, triple or quadruple. As reported by Merkatz et al., (Merkatz et al., 1984) in 1984, maternal serum alpha-fetoprotein (MSAFP) levels were lower in pregnancies wherein the child was born with chromosomal abnormalities, predominantly Down syndrome usually combined with maternal age (Cuckle et al., 1984; Fuhrmann et al., 1984).
It is known to allow an additional 20% of all accepted pregnancies to be identified of Down syndrome (Palomaki and Haddow, 1987). However, the reason for these low levels of AFP is still unclear and more studies on the same are required. (Chard, 1991) Bogart et al. (Bogart et al., 1987) showed that second trimester maternal serum human chorionic gonadotropin (hCG) levels are generally higher in maternal serum when fetal Down syndrome is present. They noted that hCG appeared to be superior to MSAFP in detecting fetal chromosome abnormalities. Because of the widespread availability of hCG assays for pregnancy detection and monitoring, a rapid introduction of the testing as an adjunct to Down syndrome screening was possible. Similarly, analysis of second trimester maternal serum indicated that a reduction of unconjugated estriol (uE3) was also present and that this marker could also be used for Down syndrome screening (Canick et al., 1988; Wald et al., 1988). Although there has been some controversy as to the value of this marker (Macri et al., 1990), the cumulative data from multiple studies indicated that uE3 is nearly as useful as hCG and is more powerful than MSAFP in distinguishing between affected and unaffected pregnancies. The use of inhibin as an additional marker for Down syndrome screening was first suggested by Van Lith et al (Van Lith et al., 1992).

Ultrasounds can also be used in the first and second trimesters to assess several soft markers such as nasal hypoplasia/absent nasal bone (a ratio of the biparietal diameter (BPD) to nasal bone of greater than 11.0 was the best definition of nasal bone hypoplasia associated with aneuploidy) (Manohar, 2016), nuchal translucency (measurement of the fluid in the neck region on first trimester ultrasound) (Arias et al., 2019), short femur length (a measurement below the 2.5th percentile for gestational age or a measurement that is less than 0.9 of that predicted by the measured biparietal diameter) (Nyberg et al., 1993) and short humerus length.

This questionnaire-based study was performed among dental students to assess their knowledge and awareness regarding the screening techniques employed for the prenatal diagnosis of Down syndrome. Previously our department has published extensive research on prosthetic dentistry (Ajay et al., 2017; Ashok and Suvitha, 2016; Duraisamy et al., 2019; Ganapathy et al., 2016; Jain et al., 2018; Jyothi et al., 2017; Kannan and Others, 2017; Ranganathan et al., 2017; Venugopalan et al., 2014), on effect of various drugs (Selvan and Ganapathy, 2016; Subasree et al., 2016), oral hygiene status of women (Basha et al., 2018), on the effect of impregnated gingival retraction cords (Kannan and Venugopalan, 2018), on the medical management of cellulitis (Vijayalakshmi and Ganapathy, 2016), this vast research experience has inspired us to research this topic. This study aims to assess the knowledge and awareness of prenatal screening techniques for Down syndrome among dental students studying at a private dental hospital in Tamilnadu, India.

2. MATERIALS AND METHODS

Background:

The questionnaire-based study was conducted among the students studying at a private dental college to assess their knowledge on gestational screening techniques for Down Syndrome. It was conducted in the city of Chennai, Tamilnadu, India during January 2020.

Study design:

A questionnaire was created on Google Forms and the subjects were administered with a structured questionnaire encompassing their knowledge and awareness of different techniques employed to conduct prenatal screening for Down Syndrome. The Multiple-Choice Questionnaire developed, had 11 questions and it was made sure that individuals gave their first natural response and attempted all the questions spontaneously. Anonymity was maintained and their responses were noted and tabulated. Ethical approval to conduct the study was obtained from the ethical review board of Saveetha Institute of Medical and Technical Sciences.

Inclusion criteria:

3rd, 4th students and interns studying at a private dental college were included in the study

Exclusion criteria:

Post graduate students, professors were excluded from the study. Incomplete responses were excluded due to the risk of bias.

Statistical analysis:

The responses were tabulated and Chi square tests were performed using SPSS software by IBM

Limitations of study:

The study was conducted only in one private dental hospital and thus confined to one metropolitan area.

3. RESULTS AND DISCUSSION

Among 106 students who participated in the survey based original study, 40 (37.7%) were interns, 33 (31.13%) were third year students and the remaining 33 were fourth year students (Table 1). Regarding the chromosome affected in Down syndrome, the majority of the students, 71 in number answered correctly as chromosome 21, among which 16.9% were third year students, 16.0% were fourth year students and 33.9% were interns ($p<0.05$) as depicted by Graph 1. However, 24 students leaned towards the answer, chromosome 12 among which majority were third year students (11.32%). When asked about their awareness regarding the usage of ultrasound scanning techniques to screen for Down syndrome, 70 out of 106 students answered yes out of which 13.21% were third year students, 24.53% were fourth year students and 28.3% were interns (p value < 0.05) as depicted by Graph 2. Question regarding the awareness of the students about maternal serum screening during second trimester evoked a positive response from fourth years (24.53%) and interns (28.30%) whereas 28.30% of the third-year students were unaware of the same with the p value < 0.05 (Graph 3). Majority of the interns (17.92%) were aware of the soft markers assessed in ultrasound scans in the gestational screening for Down syndrome and 2.83% of third years, 3.77% of fourth year students and 9.43% of the interns were not sure or aware of the soft markers. Nuchal fold thickness and nasal bone was the most answered option among fourth year students (10.38%) whereas femur length was the most chosen answer among third year students (15.09%) as depicted by Graph 4 (p value $<$ 0.05). Majority of the students felt that prenatal screening should be a part of routine gestational screening with a greater number being interns however majority of the third-year students opted that it should not be employed until advised (15.09%) as depicted by Graph 5.

Down syndrome is caused by the presence of an additional copy of chromosome 21 (Turpin et al., 1959). This additional copy is usually the result of a maternal meiotic nondisjunction event but approximately 4% of cases are attributable to the unbalanced segregation of a Robertsonian translocation. In approximately 1% of cases, mosaicism is

present and these individuals may show a milder phenotype. (Benn, 2002a) In the absence of prenatal screening and diagnosis, it can be estimated that Down syndrome prevalence at birth in the United States would currently exceed 1 in 600 (Egan et al., 2000). Approximately 85–90% of individuals born with Down syndrome can be expected to survive to 1 year of age (Baird and Sadovnick, 1987; Mikkelsen et al., 1990) and over 50% will be expected to survive beyond 50 years (Baird and Sadovnick, 1989). This disorder is therefore one of the most important potential causes of mental retardation in the population. Although ultrasonography is the essential part of the early screening strategy, additional biochemical parameters are also recommended as these are independent of the ultrasound markers and increase the detection rates (Spencer et al., 1999). The application of such biochemical markers to pregnancies achieved by assisted reproduction techniques has not been fully investigated.

Down syndrome is caused by the aneuploidy of chromosome 21 and when questioned about the same among dental students, the majority of the students, mainly interns answered it correctly with p value < 0.05 stating a significant difference between the knowledge among interns and the other subjects. 3rd year students were slightly well versed about the chromosome affected when compared to the fourth years.

An ultrasound examination is commonly performed for patients with maternal serum screen-positive results. This ultrasound, minimally, may be used to correct a major error in gestational age that may have been sufficient to explain the screen-positive result. Second trimester ultrasound may identify specific anatomic anomalies and/or ‘‘markers’’ that have been associated with Down syndrome. These markers include increased nuchal fold thickness, short femur and humerus, echogenic cardiac foci, renal pyelectasis, echogenic bowel and presence of choroid plexus cysts (Drugan et al., 2000; Smith-Bindman et al., 2001)

Because nuchal fold thickness and proximal long bone measurements can be treated as continuous variables, it is possible to combine these markers into a multivariate Gaussian marker model that can include maternal serum analytes. Recently, a protocol that combined the quadruple test with nuchal thickness and long bone measurements was developed [117]. A provisional study conducted by Benn et al indicated combined second trimester screening might achieve an approximately 90% detection rate at the 5% false-positive standard (Benn, 2002a). There is considerable potential for second trimester ultrasound biometry to help identify fetal Down syndrome given the level of detail available in the second trimester relative to that available in the first trimester, it seems reasonable to expect that Down syndrome identification through a second trimester scan may ultimately prove to be even more effective than that currently achievable in the first trimester. (Benn, 2002b)

Knowledge regarding the usage of ultrasound scans to prenatally screen for Down syndrome was assessed, and a majority of interns and third years were significantly (p value < 0.05) aware of the same. Greater number of third years were well versed in this than the interns. 17.92% of the fourth-year students were not aware of such screening techniques. This may be explained by the advent of seminars and research summits followed by the active participation of the younger students. On the other hand, a greater number of interns and fourth year students were significantly aware of maternal serum screening tests performed to check for chromosomal abnormalities in fetuses whereas the majority of the third-year students were not well informed (p value < 0.05).

When asked in depth about the soft markers that are assessed during prenatal ultrasound screening, significant number of interns (17.92%) were aware of all the soft markers being assessed such as femur length, humerus length, nuchal fold thickness, nasal bone whereas 16.03% of the total subjects were not sure of the abnormalities being assessed in ultrasound

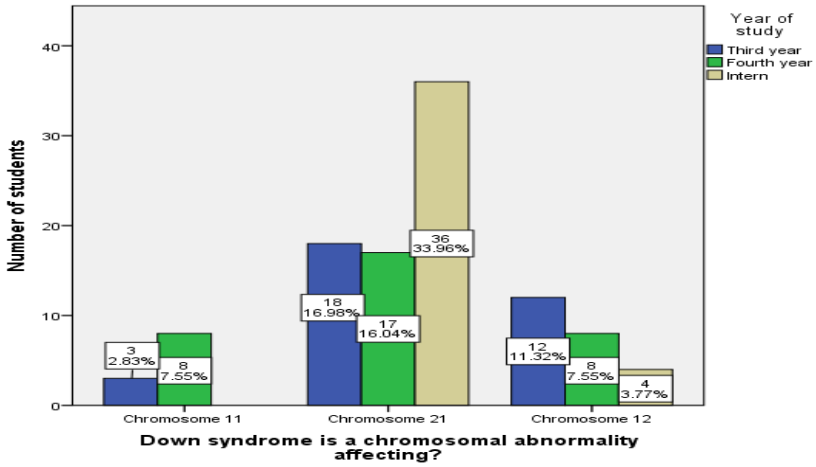
scans. Greater number of fourth year students were unsure of this technique when compared to the third years (p value < 0.05).

In a multicultural country like India, prenatal screening is often looked down upon as there are multitude scenarios of it being used in an unethical manner of gender identification and often not performed. However, the concept of prenatal screening goes both ways as it gives a choice to the family regarding continuation of the gestation as well as helping the family to be prepared for bringing up a child with Down syndrome or other chromosomal disorders. Maternal serum tests are initially performed and those who screen positive are advised to undergo amniocentesis. When the dental students were asked about their view regarding prenatal screening, the majority of the interns significantly felt that it should be a part of routine screening excluding amniocentesis whereas significant number of third- and fourth-year students felt that it should not be advised until absolutely necessary (p value> 0.05). This can be explained by increased exposure of the interns to patients and their issues and their urge to hasten diagnosis which saves time and energy.

There is insufficient knowledge regarding prenatal screening for chromosomal abnormalities among all the dental students however this can be changed by conducting seminars and holding workshops on the same as holding this knowledge is crucial and should be given more importance during anatomy lectures or radiology lectures. The distinction between screening and the fully diagnostic tests for fetal aneuploidy will ultimately become less apparent. Amniocentesis and chorionic villus sampling may then only be offered in the few cases where an abnormality has already been established with near certainty. An achievable goal in Down syndrome screening is a level of efficacy in which amniocentesis and chorionic villus biopsy areno longer used as initial or primary diagnostic tools but, instead, are only offered to confirm and precisely define the chromosomal basis for an anomaly.

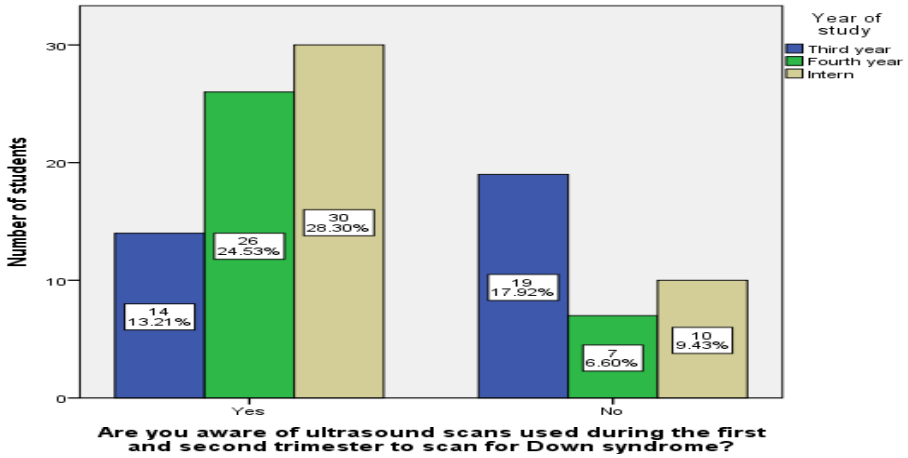
Year of study	Frequency	Percentage
3rd year students	33	31.1%
4th year students	33	31.1%
Interns	40	37.7%

Table 1: Frequency and percentage of the number of students in each group

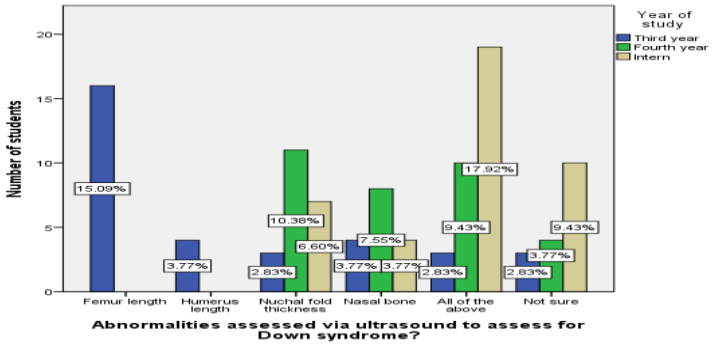


Graph 1: Bar graph representing association between question of the chromosome being affected in Down syndrome and year of study of the dental student. X axis represents the chromosome affected and Y axis represents the number of

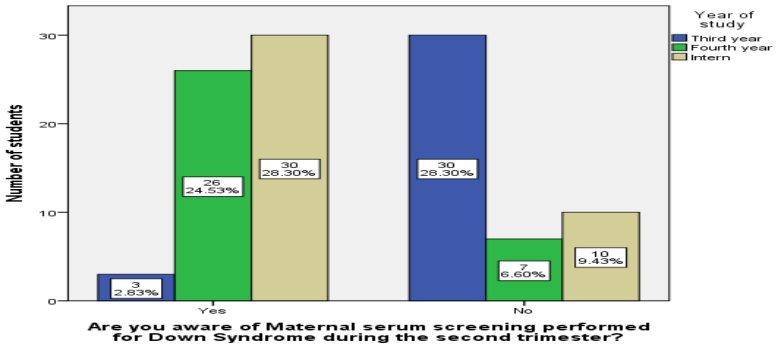
students in each category. Chi square test, p value: 0.000313: significant. There was a significant difference in knowledge among interns and the other subjects. Interns and 3rd year students were slightly well versed about the chromosome affected when compared to the fourth years.



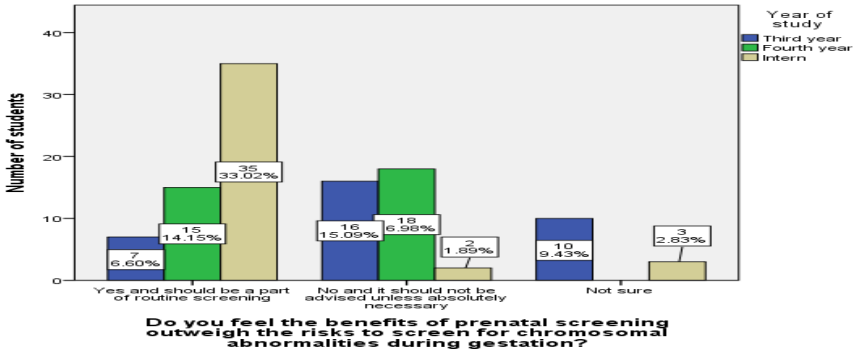
Graph 2: Bar graph representing association between question regarding awareness of usage of ultrasounds to diagnose Down syndrome and year of study of the dental student. X axis represents if the student was aware or not and Y axis represents the number of students in each category. Chi square test, p value: 0.002443: significant. Greater number of third years were well versed in this than the interns. 17.92% of the fourth-year students were not aware of such screening techniques



Graph 3: Bar graph representing association between the question of the soft markers or abnormalities assessed via ultrasound screening of Down syndrome and year of study of the dental student. X axis represents the soft markers assessed and Y axis represents the number of students in each category. Chi square test, p value: 0.000000: significant. The majority of interns were aware of all the soft markers being assessed whereas a greater number of fourth year students were unsure of this technique when compared to the third years.



Graph 4: Bar graph representing association between question regarding awareness of usage of maternal serum tests to diagnose Down syndrome and year of study of the dental student. X axis represents if the student was aware or not and Y axis represents the number of students in each category. Chi square test, p value: 0.000000: significant. A greater number of interns and fourth year students were significantly aware of maternal serum screening tests performed to check for chromosomal abnormalities in fetuses.



Graph 5: Bar graph representing association between the question regarding their opinion on prenatal screening and year of study of the dental student. X axis represents the student's opinion and Y axis represents the number of students in each category. Chi square test, p value: 0.000000: significant. the majority of the interns significantly felt that it should be a part of routine screening excluding amniocentesis whereas third- and fourth-year students felt it should not be performed until absolutely necessary.

4. CONCLUSION

In our study, it can be concluded that within the limits of the study, the interns had better knowledge regarding prenatal screening techniques for Down syndrome than third- and fourth-year students. Seminars, workshops and conferences on the same are the need of the hour to initiate further studies and thus educate dentists and public health programs to create awareness among the general population.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

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