

Awareness On Apert Syndrome Among Dental Students

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Abstract

Introduction: Apert syndrome (AS) is a rare genetic disorder that is characterized by craniosynostosis (premature fusion of cranial structures), acrocephaly (premature closure of lambdoid and coronal sutures) , syndactyly of the hands and feet and often combined with anomalies of other organs. The most readily observed dental mal-relationships are severe maxillary anterior open bite and a severely crowded and retrusive maxillary arch due to the constricted secondary palate. The aim of this study is to examine the awareness of dental students about Apert syndrome due to its large amount of oral manifestations.

Materials and Methods: A cross sectional study involving students of Saveetha Dental College, Chennai, India were taken. A self-structured questionnaire containing 11 questions was framed and circulated among dental students of 100 people. The questions enquired about the awareness of AS among dental students. Google forms were used to circulate the questions and the responses were collected, the data analysis was carried out using SPSS software. Chi square test was used for statistical analysis and p value < than 0.05 was considered as significant.

Results: Out of the participants, 58% were females and the remaining 42% were males. Majority of the participants were unaware about the term Apert syndrome. Most of them did not know about the cause, and main characteristics of the syndrome. Some questions were wrongly answered and the students took to the option of ‘not aware’ as well.

Conclusion: In conclusion, it can be said that neither gender is very aware about the features, symptoms, characteristics, oral manifestations and treatment of Apert syndrome and knowledge about the same should be spread.

Keywords: Apert syndrome, syndactyly, craniosynostosis, acrocephaly

INTRODUCTION

Apert syndrome (AS) is a rare genetic disorder that is characterized by craniosynostosis (premature fusion of cranial structures), acrocephaly (premature closure of lamboid and coronal sutures), syndactyly of the hands and feet and often combined with anomalies of other organs(1). Craniosynostosis involves premature fusion of one or more neurocranial sutures and associated dysmorphologies of the cranio-facial complex(2,3). Acrocephaly is a type of craniosynostosis in which there is premature closure of the lambdoid and coronal sutures, resulting in an abnormally high, peaked, or cone-shaped cranium(4). Syndactyly is the condition of having some or all of the fingers or toes wholly or partly united, either naturally (as in web-footed animals) or as a malformation(5). AS incidence is reported to be 1 in 65,000 live births and both males and females are affected equally, accounting for about 4.5% of all cases of craniosynostosis. Study analysis report that 98% cases are a result of one of two heterozygous mutations in exon IIIa of fibroblast growth factor receptor 2 gene (FGFR2) encoding the amino acid substitutions Ser252Trp or Pro253Arg(6). FGFR2 is one of four transmembrane FGFRs that mediate signalling downstream of fibroblast growth factor ligands and plays a vital role in skeletal development and disease(7).

The newborn infant presenting AS shows a fused coronal suture and agenesis of the sagittal and metopic sutures, which results in a wide defect extending from the glabella to the posterior fontanelle(8). Additionally, the sphenoccipital, sphenothmoidal, and frontoethmoidal sutures fuse early; resulting in a turribrachycephaly skull. The typical appearance includes a flat, elongated forehead with bitemporal widening and occipital flattening. Craniofacial deformities specific to Apert syndrome (AS) include, acrocephaly (cone-shaped calvarium), prominent forehead, proptosis, hypertelorism, and flattened nose with a low bridge(9). The most readily observed dental mal-relationships are severe maxillary anterior open bite and a severely crowded and retrusive maxillary arch due to the constricted secondary palate. Therefore, the skeletal class III is not the result of a prognathic mandible, but is due to the

sagittal maxillary hypoplasia(10). Dental anomalies include delayed and ectopic eruption, shovel-shaped incisors, crowding of teeth, especially in the maxilla, anterior open bite, bilateral crossbite, mandibular overjet, midline deviation, pseudocleft, high-arched palate, transverse, and sagittal maxillary hypoplasia(11). Mandibles are generally normal in size, and pseudo prognathism can be seen. Rarely symptoms related to the central nervous system, cardiac, gastrointestinal, and urogenital system, and vertebral anomalies have been reported(12). Crouzan, Pfeiffer, Muenke and Saethre-Chotzen syndrome are characterised by craniosynostosis and hence their diagnosis is clinically overlapped with that of Apert syndrome. Other malformations include abnormalities of the skin, skeleton, brain and other internal organs. Mental ability varies widely from normal to severe deficiency, although not lethal but many cases result in death due to abnormalities in respiratory or cardiovascular systems(13).

Radiographs of hands, feet, and skull show syndactyly of hands and feet, malformation of midfacial bones, and craniosynostosis of skull(14). Prenatal detection of specific FGFR mutations now allows definitive antenatal diagnosis of AS, other craniosynostosis syndromes, and skeletal dysplasias(15). Prenatal detection of the syndrome became feasible only in recent years after the advent of routine prenatal ultrasound screening for fetal anomalies. Plain skull radiographs including anteroposterior, lateral, and Towne's projection are usually done(16). Radiographs of hands and feet are taken to see syndactyly of hands and feet. Now, three-dimensional computed tomography (CT) scans have added a further dimension in planning surgery of these patients and for objective assessment of operative outcome(17).

Ideally, treatment of AS begins at birth with proper diagnosis, identification of the child's individual needs, and a proper facility to administer what is needed. Treatment involves multidisciplinary teamwork including craniofacial surgeon, neurosurgeon, neurologist, ENT (ear, nose, and throat), audiologist, pediatrician, speech pathologist, oral surgeon, psychologist, and an orthodontist(18). Surgical

care involves early release of the coronal suture and frontoorbital advancement with reshaping to allow proper brain growth and reduce dysmorphic and unwanted skull growth changes. Craniotomy is often performed during the 1st year of life to treat the craniosynostosis(19). Frontofacial advancement and midface advancement can be performed later to correct the proptosis and midface hypoplasia. Coordinated orthodontic therapy is often necessary to bring unerupted teeth into place and improve occlusion(20). Our team has extensive knowledge and research experience that has translate into high quality publications(21–29),(30–35),(36–42)

The aim of this study is to examine the awareness of dental students about Apert syndrome due to its large amount of oral manifestations.

MATERIALS AND METHODS

A cross sectional study involving students of Saveetha Dental College, Chennai, India were taken. Ethical approval was obtained from the international review board prior to the start of the study. Inclusion criteria-Students of Saveetha Dental College. Exclusive criteria-Students studying in institutions other than Saveetha

Dental College. This study excludes the age criteria and the year of study of the students. A questionnaire was set up and circulated among dental students of 100 people. The sampling method used in this study was non- probability convenient random survey sampling. To minimize the bias certain measures were taken that include, to avoid leading questions, use of simple language to frame the questions and avoidance of difficult concepts among common people. A self-structured questionnaire containing 11 questions was framed which was checked for validity by three internal experts (from Saveetha Dental College) and also by three external experts (outside Saveetha Dental College). The questions enquired about the awareness of AS among dental students. Google forms were used to circulate the questions and the responses were collected, the data analysis was carried out using SPSS software. Chi square test was used for statistical analysis and p value < than 0.05 was considered as significant.

RESULTS

Figure 1. Shows the gender distribution of the dental students who answered the survey. Male population is 42% and the female population is 58%.

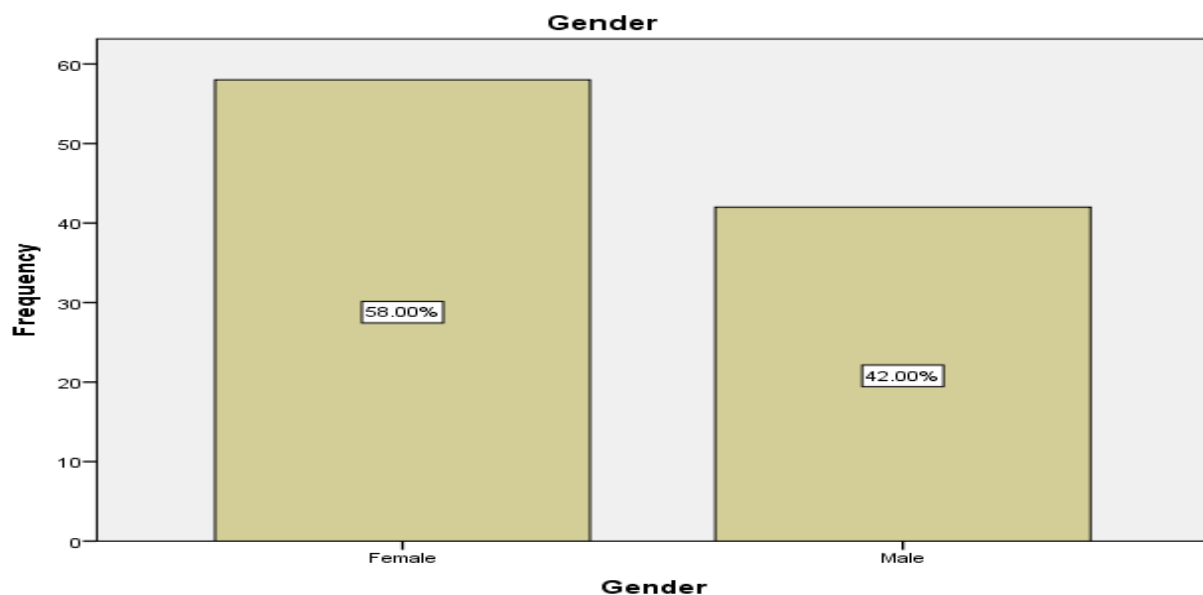


Figure 2. depicts the correlation graph between gender of the participants and whether they are

aware of what Apert syndrome is. Blue colour denotes no, green colour denotes yes. Among

females, 31% answered as no, 27% answered as yes. Whereas among the males, 22% responded as no, 20% of males answered yes. Chi square test

was evaluated for this graph with a p value of $p=0.142$ ($p>0.05$). Hence the value is statistically insignificant.

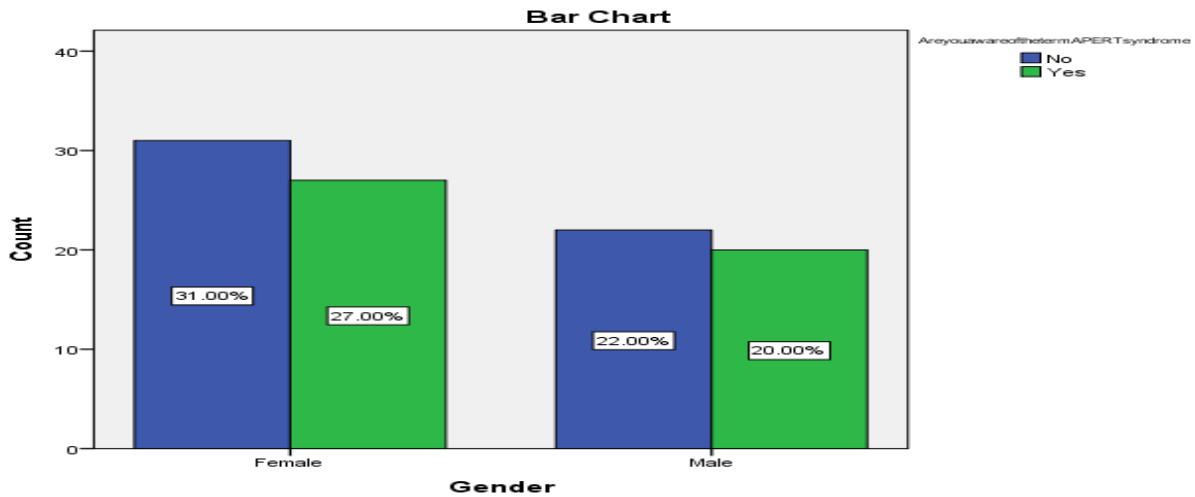


Figure 3. depicts the correlation graph between gender of the participants and their awareness on what Apert syndrome is. Blue colour denotes defect in facial muscles, green colour denotes distinctive malformations of the skull, face, hands and feet, purple colour denotes overgrowth of ligaments and yellow colour denotes not sure. Among females, 5% answered as defect in facial muscles, 23% answered as distinctive malformations in the skull, face, hands and feet,

3% as overgrowth of ligaments and 27% answered as not sure. Whereas among the males, 7% answered as defect in facial muscles, 15% answered as distinctive malformations in the skull, face, hands and feet, 2% as overgrowth of ligaments and 18% answered as not sure. Chi square test was evaluated for this graph with a p value of $p=0.128$ ($p>0.05$). Hence the value is statistically insignificant.

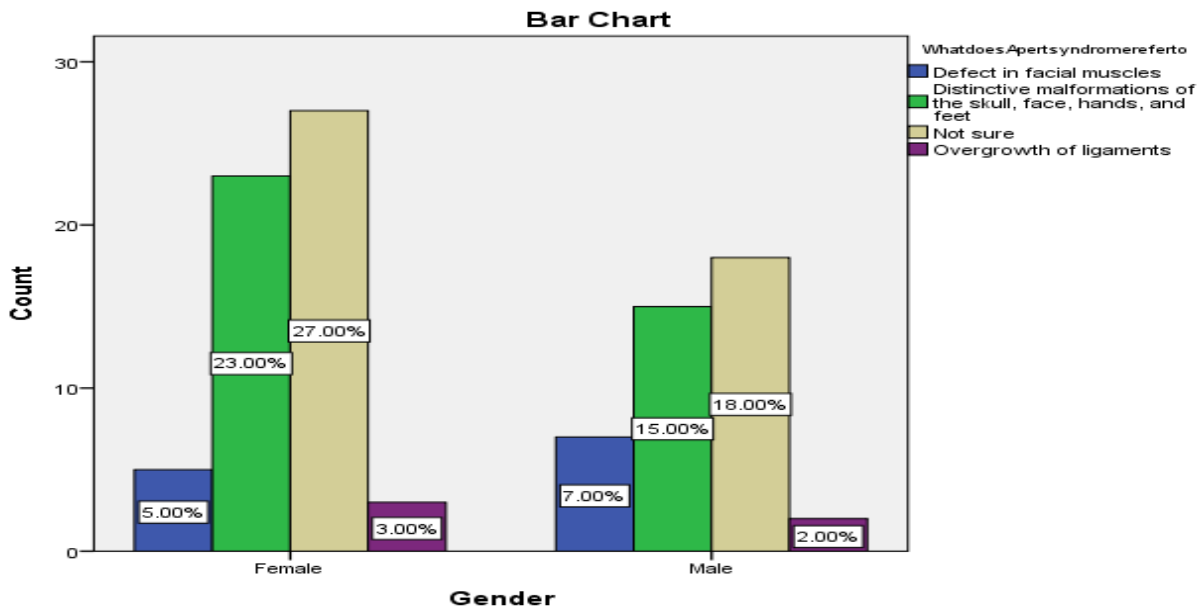


Figure 4. depicts the correlation graph between gender of the participants and their awareness on what type of disease Apert syndrome is. Blue

colour denotes rare acquired syndrome, green colour denotes rare genetic syndrome, and yellow colour denotes not aware. Among

females, 10% answered as a rare acquired defect, 28% answered as a rare genetic syndrome, and 20% answered as not aware. Whereas among the males, 5% answered as a rare acquired defect, 19% answered as a rare genetic syndrome, and

18% answered as not aware. Chi square test was evaluated for this graph with a p value of $p=0.078$ ($p>0.05$). Hence the value is statistically insignificant.

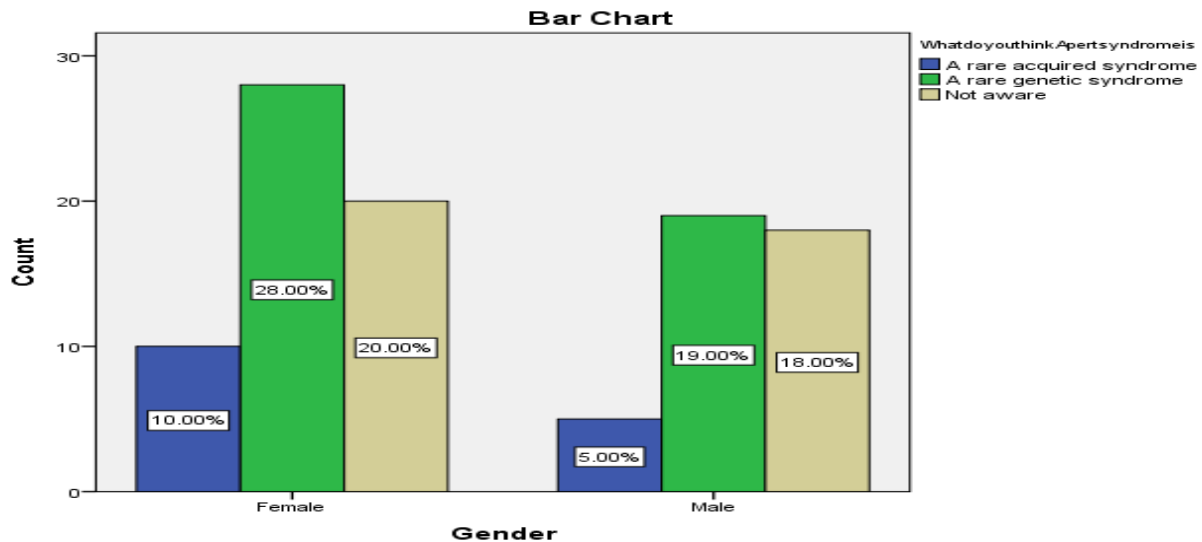


Figure 5. depicts the correlation graph between gender of the participants and their awareness on the characteristic feature of Apert syndrome. Blue colour denotes craniosynostosis, green colour denotes learning disabilities, and yellow colour denotes not aware and purple colour denotes overgrowth in childhood. Among females, 20% answered as craniosynostosis, 8% answered as learning disability, 25% answered as

not aware and 5% answered as overgrowth in childhood. Whereas among the males, 12% answered as craniosynostosis, 6% answered as learning disability, 17% answered as not aware and 7% answered as overgrowth in childhood. Chi square test was evaluated for this graph with a p value of $p=0.312$ ($p>0.05$). Hence the value is statistically insignificant.

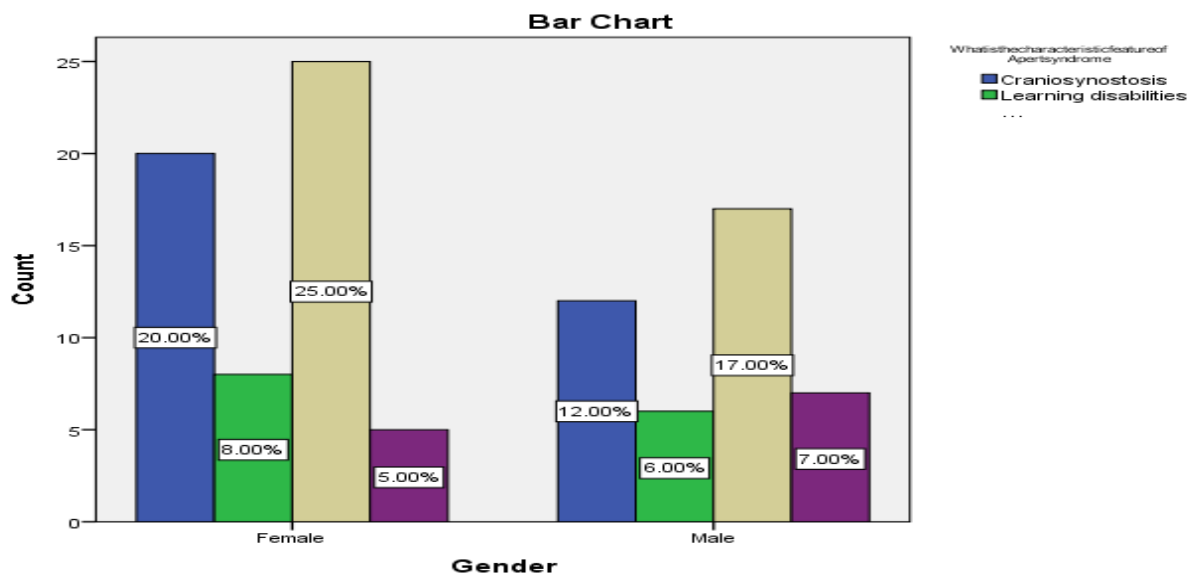


Figure 6. depicts the correlation graph between gender of the participants and their awareness on

the cause of Apert syndrome. Blue colour denotes mutation in genes, green colour denotes not sure,

yellow colour denotes transduction in genes and purple colour denotes translocation in genes. Among females, 11% answered as mutation in genes, 30% answered as not sure, 6% answered as transduction in genes and 11% as translocation in genes. Whereas among the males, 11%

answered as mutation in gene, 20% answered as not sure, 3% answered as transduction in gene and 8% as translocation in gene. Chi square test was evaluated for this graph with a p value of $p=0.126$ ($p>0.05$). Hence the value is statistically insignificant.

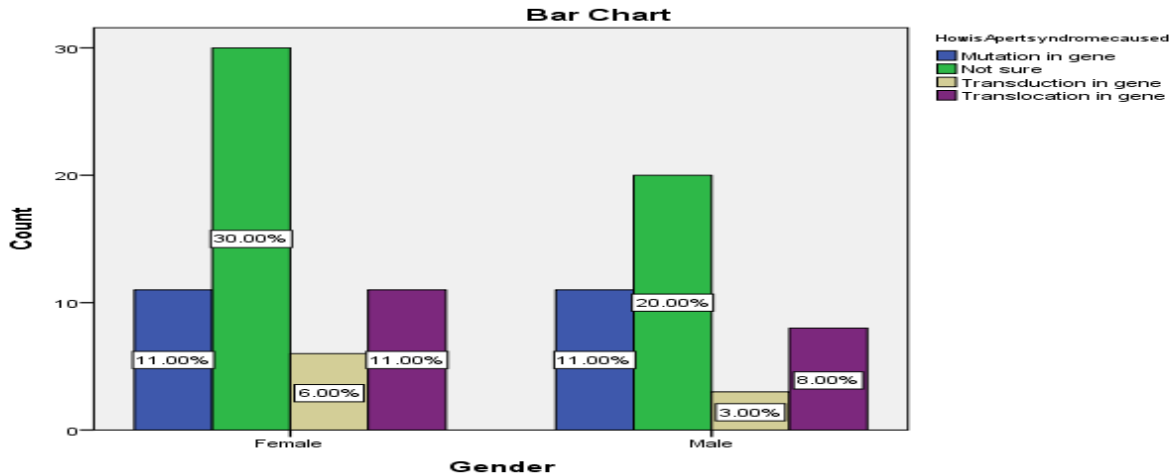


Figure 7. depicts the correlation graph between gender of the participants and their awareness on mutation in which gene causes Apert syndrome. Blue colour denotes FGFR2 gene, green colour denotes HLA-DRB1 gene, yellow colour denotes not sure and purple colour denotes NSD1 gene. Among females, 16% answered as FGFR2 gene, 6% answered as HLA-DRB1 gene, 31% answered as not sure and 5% answered as NSD1 gene. Whereas among the males, 11% answered as FGFR2 gene, 5% answered as HLA-DRB1 gene, 21% answered as not sure and 5% answered as NSD1 gene. Chi square test was evaluated for this graph with a p value of $p=0.111$ ($p>0.05$). Hence the value is statistically insignificant.

answered as not sure and 5% answered as NSD1 gene. Whereas among the males, 11% answered as FGFR2 gene, 5% answered as HLA-DRB1 gene, 21% answered as not sure and 5% answered as NSD1 gene. Chi square test was evaluated for this graph with a p value of $p=0.111$ ($p>0.05$). Hence the value is statistically insignificant.

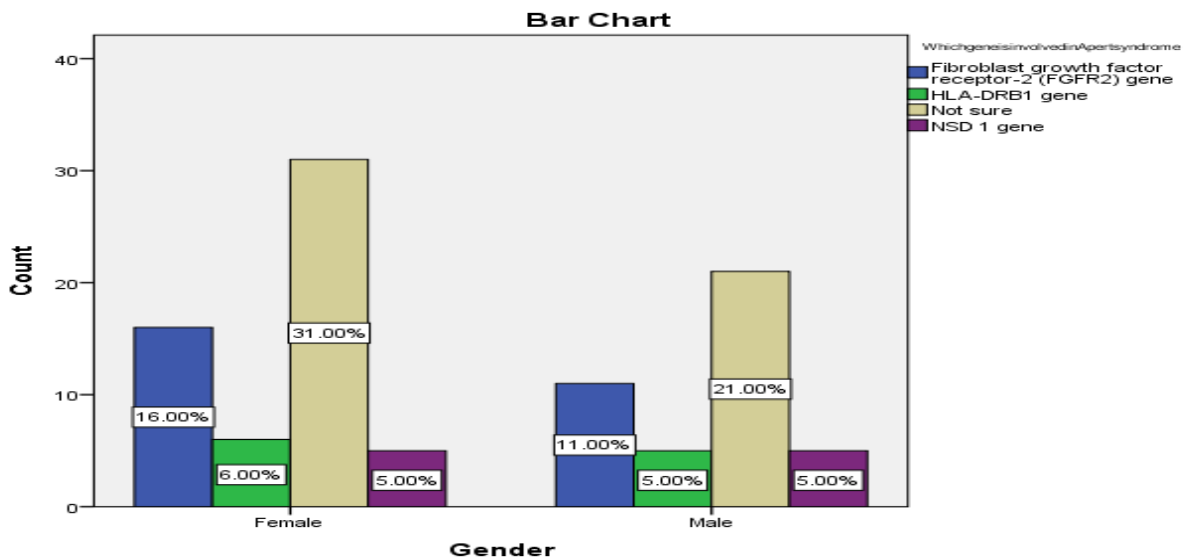


Figure 8. depicts the correlation graph between gender of the participants and their awareness on which disease Apert syndrome is a severe and asymmetric form of. Blue colour denotes

Crouzons syndrome, green colour denotes not aware, yellow colour denotes Pfeiffer syndrome and purple colour denotes SOTOS syndrome. Among females, 14% answered as Crouzons

syndrome, 27% answered as not aware, 13% answered as pfeiffer syndrome and 4% answered as SOTOS syndrome. Whereas among the males, 8% answered as Crouzons syndrome, 21% answered as not aware, 8% answered as pfeiffer

syndrome and 5% answered as SOTOS syndrome. Chi square test was evaluated for this graph with a p value of $p=0.291$ ($p>0.05$). Hence the value is statistically insignificant.

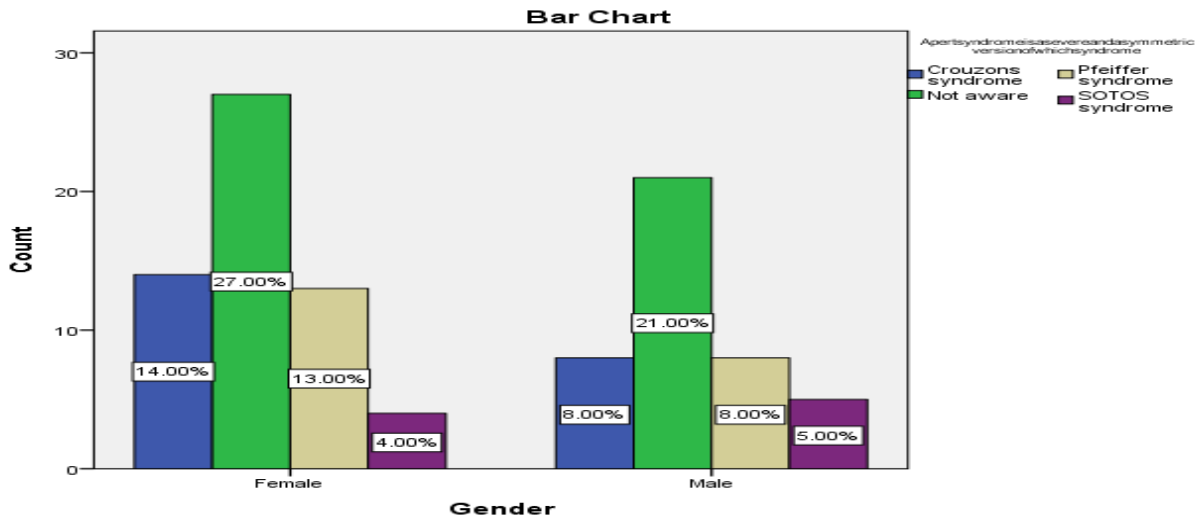


Figure 9. depicts the correlation graph between gender of the participants and their awareness on the symptoms of Apert syndrome. Blue colour denotes all of the above, green colour denotes palatal abnormalities such as cleft palate, yellow colour denotes underdeveloped midfacial regions and purple colour denotes spaced eyes. Among females, 36% answered as all of the above, 2% answered as palatal abnormalities, 10%

answered as underdeveloped midfacial regions and 10% answered as spaced eyes. Whereas among the males, 24% answered as all of the above, 4% answered as palatal abnormalities, 5% answered as underdeveloped midfacial regions and 9% answered as spaced eyes. Chi square test was evaluated for this graph with a p value of $p=0.159$ ($p>0.05$). Hence the value is statistically insignificant.

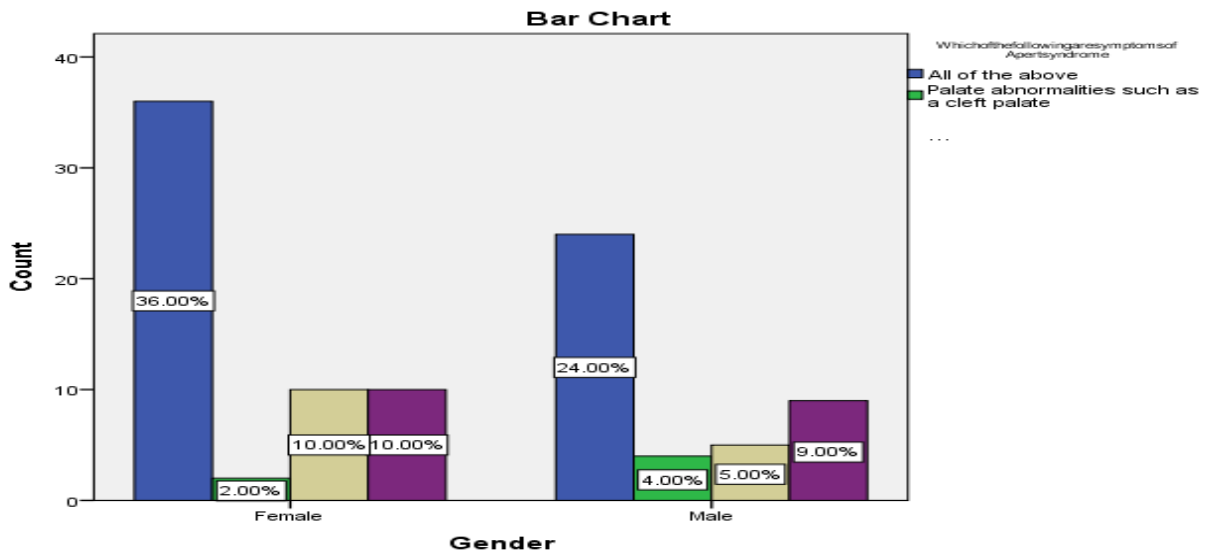


Figure 10. depicts the correlation graph between gender of the participants and their awareness on

the oral manifestations of disease Apert syndrome. Blue colour denotes all of the above,

green colour denotes crowding, yellow colour denotes delayed teeth growth and purple colour denotes open bite. Among females, 41% answered as all of the above, 7% answered as crowding, 4% answered as delayed teeth growth and 6% as open bite. Whereas among the males,

28% answered as all of the above, 3% answered as crowding, 2% answered as delayed teeth growth and 9% as open bite. Chi square test was evaluated for this graph with a p value of $p=0.118$ ($p>0.05$). Hence the value is statistically insignificant.

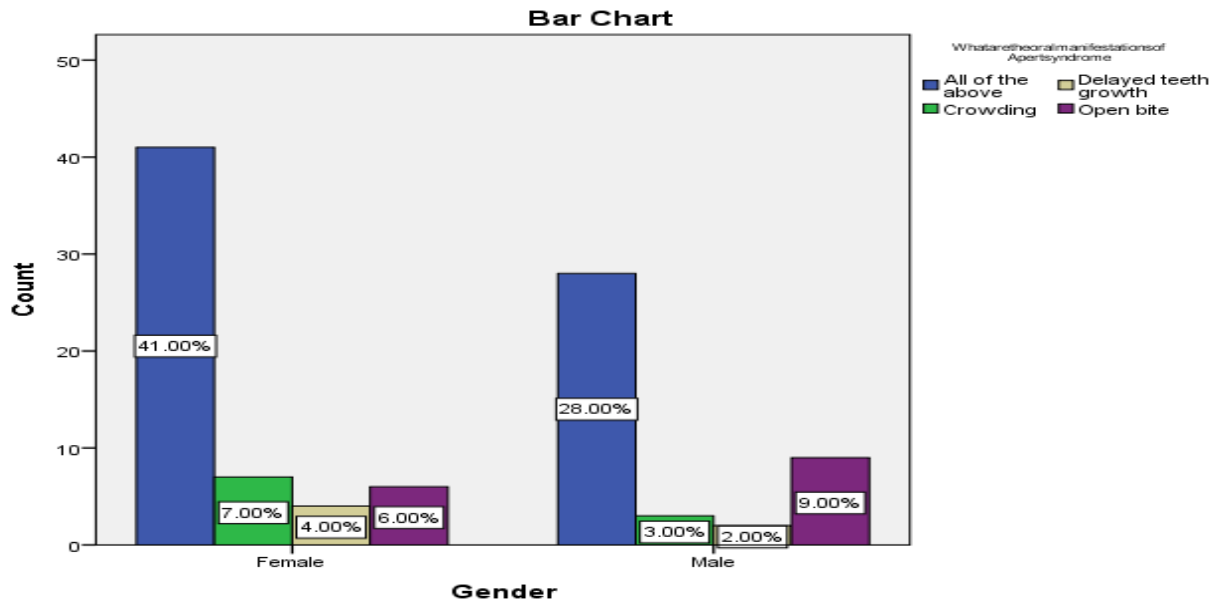


Figure 11. depicts the correlation graph between gender of the participants and their awareness on the age when Apert syndrome can be detected. Blue colour denotes 5-10 years of age, green colour denotes adolescence, and yellow colour denotes at birth/infancy. Among females, 20% answered as 5-10 years of age, 13% answered as

adolescence, and 25% answered as at birth/infancy. Whereas among the males, 18% answered as 5-10 years of age, 12% answered as adolescence, and 12% answered as at birth/infancy. Chi square test was evaluated for this graph with a p value of $p=0.062$ ($p>0.05$). Hence the value is statistically insignificant.

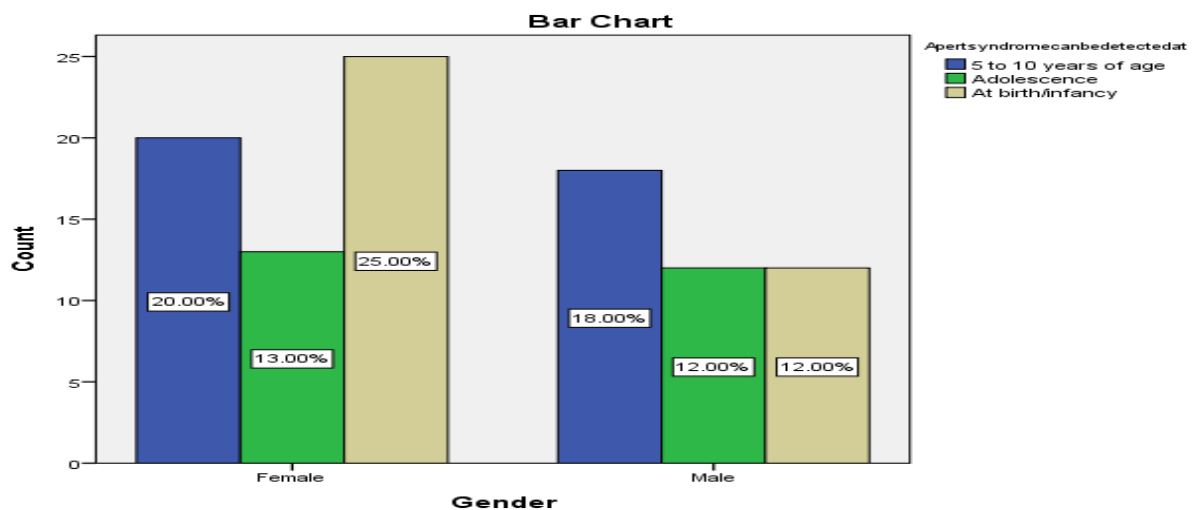
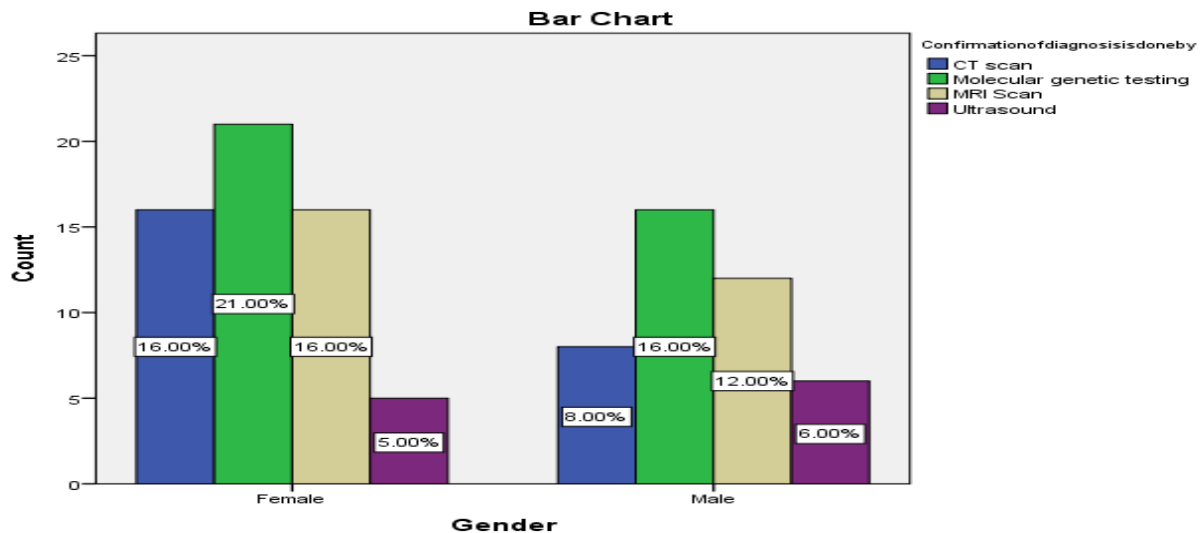


Figure 12. depicts the correlation graph between gender of the participants and their awareness on

the method to confirm Apert syndrome. Blue colour denotes CT scan, green colour denotes

molecular genetic testing, yellow colour denotes MRI scan and purple colour denotes ultrasound. Among females, 16% answered as CT scan, 21% answered as molecular genetic testing, 16% answered as MRI scan and 5% answered as ultrasound. Whereas among the males, 8%

answered as CT scan, 16% answered as molecular genetic testing, 12% answered as MRI scan and 6% answered as ultrasound. Chi square test was evaluated for this graph with a p value of $p=0.078$ ($p>0.05$). Hence the value is statistically insignificant



DISCUSSION

A total of 100 dental students participated in this study, where 58 were females and the remaining 42 were male students (figure 1). From the results we can observe that most of the people were unaware of Apert syndrome. Most of them (31% in females and 22% in males) weren't aware about the term Apert syndrome (figure 2). Figure 3 shows that a good amount of them knew that Apert syndrome is distinctive malformations in the skull, face, hands and feet. It is a combination of three main symptoms that is, craniosynostosis, acrocephaly and syndactyly(43). In figure 4, it can be observed that the majority of the dental students (28% in females and 19% in males) know that Apert syndrome is a rare genetic syndrome and cannot be acquired. According to figure 5, Apert syndrome has characteristic features such as craniosynostosis, acrocephaly and syndactyly, however the students were confused with the characteristics and opted for the other options as well. This graph thus shows the unawareness of the students towards this disease. Apert syndrome is caused by a mutation in the gene, not transduction or translocation in

the gene and awareness about this fact is very high, wherein most of the students were able to answer this question correctly (figure 6). According to figure 7, a mutation in the fibroblast growth factor receptor 2 gene (FGFR-2 gene) causes Apert syndrome. Most of the students answered this correctly in opposition to the HLA-DRB1 gene and NSD1 gene. This syndrome is a severe form of Pfeiffer syndrome(44) and it can be seen in figure 8, that the majority of the students are unaware about this fact. Many students were misled by the disease Crouzons syndrome which is nowhere related to the topic in hand. Apert syndrome has multiple symptoms, such as craniofacial deformities including acrocephaly (cone-shaped calvarium), prominent forehead, proptosis, hypertelorism, and flattened nose with a low bridge(45). Dental anomalies include delayed and ectopic eruption, shovel-shaped incisors, crowding of teeth, especially in the maxilla, anterior open bite, bilateral crossbite, mandibular overjet, midline deviation, pseudocleft, high-arched palate, transverse, and sagittal maxillary hypoplasia(46). Mandibles are generally normal in size, and pseudoprognathism can be seen. Rarely symptoms related to the

central nervous system, cardiac, gastrointestinal, and urogenital system, and vertebral anomalies have been reported(47). Figure 9 and figure 10 show the awareness level of the dental students in accordance to the symptoms of the syndrome along with its oral manifestations. Radiographs such as CT scan are most helpful in assessing the condition of the patient, and figure 11 shows that the participants got confused with this question and opted for other scans such as MRI scan as well. Ideally, treatment of AS begins at birth with proper diagnosis, identification of the child's individual needs, and a proper facility to administer what is needed(47,48). Treatment involves multidisciplinary teamwork including craniofacial surgeon, neurosurgeon, neurologist, ENT (ear, nose, and throat), audiologist, pediatrician, speech pathologist, oral surgeon, psychologist, and an orthodontist(47–49). Most of the dental students are aware about this, as seen in figure 12.

CONCLUSION

It can be concluded that the majority of the dental students are unaware about the syndrome. The population needs to be knowledgeable about Apert syndrome in order to manage its symptoms and provide a stable and successful treatment plan for the betterment of the patients. Long-term documentation of such cases and multicentre audit will enhance our understanding and improve our future management of Apert syndrome and its associated conditions.

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CONFLICT OF INTEREST

The authors declare that there were no conflicts of interest in the present study.

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