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Awareness On Noonan Syndrome Among Dental Students

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Abstract

Background: Noonan syndrome is a disorder that involves unusual facial characteristics, short stature, heart defects present at birth, bleeding problems, developmental delays, and malformations of the bones of the rib cage.Noonan syndrome is caused by changes in one of several autosomal dominant genes.

Aim: To Evaluate the level of awareness and to create awareness about noonan syndrome and its oral manifestation among dental students

Materials and Methods: An online study was conducted among the general population of Chennai using Google forms .The study was conducted in March-May 2020 .A total of 100 individuals attended the Survey consisting of 20 questions. The results were analysed using SPSS software, Chi square test was done with p value set as 0.05 as level of significance. and were depicted as pie charts and bar graphs.

Results: According to the findings of this research, the majority(57%) of them were not aware of noonan syndrome which was found to be statistically significant p 0.007($p>0.05$) . And in correlation with the year of study most of the 2nd , 3rd and 4th year students are aware about the syndrome

Conclusion:within the limits of the study ,the results of this survey show that the majority of the questioned subjects were not aware about the noonan syndrome , its clinical manifestations, diagnosis and treatment .

Keywords: autosomal dominant, genetic mutation, noonan syndrome, Syndrome, unusual facial characteristics, RAS-MAPK signaling pathways, germline mutation.

INTRODUCTION

Noonan syndrome is a multisystem condition with a wide range of genetic and clinical features. Jacqueline Noonan initially proposed it after studying nine individuals with pulmonic stenosis (PS), chest abnormalities, and distinctive facial dysmorphic characteristics such as hypertelorism, ptosis, low-set ears, and a webbed neck.(1) . NS and other similar diseases are caused by germline mutations in the RAS-MAPK (mitogen-activated protein kinase) pathway.(2) (3,4).

PTPN11, SOS1, RAF1, BRAF, HRAS, KRAS, NRAS, SHOC, MAP2K1, MAP2K2, and CBL are among the genes involved in this pathway. NS has recently been linked to mutations in the genes RIT1, RASA2, and A2ML1. As a result, NS is known as a heterogeneous condition.(5,6) . Patients with NS are prone to leukaemia and certain solid cancers because PTPN11 and other genes including KRAS, HRAS, NRAS, and BRAF play critical roles in the RAS-MAPK pathway. (7).Despite the fact that the majority of NS cases have autosomal dominant characteristics, autosomal recessive transmission has been observed in a few cases. In NS instances, both sporadic and familial modes of transmission have been described, although the majority of cases follow a sporadic pattern, which is thought to be the result of novel mutations.(2,8) .

Reduced postnatal development, unique facial dysmorphism, a wide range of congenital heart defects (CHDs), learning problems, short stature, renal anomalies, lymphatic malformations, bleeding disorders, and skeletal deformities are all symptoms of Noonan syndrome.(9,10) .Clinical similarities have been found between Noonan and other autosomal dominant illnesses such as LEOPARD syndrome, cardio-facio-cutaneous syndrome, NS-like syndrome with loose anagen hair, and Costello syndrome because to the vast range of phenotypic characteristics in NS.(6). Changes in one of several autosomal dominant genes are the cause of Noonan syndrome.

Clinical symptoms and signs are used to make the diagnosis of Noonan syndrome. Normal chromosomal studies are seen in people with Noonan syndrome. (11)(6) Individuals with Noonan syndrome receive treatment based on their specific symptoms. (8) People with Noonan's syndrome have a lifetime that is similar to that of the general population; nevertheless, Noonan's syndrome is linked to a number of health problems that can contribute to death.(1)

Cardiovascular disease problems are the leading cause of death in people with Noonan syndrome.(12) It is important that Dental professionals should be made aware of it due to its various oral manifestations . Our team has extensive knowledge and research experience that has translate into high quality publications(13–21),(22–27),(28–34)

The research is needed to assess and create awareness on the Noonan syndrome among dental students.There is no previous study done on the Noonan syndrome and it's awareness .The aim of the study is to create awareness on Noonan syndrome among dental students

MATERIALS AND METHOD:

A cross sectional Questionnaire survey was conducted among the dentists of Chennai, Vellore Tamilnadu, India during November - December 2020. A total of 100 participants were assessed using a structured questionnaire consisting of 15 close-ended questions regarding participants' demographic details, symptoms , causes , manifestation about noonan syndrome etc. All the collected data were then analyzed in IBM SPSS (Version 23) .The descriptive statistical analysis was done and chi square test was carried out to determine the association between the variables with p value set as 0.05 as level of significance. The results were depicted in the form of pie charts and graphs

RESULTS :

This study provides responses from a total of 100 participants (Table 1), with a large number of them being female (51%) and male (49%) respectively, resulting in a gender-balanced response.40 % of the respondents are between the ages of 18 and 22, 31% of them are between the ages of 23and 28, 15% are between the ages of 29 and 33 and the remaining 14% are over 34.(Table 1)

Among the 100 Participants ,12% are 1st year students , 22% are 2nd year students, 24 are 3rd

year students,18 are 4th year students,12 are CRRI and 12 are PG students.(Figure 1)

When people were asked if they were aware of Noonan syndrome, Majority(57.43%) said No while 42.57% said Yes , which shows that the majority of them were not aware of Noonan Syndrome (Figure 2). And then a question, can anyone have Noonan syndrome? . Majority(66.34%) says No while 33667% says Yes (Figure 3).

And when a question about predisposition and cause of the syndrome is asked , Majority(59.41%) says the syndrome doesn't have familial predisposition while 40.50% says it has familial predisposition (Figure 4) . And the Majority(38.61%) says that the syndrome is caused by Microbial Infection , 26.73% says Gene Alteration , 24.75% says Lack of nourishment and the rest 9.90% says Adverse effect of medication(Figure 5).

When the question was asked about the symptoms of the syndrome Majority(37.62%) said short stature , 30.69% said Unusual facial features , 16.83% said Blindness and the rest 14.85% said Fatty Liver (Figure 6) .

In response to the question, children with Noonan syndrome Prone congenital heart defects . Majority(52.48%) said No while 47.52% says Yes

Oral manifestations of Noonan syndrome were asked . Many (40.59%) says High Arched Palate , 28.71% says micrognathia , 21.78% says Dental Malocclusion and the rest 8.91% says dental anomalies, out of which all 4 are the oral manifestation of Noonan Syndrome.

And when asked about the permanent cure Noonan syndrome, Majority(51.49%) says yes, it is permanently curable while 48.51% says No

In association between Year of study of participants and responses on awareness of noonan syndrome. Majority of the students were not aware , and among the few, the majority 2nd year students were more aware about the syndrome , And on analysis there was statistical significance between Year of study groups and awareness in Noonan Syndrome which was statistically significant (p>0.05)

		Gender		
		Female	Male	Total
Age	18-22	24	16	40
	23-28	10	21	31
	29-33	11	4	15
	34 and above	6	8	14
Total		51	49	100

Table 1: Demographic details of participants

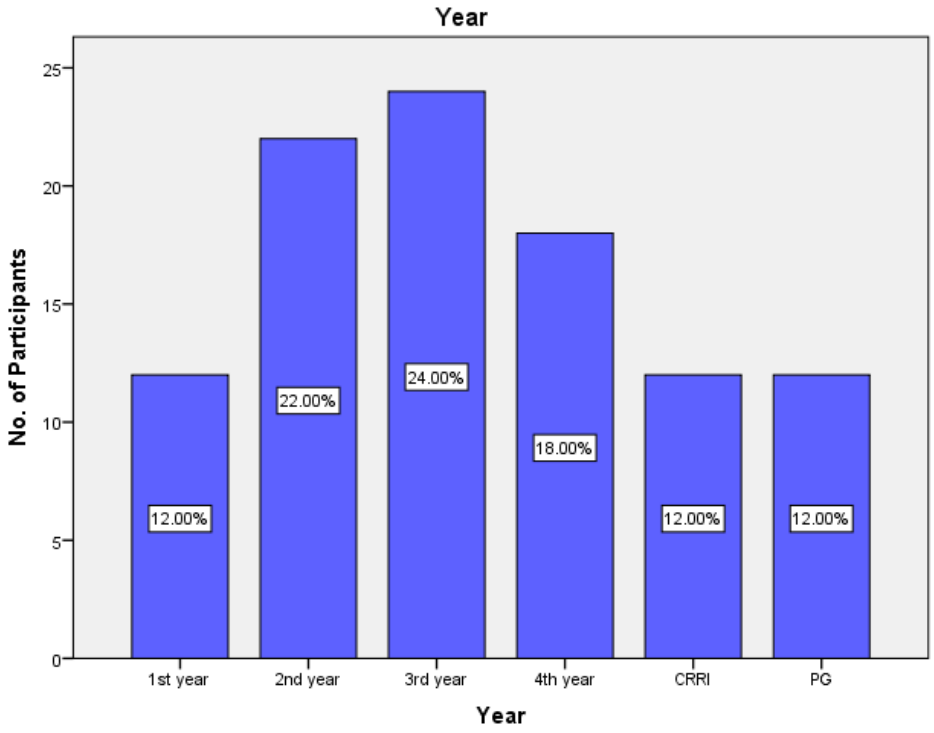

Figure 1: Graph shows the percentage of study population participated in each year

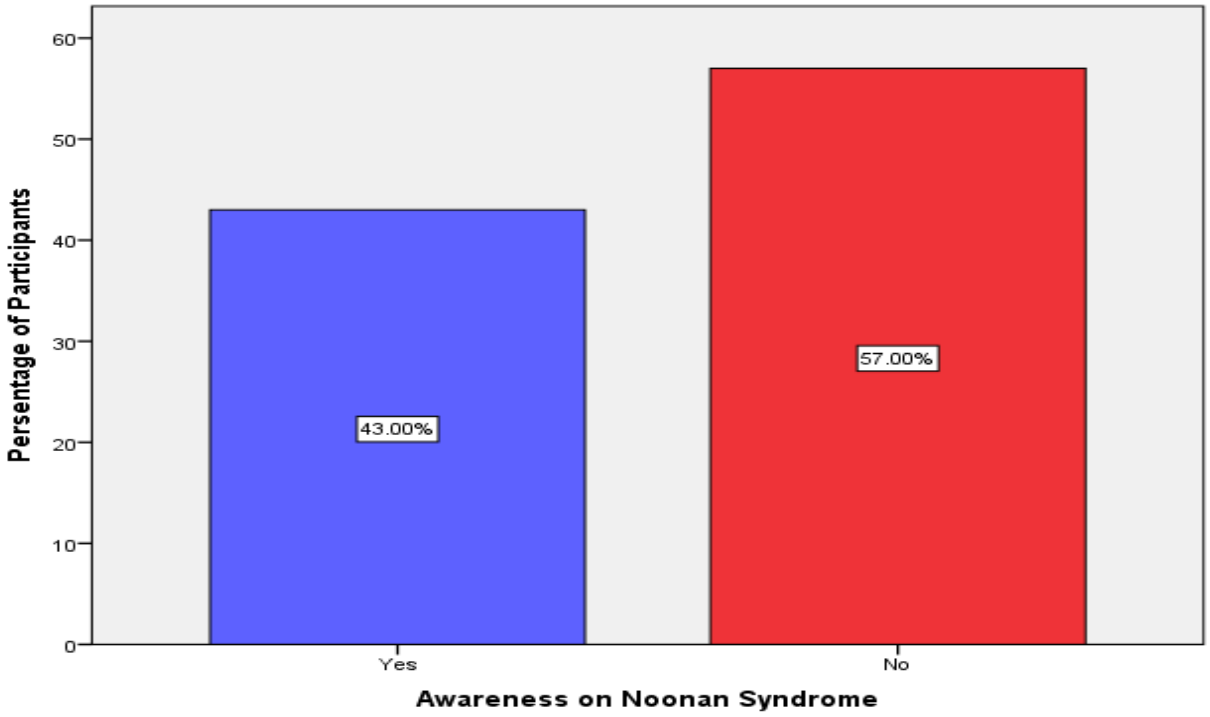

Figure 2 Pie chart depicts the percentage of distribution on responses to the question heard of Noonan syndrome . Majority(57%) says No (Red) while 43% says Yes(Blue)

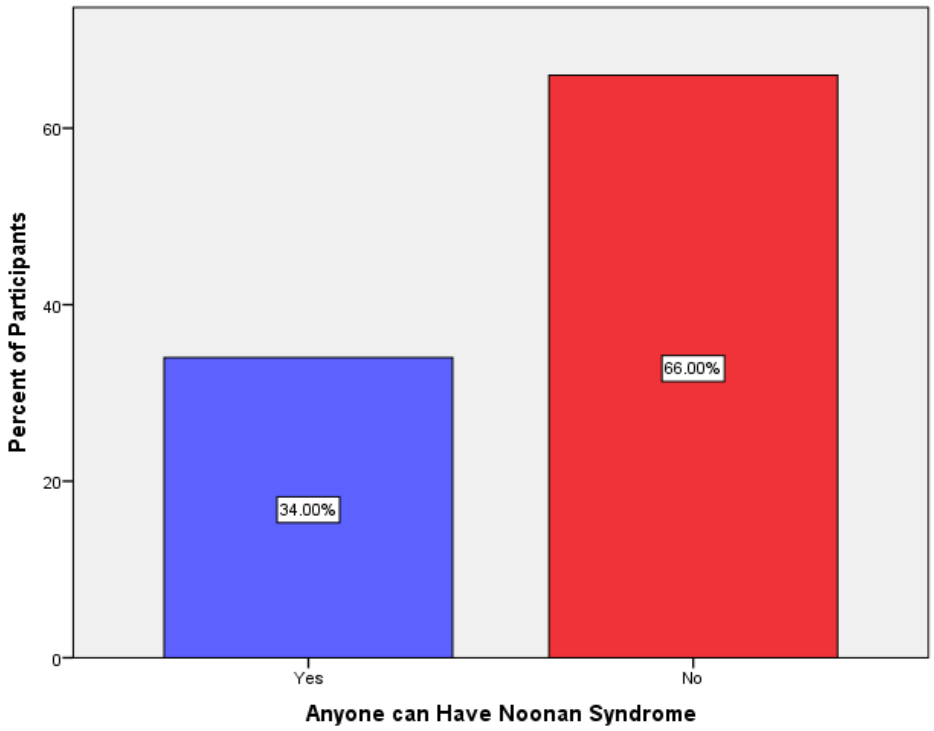

Figure 3 Pie chart depicts the percentage of distribution on responses to the question anyone can have Noonan syndrome . Majority(66%) says No (Red) while 34% says Yes(Blue)

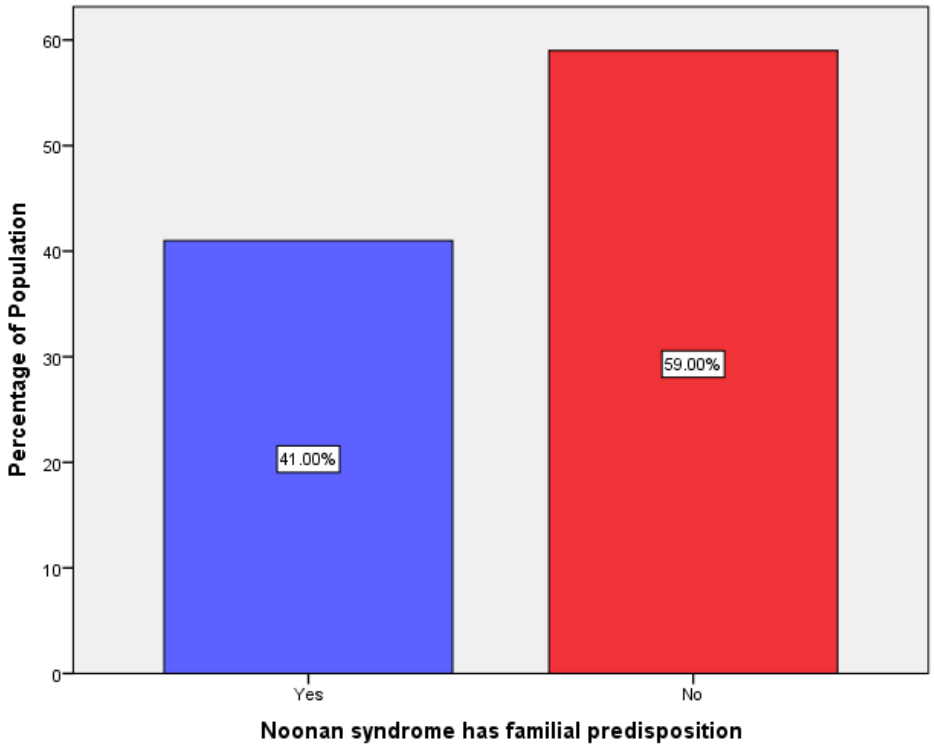

Figure 4 Pie chart depicts the percentage of distribution on responses to the question Noonan syndrome has familial predisposition. Majority(59%) says No (Red) while 41% says Yes(Blue)

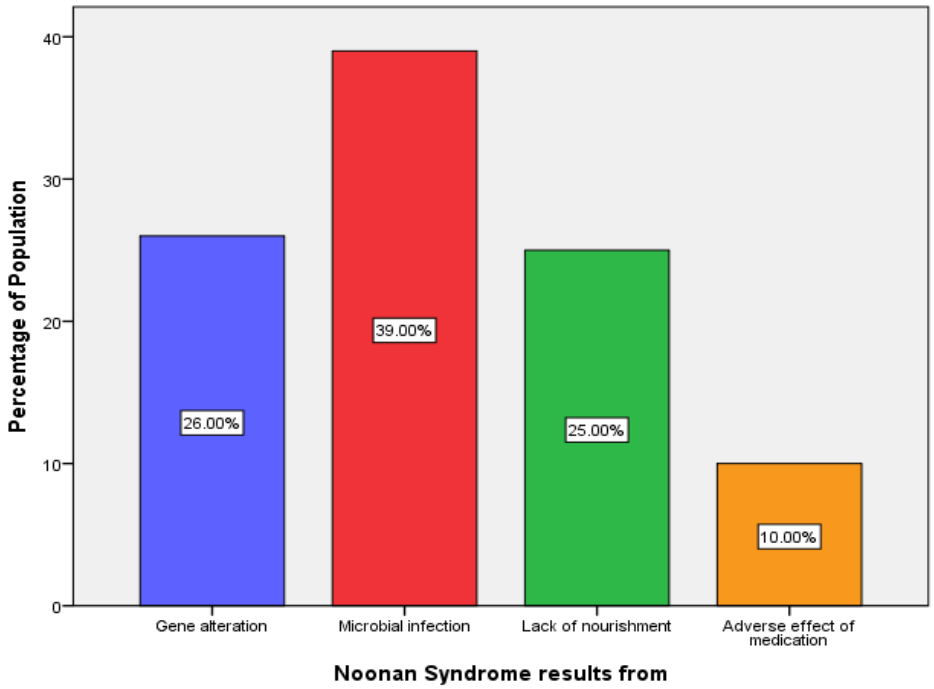

Figure 5 Pie chart depicts the percentage of distribution on responses Noonan syndrome caused by . Majority(39%) says Microbial Infection(Red) , 26% says Gene Alteration (Blue), 25% says Lack of nourishment (Green) and rest 10% says Adverse effect of medication(Orange).

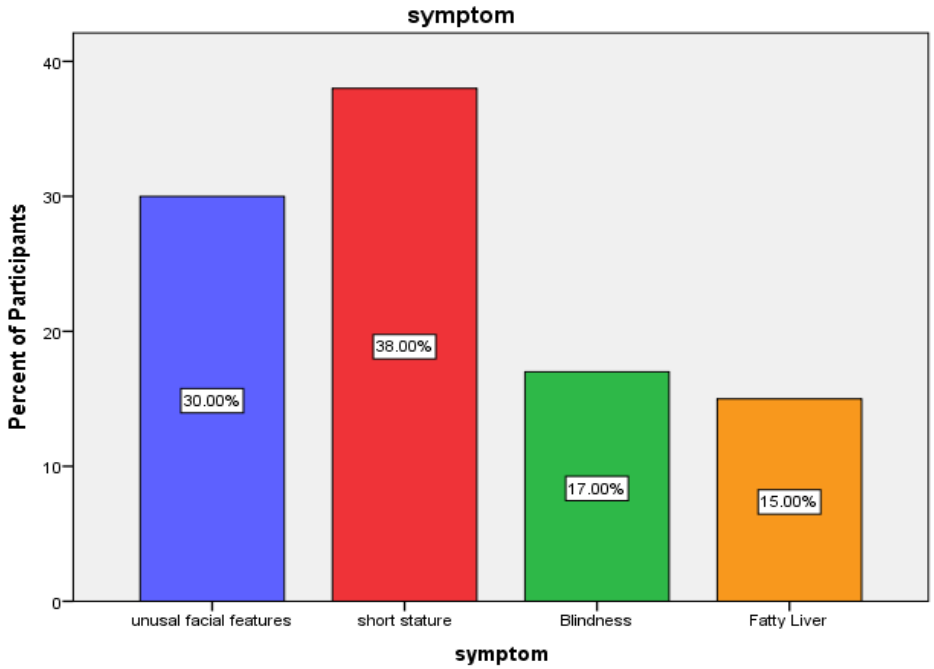

Figure 6 Pie chart depicts the percentage of distribution on responses to the question symptoms Noonan syndrome . Majority(38%) says short stature(Red) , 30% says Unusual facial features (Blue), 17% says Blindness (Green) and the rest 15% says Fatty Liver (Orange).

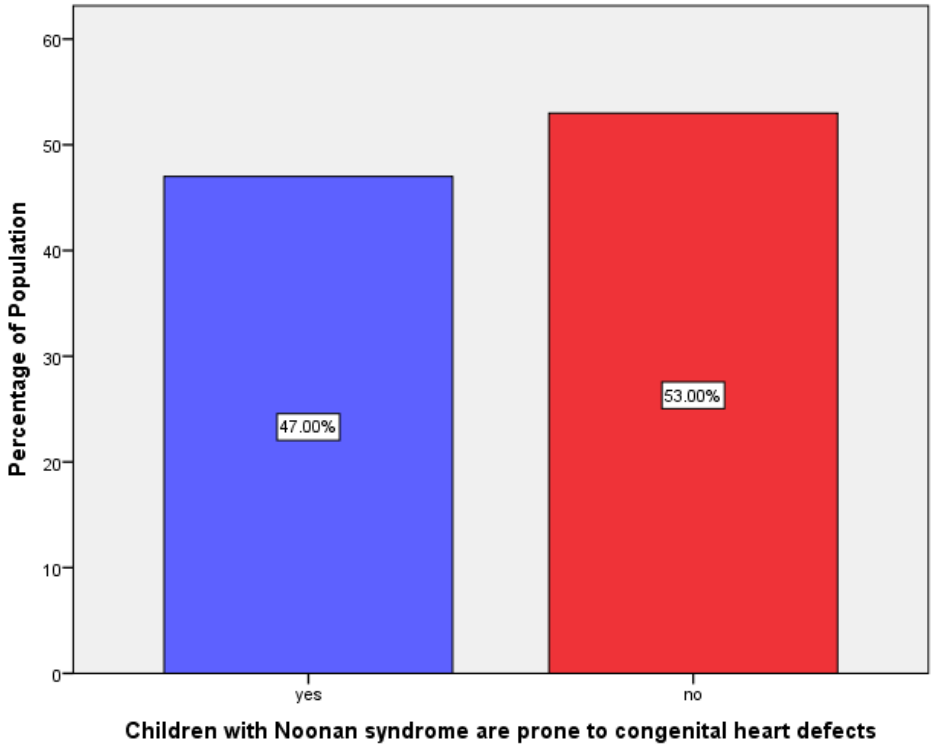

Figure 7 Pie chart depicts the percentage of distribution on responses to the question children with Noonan syndrome have congenital heart defects . Majority(53%) says No (Red) while 47% says Yes(Blue)

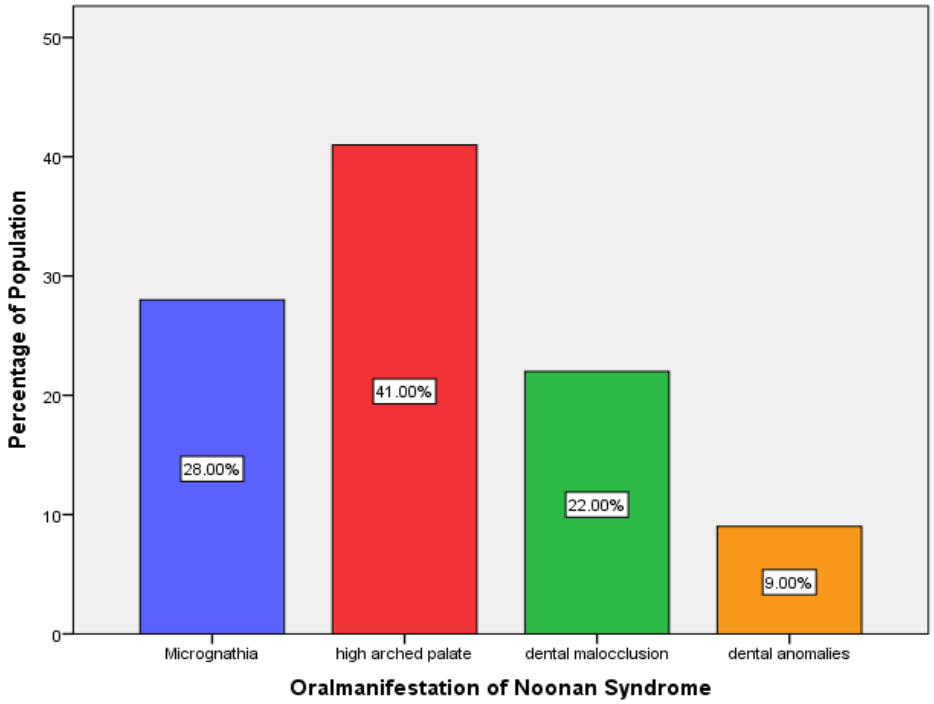

Figure 8 Pie chart depicts the percentage of distribution on responses to question oral manifestation of Noonan syndrome . Majority(41%) says High Arched Palate(Red) , 28% says micrognathia (Blue), 22% says Dental Malocclusion (Green) and the rest 9% says dental anomalies(Orang

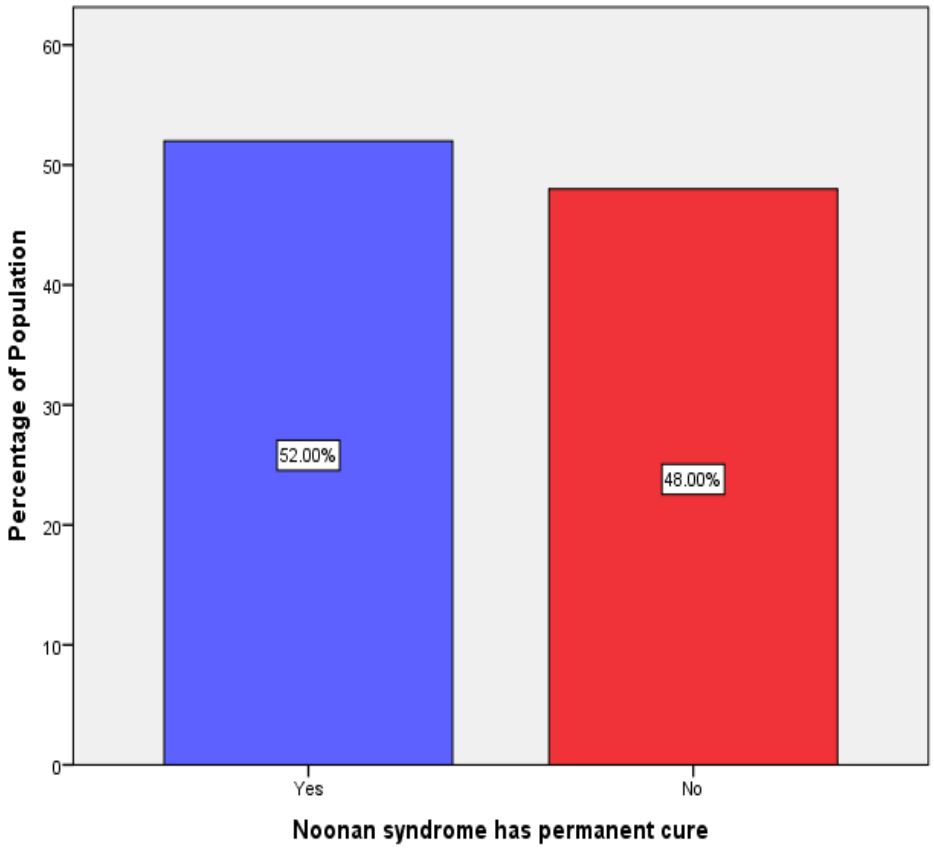

Figure 9 Pie chart depicts the percentage of distribution on responses to the question Noonan syndrome has permanent cure. Majority(52%) says yes (Blue) while 48% says No(Red)

In Correlation between Year of study of participants and responses on symptoms of noonan syndrome. Majority of the students answered Short Stature , In which 2nd , 3rd and 4th year students However on analysis there was no statistical significance between Year of study groups and symptoms of Noonan Syndrome .

In correlation between Year of study of participants and responses on oral manifestation of noonan syndrome. Majority of the students answered High Arched Palate, but the majority of third years were aware all the four were oral manifestations of the syndrome. However on analysis there was no statistical significance between Year of study groups and oral Manifestation of Noonan Syndrome .

In association between Year of study of participants and responses on Permanent cure for noonan syndrome.Majority of the students answered Yes, but majority of 4th years were aware that there is no permanent cure for the syndrome. However on analysis there was no statistical significance between Year of study groups and cure for Noonan Syndrome ,Which says that none of the year students in the study population was not clearly aware about the syndrome .

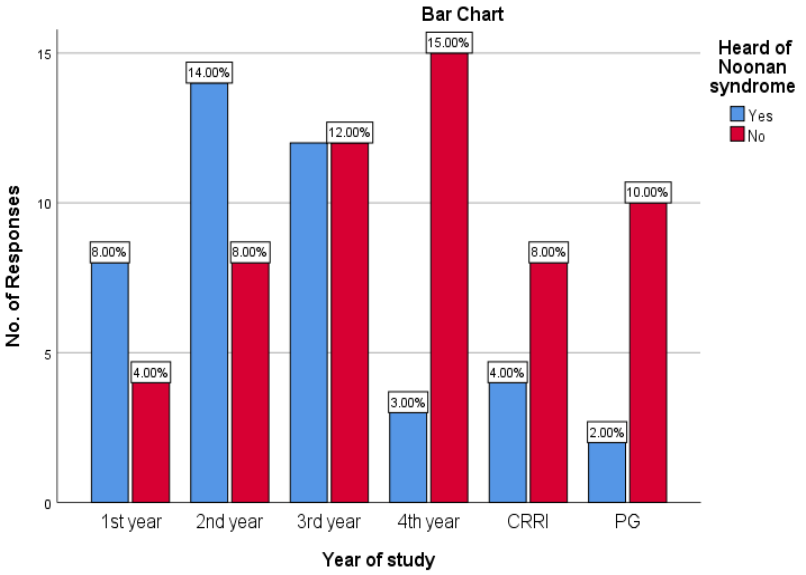

Figure 10 Bar chart represents the association between Year of study of participants and responses on awareness of noonan syndrome. X axis represents the year of study of participants and Y axis represents number of responses.Blue denotes Yes and red denotes No. Majority of the students answered No , However , Majority of 2nd year students were more aware of the syndrome , This difference was statistical significance (chi square test, p value = 0.007;p>0.05 statistically significant)

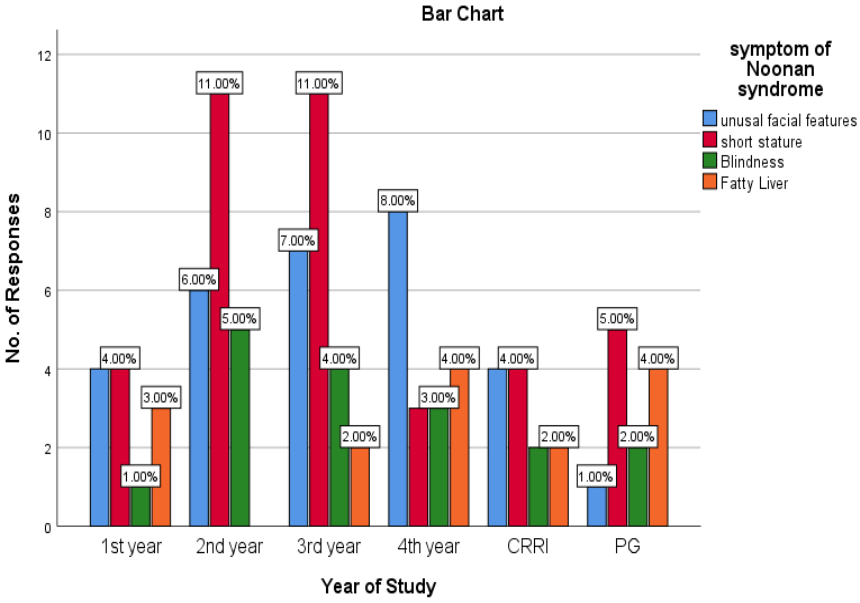

Figure 11 Bar chart represents the association between Year of study of participants and responses on symptoms of noonan syndrome. X axis represents the year of study of participants and Y axis represents number of responses.Blue denotes unusual facial features , red denotes Short stature, green denotes Blindness and Orange denotes Fatty Liver. Majority of the students answered Short Stature, However Most of the 4th year students were aware unusual facial features were the most common symptom of Noonan syndrome. This difference was not statistical significance (Chi square test , p value = 0.386(p>0.05 statistically not significant)

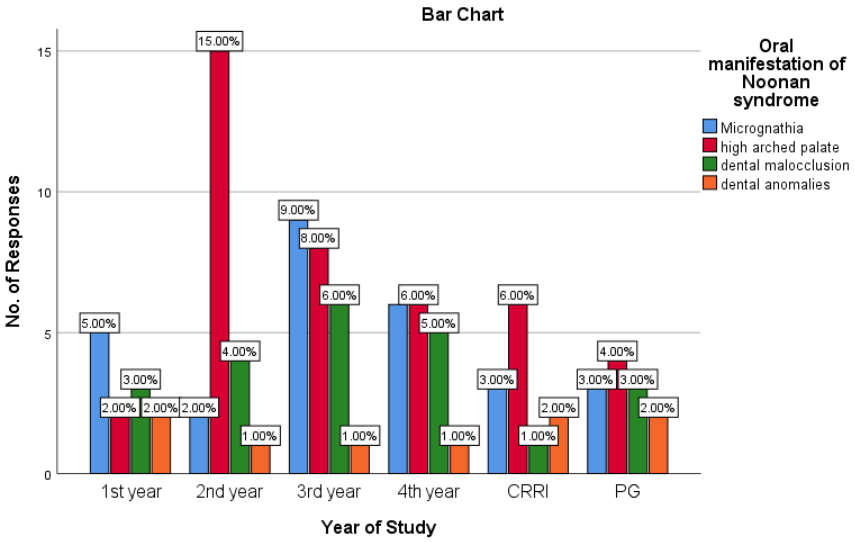

Figure 12 Bar chart represents the association between Year of study of participants and responses on oral manifestation of noonan syndrome. X axis represents the year of study of participants and Y axis represents number of responses.Blue denotes Micrognathia , red denotes High Arched Palate, green denotes Dental Malocclusion and Orange denotes Dental Anomalies. Majority of the students answered High Arched Palate, However , Majority of 4th year students were aware all 4 given symptoms were the oral manifestation of the syndrome.This difference was not statistical significance (Chi square Test, p value = 0.338;p>0.05 statistically not significant)

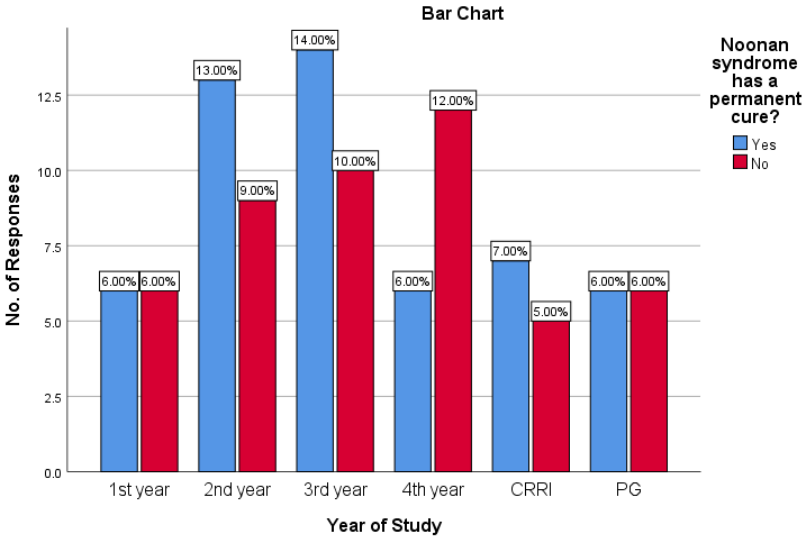

Figure 13 Bar chart represents the association between Year of study of participants and responses on Permanent cure for noonan syndrome. X axis represents the year of study of participants and Y axis represents number of responses.Blue denotes Yes and red denotes No. Majority of the students answered Yes, However Most of the 4th year were aware that there is no permanent cure to Noonan syndrome on analysis there was no statistical significance between Year of study groups and cure for Noonan Syndrome . This difference was not of statistical significance . (Chi square value 3.572 , p value = 0.612 p>0.05 statistically not significant)

DISCUSSION:

In the present study it was found that most of the students in the study population were not aware of the Noonan syndrome(Figure 2).Noonan Syndrome is still not widely known let alone understood and this can still be true in the medical and educational fields as well as in the public in general . In India, Noonan Syndrome affects 1 in 1,000 to 1 in 2,500 live births, although 50 percent of those affected go untreated or are misdiagnosed due to a lack of understanding about the condition.(35).

Although the majority of our participants said that the condition may affect anybody (Figure 3), previous research has revealed that Noonan syndrome is a hereditary disease that inhibits normal development in many parts of the body.(36)(37),This suggests that the condition can affect anyone.

The signs and symptoms of Noonan syndrome vary widely from person to person and can range from moderate to severe.Characteristics may be linked to the mutation's location in the gene. One of the major clinical characteristics that leads to a diagnosis of Noonan syndrome is facial appearance. (38) (39)(8,39)(40).At birth, children with Noonan syndrome are generally of average height and weight. However, by the time they are two years old, they may realise that they are not growing as rapidly as other children their age. Puberty normally begins a few years later than it should, and the expected growth spurt that occurs with puberty is either decreased or absent.(41) Other less frequent characteristics in children include learning disabilities, eating issues, behavioural issues, and so on.(42)(43)

According to the research, the prevalence of congenital cardiac abnormalities in Noonan syndrome ranges from 50 to 80 percent.(44–46). Congenital cardiac disease affects nearly all children with Noonan syndrome. Severe stenosis of the pulmonary valve, hypertrophic cardiomyopathy, and septal abnormalities are only a few examples.It should be highlighted that the subset of individuals with Noonan syndrome and aortic coarctation has a male predominance and clinical symptoms that are similar to those of Turner syndrome, suggesting that potential lymphogenic genes on sex chromosomes are involved in these patients.(47)(47,48)

Noonan syndrome is an autosomal dominant genetic disease caused by mutations in many genes, the most common of which are PTPN11, KRAS, SOS1, RIT1, and RAF1.(49) *PTPN11* mutations have been discovered in around half of the people who are affected. (50,51).The faulty gene might be inherited from either parent or caused by a new mutation (gene alteration) in the afflicted person.Each pregnancy has a 50% chance of transmitting the faulty gene from the affected parent to the offspring. (9)

The clinical phenotypes of NS differ greatly, therefore it's crucial to understand the nature and amount of the phenotypic differences in affected people.Oral and dental symptoms of NS can develop simultaneously or independently from the overall manifestations, both of which have serious implications.(52) The most common manifestations include maxillo-mandibular discrepancies, high arched palate, micrognathia, malocclusion, anterior open-bite, posterior cross-bite, eruption disturbances, enamel defects, dental caries, eruption cysts, dilacerations, benign MGCLs of hard and/or soft tissues, odontogenic keratocysts, and dental anomalies such as hypodontia, hyperdontia (53)(54–56) Furthermore, for the best treatment outcomes, an interdisciplinary approach is required. (53)

Although there is no one cure for Noonan syndrome,(11) various aspects of the condition can be treated.Treatment for Noonan syndrome includes cardiac therapy, growth hormone therapy, physical and speech therapy, eye treatment, bleeding issue management, lymphatic problem treatment, and urologic therapy(in males)(57)(58,59)

From the perspective of a healthcare provider, this knowledge will be used to educate people. Healthcare providers can better frame their advice and guidance by considering the population's current level of awareness and attitude toward The Noonan syndrome .

There are some drawbacks to this report, such as questionnaires filled out by people who can read English and have smartphones with internet access. Since these educated demographic groups are often limited to urban areas, this cannot be applied to the whole population. The findings of

our sample may vary from those obtained from rural people.

CONCLUSION:

Overall, the results of this survey show that the study population has a poor level of awareness of Noonan Syndrome. Also the symptoms, Oral manifestation and treatment of Noonan Syndrome are still not well understood among the study population . But among the people aware , 2nd , 3rd and 4th year students were more knowledgeable about the syndrome than other year students. Exploring these findings could help healthcare professionals educate patients more efficiently when discussing about the various dental problems caused by certain syndromes

AUTHOR CONTRIBUTIONS:

Swetha G: Literature search, data collection, analysis.

Jerry Joe Chokkattu : Data verification, manuscript drafting.

Dhanraj Ganapathy: Data verification, manuscript drafting.

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CONFLICT OF INTEREST:

No conflict of interest declared

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