

INCIDENCE OF ANGULAR CHEILITIS AMONG PATIENTS VISITING PRIVATE DENTAL HOSPITAL IN CHENNAI : AN INSTITUTIONAL STUDY

Type of Article: Original Research Article

Running Title: Prevalence of Angular cheilitis among patients visiting a private dental setting in chennai - An Institutional study

Abstract:

Introduction:

Angular cheilitis is defined as the localised inflammation of the lip commissure. The angles of the mouth are more prone to inflammation as they serve as the points of interface between the squamous epithelium and oral mucosa. It is a multifactorial disease and occurs due to varied etiology. It can be due to microbial infections, poor dentures, or can be due to smoking and pan chewing habits, Nutritional deficiency or Generalised Immunosuppression. Most of the lesions respond well to the topical antifungal medications and steroids.

Aim:

The current study aims to assess the Incidence of Angular cheilitis among patients visiting the Out patient department of a private dental hospital setting

Materials and Methodology:

The study was performed in the Out patient department of saveetha dental college, under a university setting. The study was a retrospective study and the data required were procured by reviewing patient records dating between June 2019 and March 2021 and the sample size was n =125 .The data thus collected were sorted and tabulated in the excel sheet. The sorted data were then entered in the IBM SPSS software and descriptive analysis was performed. The results were interpreted in the form of pictorial graphs.

Results:

n = 125 patient records who had been diagnosed with Angular cheilitis had been retrieved. Our results show that the majority of them i.e 52% of the people were Females and 48% of them were Males.Our results also show that the people of age group 41 to 50 were the most affected with 31.20% and people with 20 to 30 years of age group were the least affected with 12.80%.

Conclusion:

Within the limitations of the study, it can be concluded that Angular cheilitis has got a predominant Female predilection and more commonly affects people of 41 to 50 years of age.

There is also a positive correlation between the Gender of the population and smoking and pan chewing habits; and Gender of the population and Iron deficiency anemia induced Angular cheilitis.

Keywords: Angular chelosis, Angular stomatitis, Commissural cheilitis, Perleche

Introduction:

Angular cheilitis is the descriptive diagnosis of inflammatory skin process of varied etiology that occurs at the labial commissure or the angle of the mouth (1) The word "Cheil" is a Greek word and refers to the lip and the word "itis" refers to inflammation. Therefore "Angular cheilitis" refers to the localised inflammation of the angle of the mouth. This localised inflammation of the lip commissure is often characterised by maceration, erythema and crust formation (2). Angular cheilitis is known by various other names such as Angular chelosis, Angular stomatitis, Commissural cheilitis and Perleche . The angles of the mouth are more prone to inflammation as they serve as the points of interface between the squamous epithelium of the face and the oral mucosa (3) . They are easily susceptible to various stresses. They serve as a mechanical dynamic hinge for the oral cavity that bears more motion and tensile forces than the other areas of the lips or oral cavity. The Angular cheilitis lesions may be symmetrical or unilateral, confined to the lips or may extend past the vermilion border of the lips. Initially the lesions appear as a grey white thickening and later develop into a roughly triangular area of erythema, edema, and finally the skin breaks down. The mucosa becomes fissured, crusted, ulcerated or atrophied. Radiating rhagades are seen in case of skin involvement (4). Chronic angular cheilitis is characterised by suppuration, exfoliation and granulation tissue formation. Generally no bleeding occurs. As we have seen the characteristics of the lesion , it is also very important to understand the varied etiology of the disease (5). Angular cheilitis is a multifactorial disease that is mostly of infectious origin and also includes other local and systemic predisposing factors also. *Candida albicans*, *Candida Stellatoidea*, *S.aureus* and *Beta haemolytic streptococci* are the microorganisms that have got direct etiology. The Hyphal form of *Candida* is found in almost 93% cases of Angular cheilitis. Though *Candida* is a normal component of the oral microbiota, the hyphal forms are known to invade the skin tissues and can cause inflammation (6). People with suppressed immunity and those who are under steroid medication are more prone, as they are more susceptible to opportunistic fungal infections (7). Other etiological factors include low vertical dimension and lack of lip support which are common in old age people and then Wearing of complete dentures, Excessive carbohydrate consumption, Vitamin deficiency, Iron deficiency, Sensitivity to denture materials and Prolonged use of antibiotics are other causes (8). Studies show that about 22% of Angular cheilitis lesions are due to irritants caused by Irritation contact dermatitis (9). Saliva contains digestive enzymes which on prolonged exposure to skin can cause digestive action on skin. Edentulous patients wearing worn out dentures have reduced lower facial height and vertical dimension that results in overclosure of the mandible (10). These cause saliva wetting in the angles of the mouth which by both digestive enzymes and yeast infection

can cause Angular cheilitis. Reduced vertical dimension can also be caused by tooth migration, wearing orthodontic appliances, and elastic tissue damage caused by ultraviolet light exposure and smoking (11,12). Another important factor leading to Angular cheilitis is Nutritional deficiency. Deficiency of folic acid, vitamin B2, vitamin B5, Zinc and minerals can cause Angular cheilitis. The exact mechanism of them causing the disease is unknown(11,12). But the fact is Deficiency of the above mentioned vitamins and minerals can cause generalised immuno compromise which can lead to opportunistic infections. On the other hand, Vitamin A hypervitaminosis can cause Angular cheilitis (11). Retinoids have the overall effect of altering differentiation and they promote shedding. There is alteration within the epidermis, particularly corneal layer. Decrease with the thickness of corneum attributes to poor barrier function and photosensitivity which will cause the formation of Angular cheilitis (11–13). On that note, Isotretinoin can cause Angular cheilitis. Other drugs such as indinavir and sorafenib are also known to cause Angular cheilitis (14). Smoke from cigarette smoking and the ingredients in pan masalas also act as irritants and causes Angular cheilitis. Allergens present in lipstick, toothpaste, acne products, cosmetics, chewing gum, mouthwash, foods, dental appliances, materials from dentures or mercury containing amalgam fillings can also cause generalised angular cheilitis (15). Further, Angular cheilitis has shown association with Sjogren's syndrome, Down's syndrome, Inflammatory bowel disease, Crohn's disease, Ulcerative colitis, HIV, neutropenia, Diabetes, Plasma cell gingivitis, Melkersson-Rosenthal syndrome and Sideropenic dysphagia. Thus Angular cheilitis may be *Candida* associated or non *Candida* associated. It can be Acute, Chronic or Refractory. Diagnosis is usually done clinically. Microbial cultures are done occasionally (16). Treatment and Management interventions involve disinfecting and cleaning dentures before and after use. In case of loss of lower facial height, construction of a new denture with an adjusted bite can help. Surgical procedures such as collagen injections are also done to restore facial contour (17). Primary treatment aims at eradicating the potential reservoirs of infection with topical antifungal medications such as clotrimazole, amphotericin B, ketoconazole, nystatin and corticosteroids such as hydrocortisone and triamcinolone are given to reduce inflammation (18). Most of the patients respond quickly to anti fungal treatment. Some long standing cases follow a relapsing and remitting course over time.

So, the current study aims to assess the Incidence of Angular cheilitis and Provision of detailed statistical report. Our team has extensive knowledge and research experience that has translate into high quality publications (19),(20),(21),(22),(23),(24),(25),(26),(27),(28),(29),(30),(31), (32),(33),(34),(35),(36),(37),(38).

Materials and Methodology:

The study was performed in the Out patient department of saveetha dental college, under a university setting. The study was a retrospective study and the data required were procured by reviewing patient records dating between June 2019 and March 2021. Reviewing all the patient

records of 5,35,951 in the given time period of about 22 months ,n =125 patient records with Angular cheilitis are found. Patients with Smoking and Pan chewing habits and Patients with systemic diseases like Diabetes mellitus, Hypertension and Anemia were also included in the study to determine the correlation between the presence of the habit or systemic disease respectively and the incidence of Angular cheilitis. Only Patients under Antibiotic therapy for at least 6 months were excluded in the study as it may affect the results of the study. The data thus collected were sorted and tabulated in the excel sheet. The sorted data were then entered in the IBM SPSS software and descriptive analysis was performed. The results were interpreted in the form of pictorial graphs.

Results:

Of reviewing patient records dating between June 2019 to March 2021, we have retrieved n= 125 patient records who had been suffering with Angular cheilitis (n=125). Our results show that the majority of them i.e 52% of the people were Females and 48% of them were males (Figure 1). 12.80% of the people with angular cheilitis were found to belong to 20 to 30 years of age, 15.20% of the people were between 31 to 40 years of age, 31.20% between 41 to 50 years of age, 16.80% between 51 to 60 years of age, 24% between 61 to 70 years of age (Figure 2). The frequency of smoking or pan chewing habits in our study population were analysed. It is found that 88% of them were non smokers, while 7.20% were smokers, 2.40% were pan chewers and 2.40% were both smokers and pan chewers (Figure 3). Further, 8.80% people were found to be diabetic while 91.20% were found to be non Diabetic (Figure 4). Similarly, 4.80% people were found to be hypertensive and 95.20% people were found to be non hypertensive (Figure 5). 3.20% of our study population wore dentures (Figure 6) and 4% were found to be anemic (Figure 7). Our study had also found an association between the Gender and the smoking or pan chewing habit among the people. The Association had found to be statistically significant with chi square value 0.008 (Figure 8). There was also a significant association found between the Gender of the population and Iron deficiency anemia induced Angular cheilitis with a chi square value of 0.028 (Figure 9)

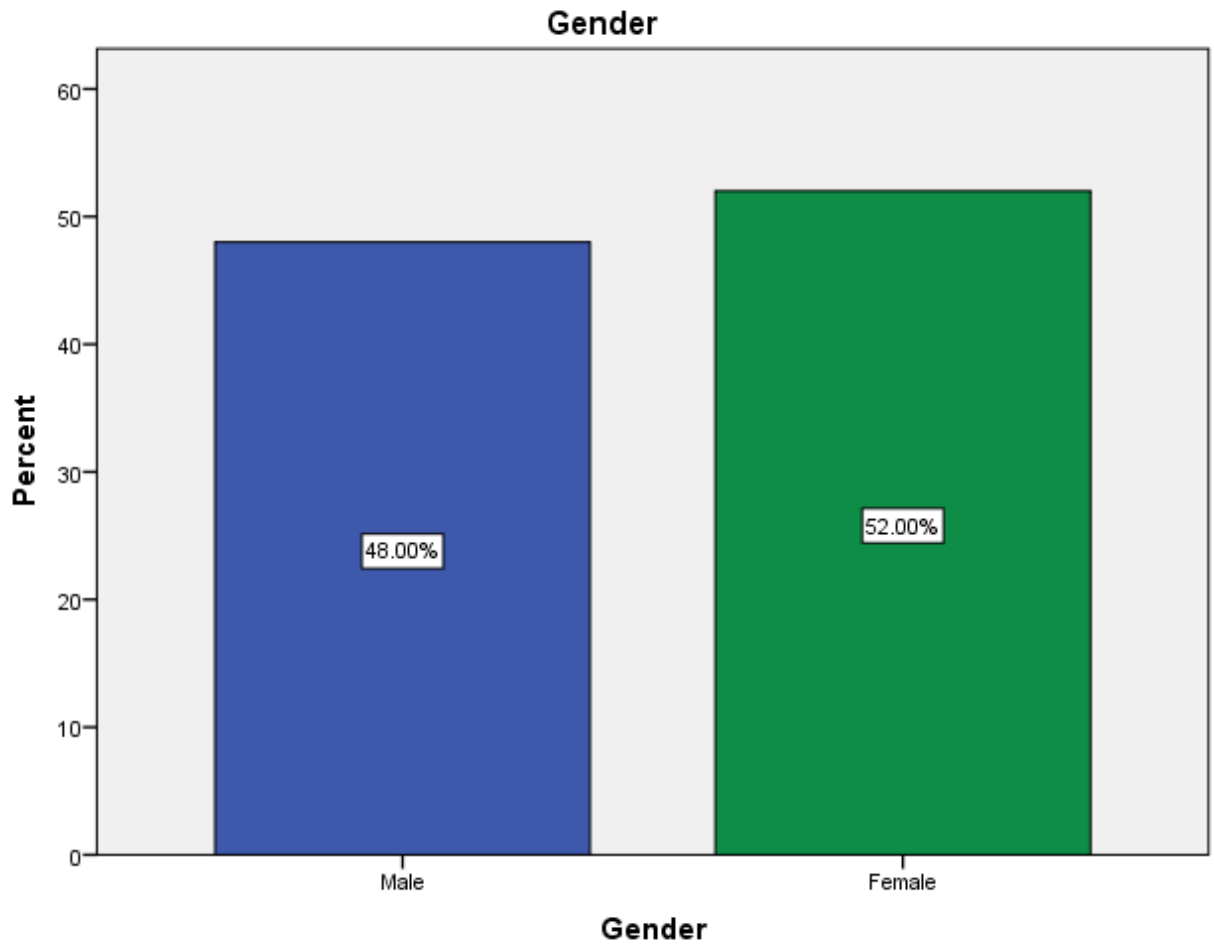


Figure 1: Shows the Incidence of Angular cheilitis in different genders of the population. The Blue zone denoted the male population and the green zone represented the female population. Incidence of Angular cheilitis in males were found to be 48% and in females it was found to be about 52%. From the graph, it is inferred that angular cheilitis had got a predominant female predilection.

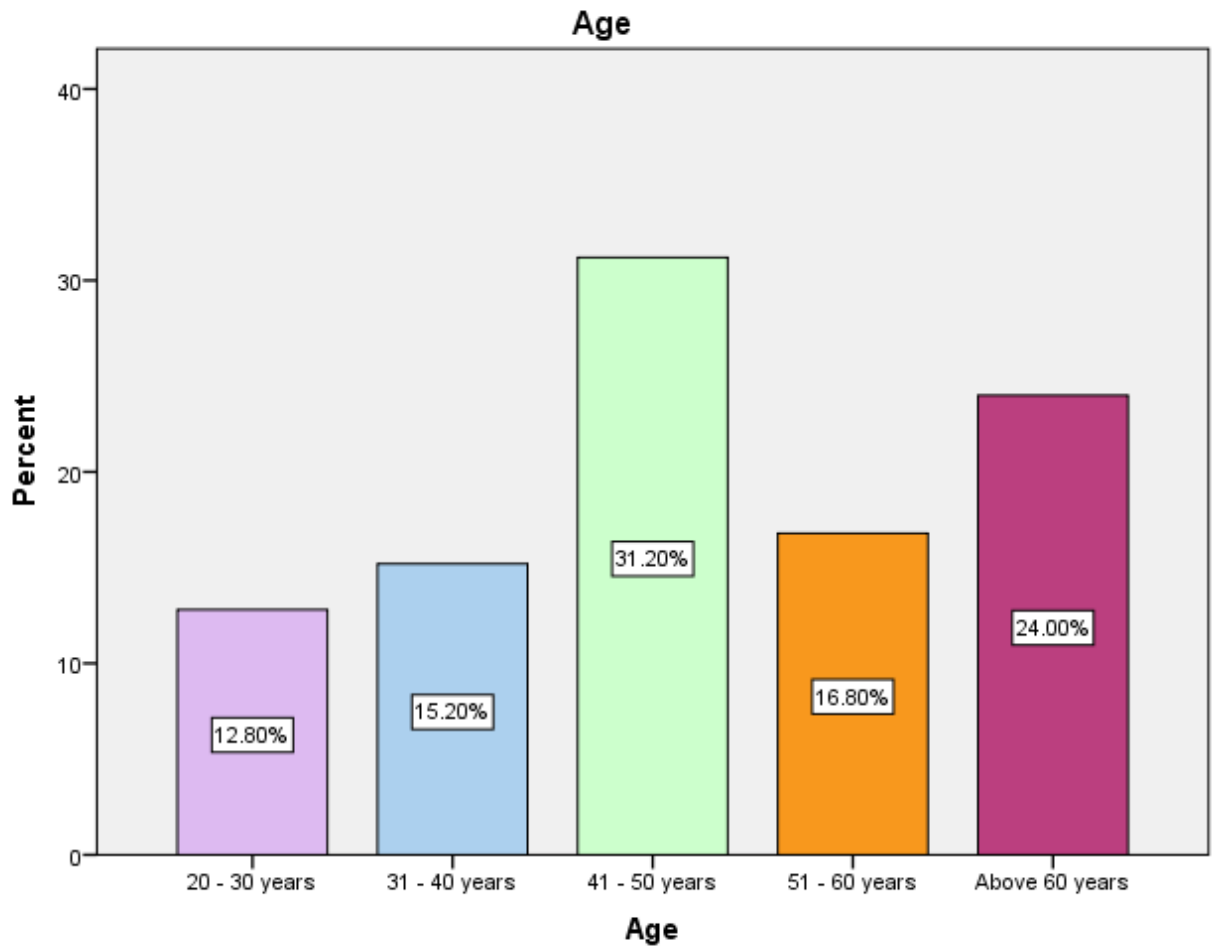


Figure 2: Shows the incidence of angular cheilitis in different age groups of the population. The violet zone represented the age group of people with 20 to 30 years age, the light blue zone represented the frequency percent of the disease in people who were 31 to 40 years old, the light green zone the frequency percent in people of 41 to 50 years old, orange zone in people of 51 to 60 years old and lastly, the purple zone above 60 years of age. The frequencies are found to be 12.80%, 15.20%, 31.20%, 16.80%, 24% respectively. From the data, we infer that angular cheilitis occurred more commonly in people of age group 41 to 50 years and less frequently in people of age group 20 to 30 years, comparatively.

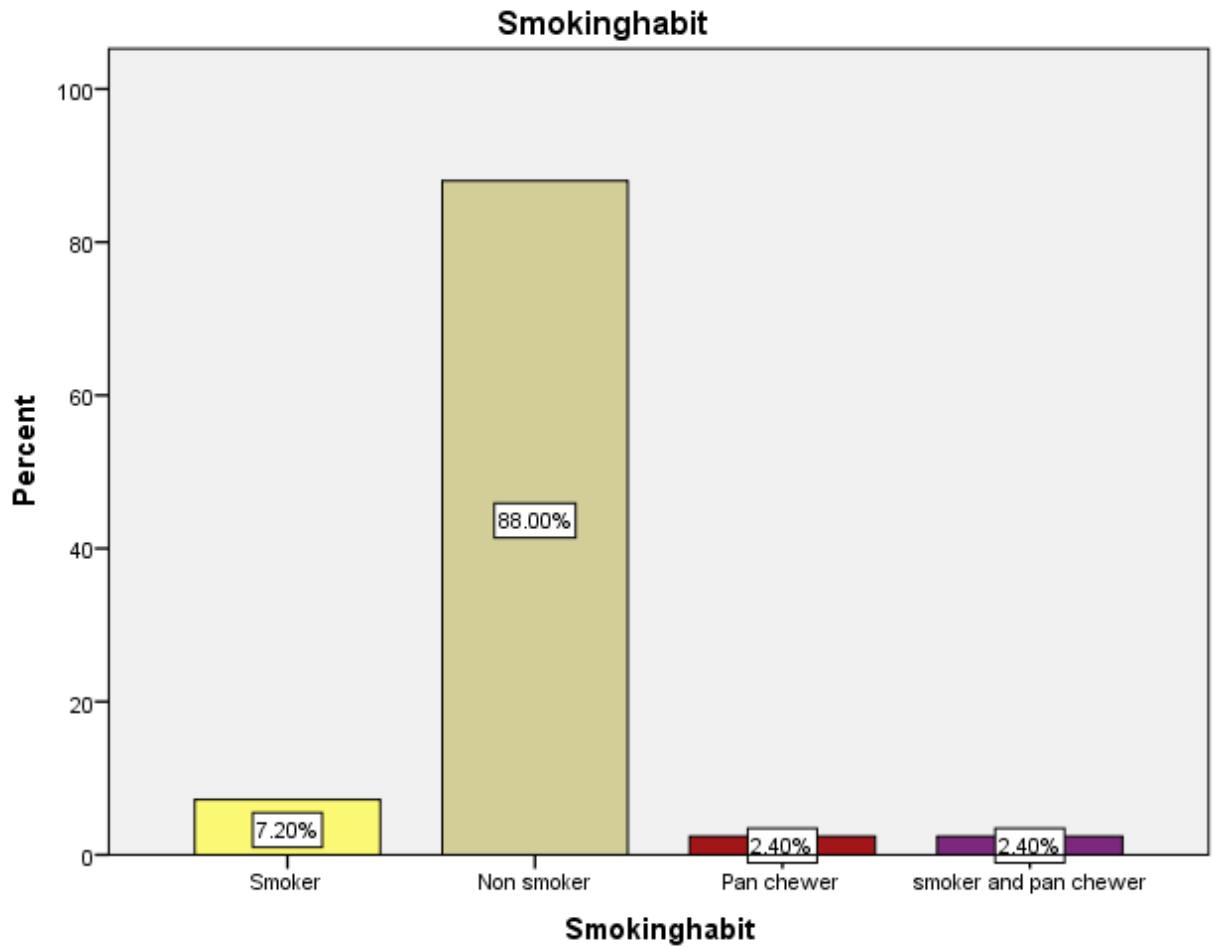


Figure 3: Shows the smoking and pan chewing habits of the study population. The yellow zone represented the smokers, the beige zone represented non smokers, the red zone represented pan chewers and the violet zone represented people who were both smokers and pan chewers. The frequencies were found to be 7.20%, 88%, 2.40% and 2.40% respectively. It is seen that most of the people were non smokers and a few were smokers with 7.20% and the no of pan chewers were comparatively very less.

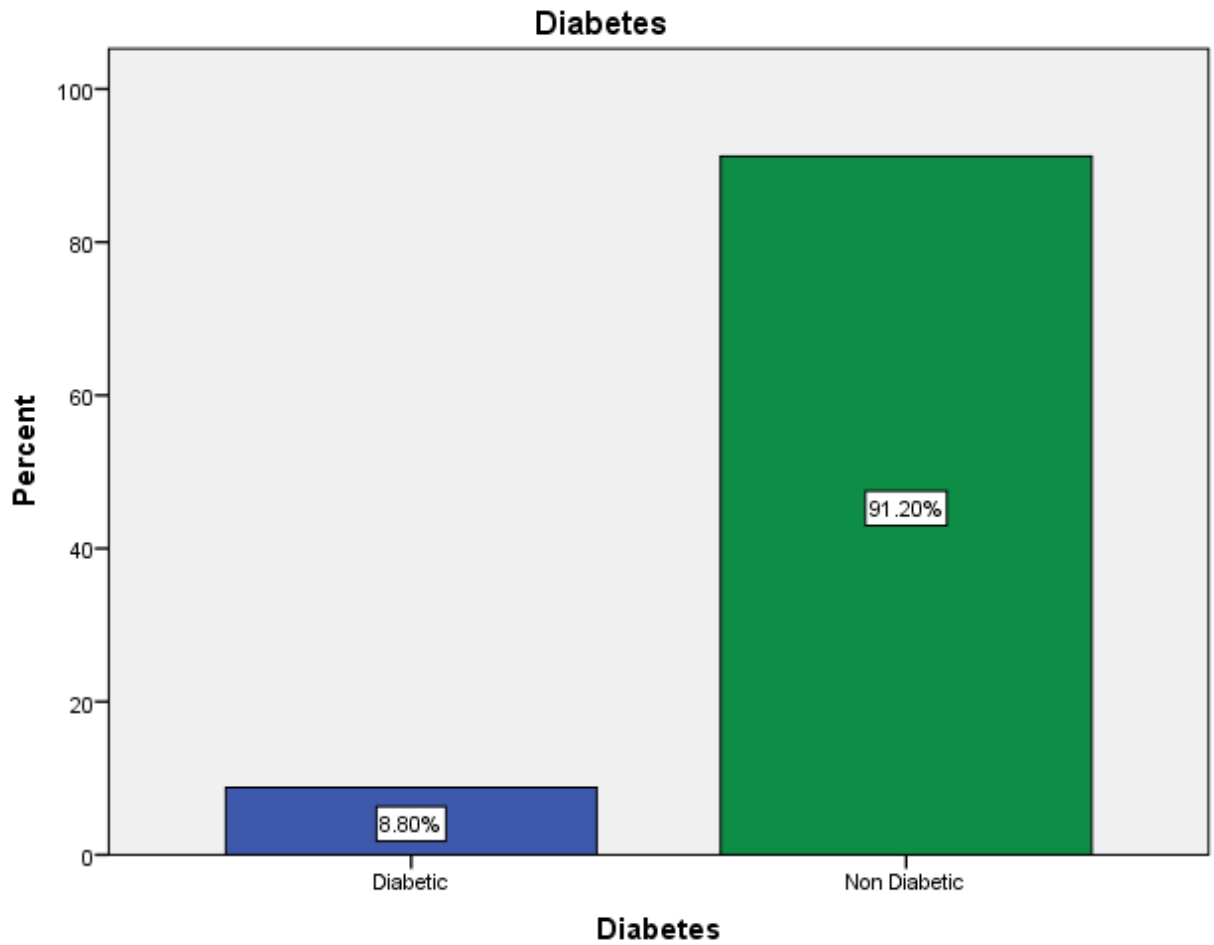


Figure 4: Shows the Percentage of people who were diabetic and non diabetic. The dark blue zone represented people who were diabetic and the dark green zone represented people who were non diabetic. 8.80% people were found to be diabetic while 91.20% were found to be non diabetic. From the graph, It is shown that most of our study population i.e 91.20% were non diabetic.

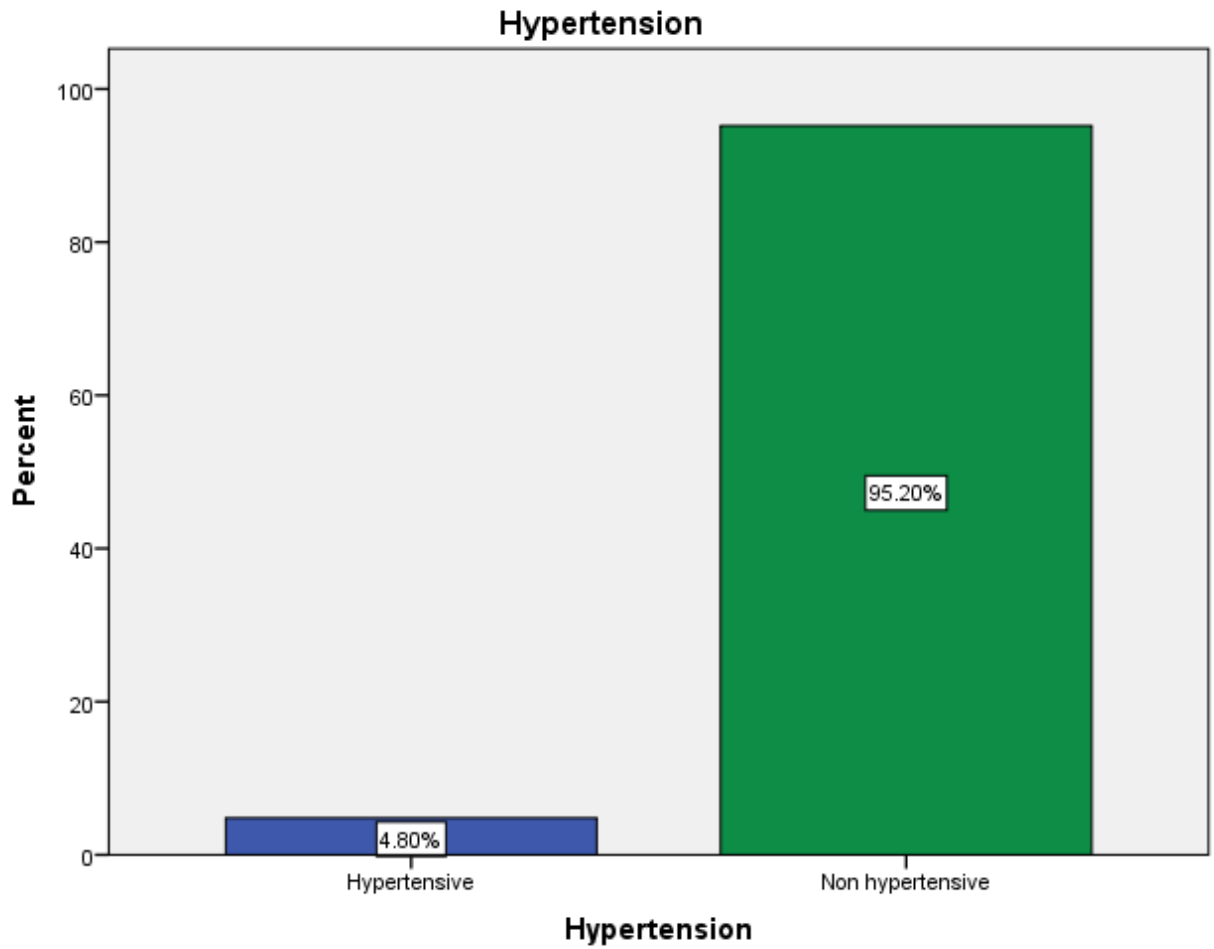


Figure 5: Shows people who were hypertensive and non hypertensive. The dark blue zone represented people who were hypertensive and the dark green zone represented people who were non hypertensive. 4.80% people were found to be hypertensive and 95.20% people were found to be non hypertensive. From the graph. It is inferred that most of our study population i.e 95.20% did not have hypertension.

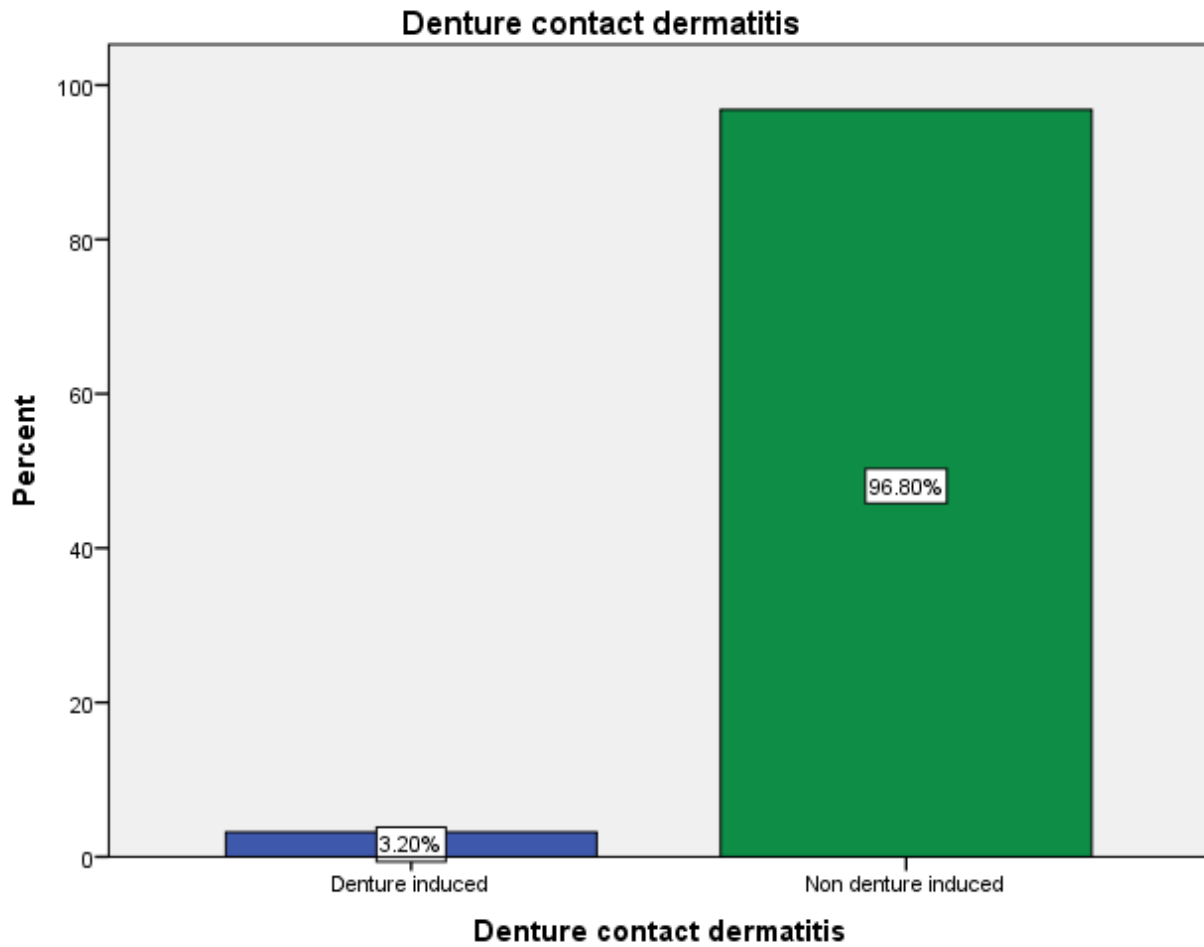


Figure 6: Shows the frequency of denture induced and non denture induced angular cheilitis among the study population. The dark blue zone represented denture induced angular cheilitis which was about 3.20% and the dark green zone represented non denture induced angular cheilitis which was about 96.80%. From the graph it is inferred that about 3.20% of our study population suffered from denture induced angular cheilitis.

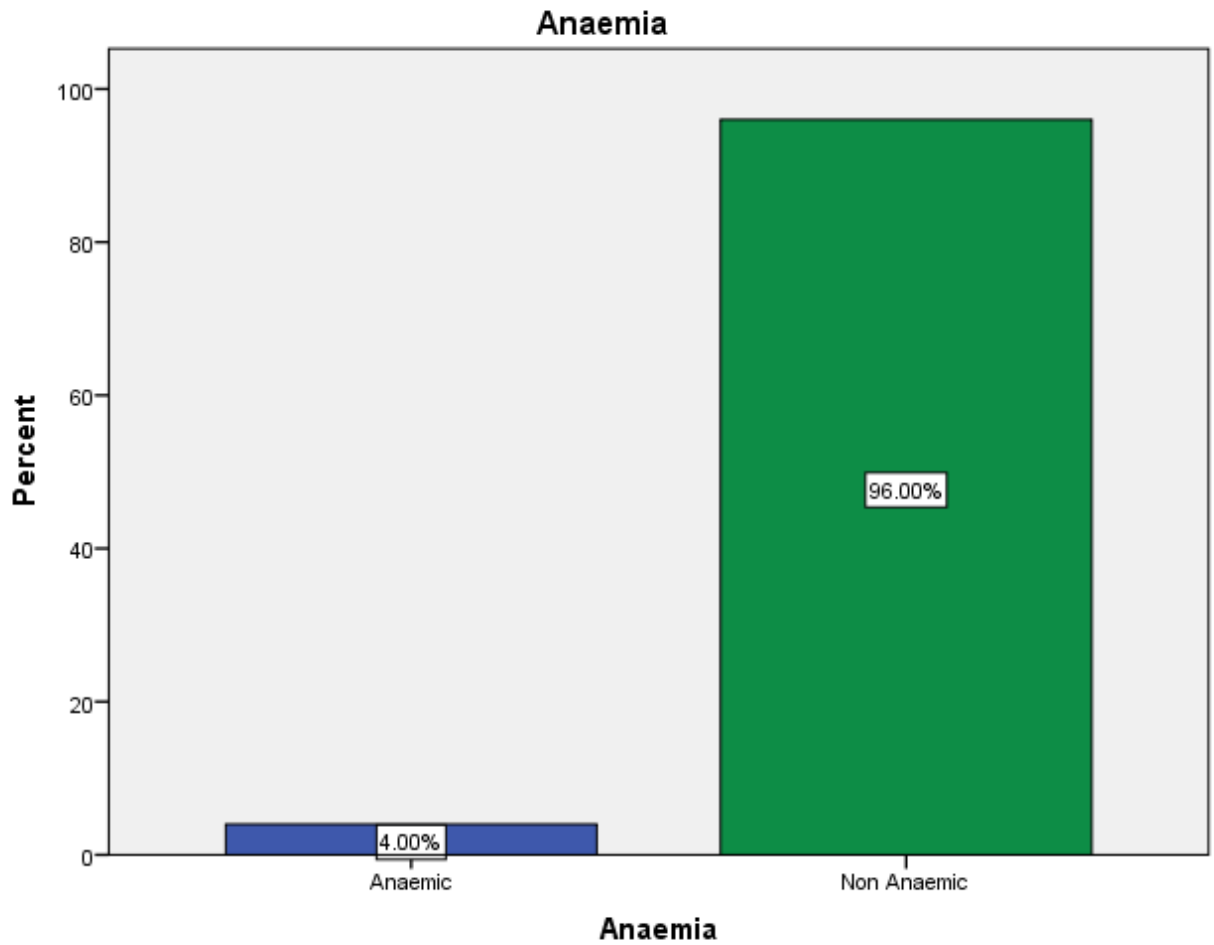


Figure 7: Shows the anemic status of people. The dark blue zone represented the people who were anaemic and the dark green zone represented people who were not anaemic. 4% people were found to be anaemic while 96% people were found to be non anaemic. From the graph it is inferred that about 4% of our study population suffered from anemia .

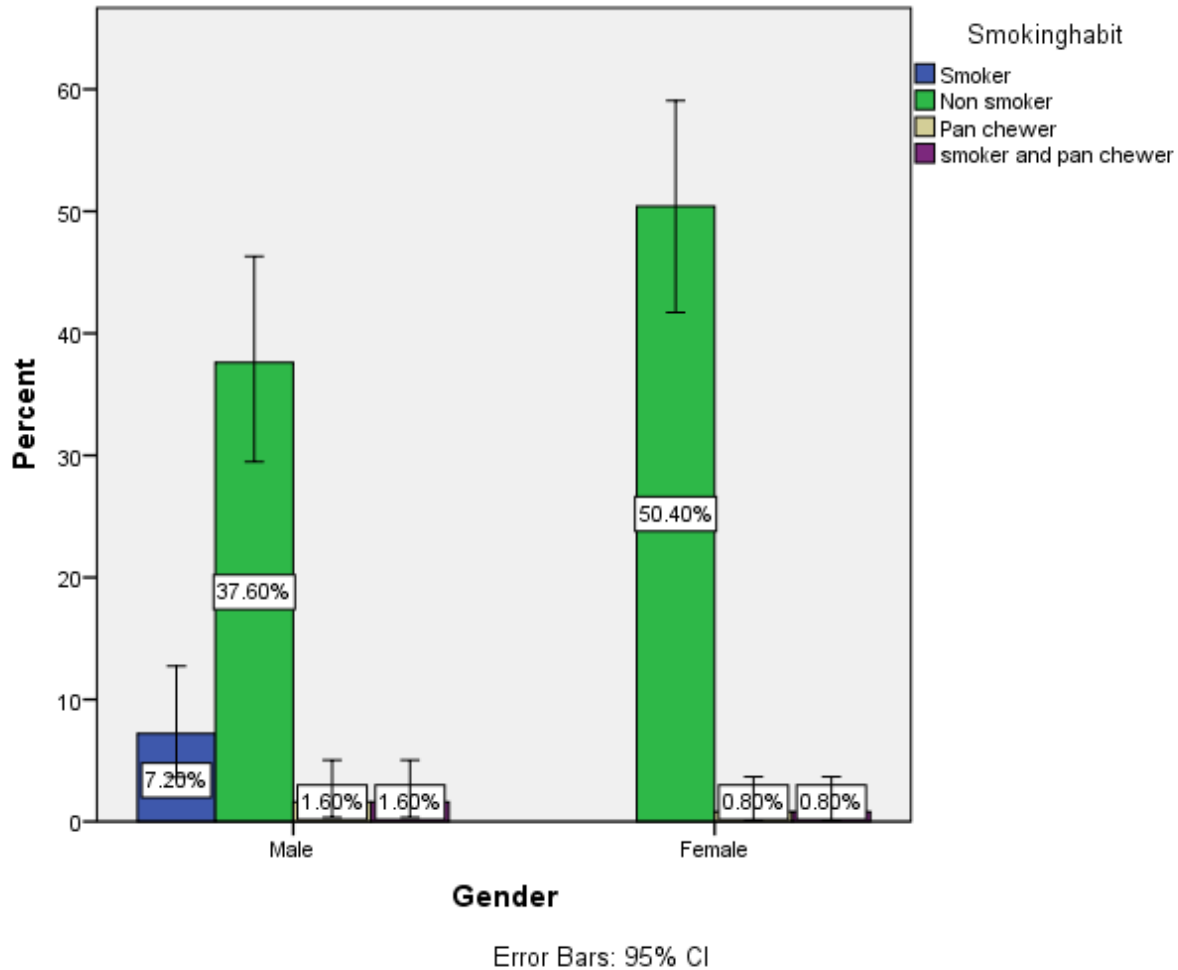


Figure 8: Shows the Association between the Gender and the Smoking and Pan chewing habit of the study population. The x axis shows the Gender of the population and y axis shows the frequency of smoking and pan chewing habit. Chi square test was done and the association was found to be statistically significant. Pearson's chi square value: 11.813, df: 3, p-value: 0.008 ($p < 0.05$). Hence statistically significant, provided males showed a higher history of smoking and pan chewing habits than Females, with 7.20% males were smokers, 1.60% were pan chewers and 1.69% were both smokers and pan chewers.

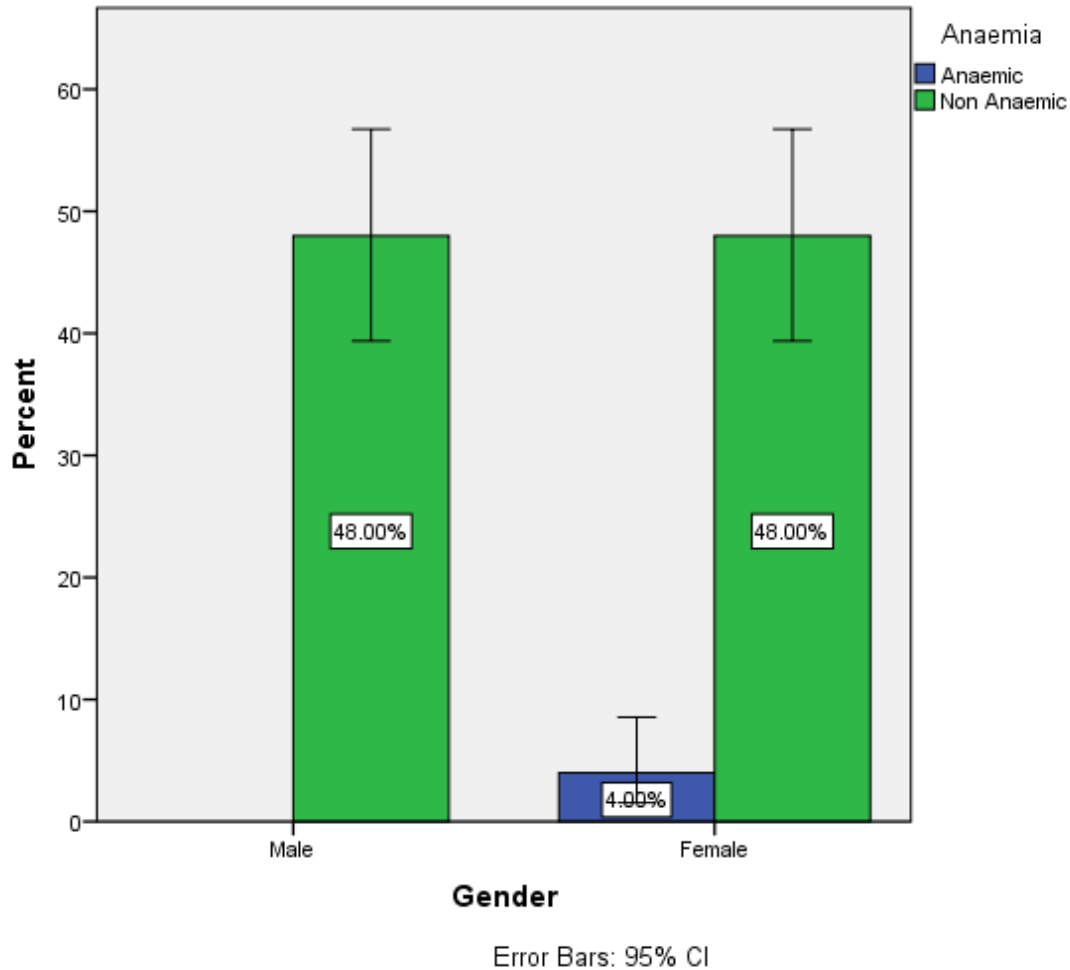


Figure 9: Shows the Association between the Gender and Iron deficiency anemia. The x axis shows the Gender of the population and the y axis shows the frequency of Anemia. Chi square test was done and the association was found to be statistically significant, p-value:0.028 ($p < 0.05$) indicating that anemia was common among female patients .

Discussion:

Angular cheilitis is a localised lip inflammation, occurring at the labial commissures. Stagnant or persistent saliva accumulation forms the basis for the disease condition. It is found that Angular cheilitis occurs more commonly in females with a frequency of 52% and least commonly in males with a frequency of 48%. This shows that Angular cheilitis has got a female predilection, though the margin of difference between both the Gender is found to be less with 4%. This may probably be due to genetic predisposition or the greater hormonal variations such as menstruation, pregnancy, menopause and anemic states that are common in women. Other reasons include opportunistic fungal infections with *Candida* species and exposure to allergens

present in cosmetics especially lip cosmetics that contain emollients and sodium lauryl sulfate and then allergens in food products. Our study also shows the frequency of different age groups of people affected. 12.80% of the people with Angular cheilitis belonged to 20 to 30 years of age, 15.20% to 31 to 40 years of age, 31.20% to 41 to 50 years of age, 16.80% to 51 to 60 years of age, 24% to 61 to 70 years of age. This shows that the people of age group 41 to 50 were most affected with 31.20%, followed by people of age group 61 to 70 years with 24% incidence rate indicating that people of older age group to be more susceptible to the disease. On the other hand people of age group 20 to 30 were the least affected. This is because older people suffer most commonly with loss of teeth. Loss of teeth causes upper lip overhanging, increasing the depth of the lip commissures. The increased depth causes persistent accumulation of saliva which finally leads to inflammation. Our results also show the Smoking or Pan chewing habit of the study population. Majority of the study population, i.e 88% of them were non smokers. Only 7.2% of them were smokers and also 2.40 % of them were pan chewers and 2.40% people had both Smoking and Pan chewing habits. Only 8.80% of our study population had Diabetes mellitus whereas 91.20% of them were free of the disorder. Similarly 4.80% of them were hypertensive and Majority of them i.e 95.20% were Non hypertensive. Our study also shows that 3.20% of the study population were denture wearers suffering with denture induced angular cheilitis or denture contact dermatitis. Poorly fabricated dentures or improper recording of centric relation will cause a reduction in the vertical dimension of the face that leads to overclosure of the mandible. This in turn causes drooling of saliva over the lip commissures which finally resulting in Angular cheilitis. Several studies have also documented that improper denture wearers are at three fold risk of getting angular cheilitis (39) and that correction of vertical dimension with properly fitting dentures can resolve angular cheilitis and also prevent its recurrence (40). Our results showed that 4% of people in the study to be anemic. All were suffering with iron deficiency anemia. Research studies show association between iron and folic acid deficiency and angular cheilitis. A twenty year old female with less hemoglobin count of 8g/dl, suffering with angular cheilitis responded well to the oral ferrous gluconate 300 mg taken twice daily. During the two year follow up course, no recurrence of angular cheilitis lesions were recorded (41) . Similarly, When patients with both angular cheilitis and low serum folate levels were treated with supplementary folic acids, the lesions disappeared in just a month (42)

In our study we had correlated the different factors that could cause Angular cheilitis like various systemic diseases, Smoking and Pan chewing habits, iron deficiency anemia and the incidence of angular cheilitis among the people. We have found two significant correlations from our study. We have found an association between the Gender of the people affected and the Smoking and Pan chewing habit of the study population. We have found the association to be statistically significant with chi square value 0.008 in which $p < 0.05$. Thus smoking and Pan chewing habit adversely affects the oral ecosystem of the microbiota causing the dominance of opportunistic organisms like *Candida albicans* and on the other hand the smoke or the ingredients in the pan

acts as an irritant that causes excessive salivation, thus causing inflammation of the labial commissures. Also we had found an association between the gender of the population and anemia induced angular cheilitis. This association was also statistically significant with chi square value 0.028. From this we infer that Iron deficiency plays a significant role in causing Angular cheilitis.

Similar studies have reported that Angular cheilitis has a female predilection, as 60% of the people with angular cheilitis in their study were females (43) and it highly correlated with our study which had 52% females with Angular cheilitis. A Similar study by Liborija et al., 2018 shows that Angular cheilitis occurs most commonly in middle aged people which also highly correlates with our study (44). Another study shows that Angular cheilitis is a common disease occurring in the age group, 30 to 60 years, which is also associated with our study. The study also states that people wearing dentures are at three fold risk of getting Angular cheilitis (39). Shulman et al., tried to find the incidence of Angular cheilitis in children and had failed to record a single case (45). Another study by Sharon et al., states that Polymicrobial infections cause most Angular cheilitis, with 60% to 75% caused by a combination of *Candida albicans* and *S. aureus* (6). A study by Park et al., states that 25% of the Angular cheilitis cases were due to Nutritional deficiency (46). A study states that Angular cheilitis is more common in Diabetic people than Non diabetic people (47). While, our study did not find any correlation between the Gender of the population and Diabetes Mellitus. Similarly Scully says that Angular cheilitis occurs more commonly in people with suppressed immunity (48).

The limitations of the study include the smaller sample size. The Geographic locations of the patients were not included in the study. Our study forms the basis for future studies with a higher population. Future analytical studies need to be done with these limitations kept in mind.

Conclusion:

Within the limitations of the study, it can be concluded that Angular cheilitis occurs more commonly in Females with 52% incidence. It also occurs commonly in people of age group 41 to 50 years of age with an incidence of 31.20%. Our study had found a significant association between the Gender of the population and smoking and pan chewing habits with a chi square value 0.008. Our study had also found a significant correlation between the Gender of the population and Iron deficiency anemia with chi square value 0.028. So we are concluding that Angular cheilitis has got a predominant Female predilection and more commonly affects people of 41 to 50 years of age. As prevention is always better than cure, practising good oral hygiene and treating the underlying disease conditions can help us keep from Angular cheilitis.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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Conflicts of interest:

The Authors declare no conflicts of interest.

DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References:

1. Riad A, Kassem I, Issa J, Badrah M, Klugar M. Angular cheilitis of COVID-19 patients: A case-series and literature review. Oral Dis [Internet]. 2020 Oct 11; Available from: <http://dx.doi.org/10.1111/odi.13675>
2. Institute NC, National Cancer Institute. Angular Cheilitis [Internet]. Definitions. 2020. Available from: <http://dx.doi.org/10.32388/ak8su8>
3. Yamunadevi A, Pratibha R, Rajmohan M, Ganapathy N, Porkodisudha J, Pavithrah D, et al. Molecular Insight into Odontogenesis in Hyperglycemic Environment: A Systematic Review. J Pharm Bioallied Sci. 2020 Aug;12(Suppl 1):S49–56.

4. Umashankar K, R. A, R. H, Ramani P, S. G. Knowledge and Attitude About COVID-19 Pathogenesis Among Oral Pathologists in Chennai [Internet]. Vol. 12, International Journal of Current Research and Review. 2020. p. 143–51. Available from: <http://dx.doi.org/10.31782/ijcrr.2020.sp17>
5. Analysis of Prevalence of Oral Squamous Cell Carcinoma in Patients with History of Chronic Irritation of Oral Tissues - A Retrospective Study [Internet]. Indian Journal of Forensic Medicine & Toxicology. 2020. Available from: <http://dx.doi.org/10.37506/ijfmt.v14i4.12511>
6. Sharon V, Fazel N. Oral candidiasis and angular cheilitis [Internet]. Vol. 23, Dermatologic Therapy. 2010. p. 230–42. Available from: <http://dx.doi.org/10.1111/j.1529-8019.2010.01320.x>
7. K M, Monica K, Vijayshree PJ, Gheena S, Ramani P, Abhilasha R, et al. IN SILICO GENE EXPRESSION ANALYSIS OF CRUCIAL CELL CYCLE CONTROL GENE CDKN2A AND CDKN2B IN HEAD AND NECK SQUAMOUS CELL CARCINOMA [Internet]. Vol. 23, Annals of Tropical Medicine & Public Health. 2020. Available from: <http://dx.doi.org/10.36295/asro.2020.232323>
8. Sinduja P, Ramani P, Gheena S, Ramasubramanian A. Expression of metallothionein in oral squamous cell carcinoma: A systematic review. J Oral Maxillofac Pathol. 2020 Jan;24(1):143–7.
9. Usatine RP. Soreness around mouth. Contact dermatitis and angular cheilitis (perlèche). J Fam Pract. 2013 Dec;62(12):767.
10. Ramani P, Krishnan RP, Karunagaran M, Muthusekhar MR. Odontogenic sarcoma: First report after new who nomenclature with systematic review. J Oral Maxillofac Pathol. 2020 Jan;24(1):157–63.
11. Lubis WH, Serelady S. ANGULAR CHEILITIS PATIENTS PROFILES AND DEMOGRAPHIC DATA AT FKG USU DENTAL HOSPITAL IN 2016 [Internet]. Vol. 19, Dentika Dental Journal. 2016. p. 138–41. Available from: <http://dx.doi.org/10.32734/dentika.v19i2.417>
12. Öhman S-C. Angular Cheilitis: A Clinical, Microbiological and Immunohistochemical Study. 1988. 30 p.
13. Degos L, Parkinson DR. Retinoids in Oncology. Springer Science & Business Media; 2012. 115 p.
14. Bhushan A. Metronidazole Induced Aphthous Ulcer with Angular Cheilitis [Internet]. Vol. 4, Pharmacy & Pharmacology International Journal. 2016. Available from: <http://dx.doi.org/10.15406/ppij.2016.04.00074>
15. Ramasubramanian A, Ramani P, Sherlin HJ, Premkumar P, Natesan A, Thiruvengadam C. Immunohistochemical evaluation of oral epithelial dysplasia using cyclin-D1, p27 and p63

expression as predictors of malignant transformation. *J Nat Sci Biol Med.* 2013 Jul;4(2):349–58.

16. E A, Aswani E, Gheena S, Pratibha R, Abilasha R, Hannah R, et al. Overexpression of HNRNPA2B1 is Associated with Poor Prognosis in Head and Neck Squamous Cell Carcinoma [Internet]. *International Journal of Current Research and Review.* 2020. p. 15–8. Available from: <http://dx.doi.org/10.31782/ijcrr.2020.122502>
17. Association of the Depth of Invasion with Lymph Node Metastasis in Oral Squamous Cell Carcinoma Patients - A Retrospective Study [Internet]. *Indian Journal of Forensic Medicine & Toxicology.* 2020. Available from: <http://dx.doi.org/10.37506/ijfmt.v14i4.12542>
18. Arduino PG. Use of Novox oil in the management of angular cheilitis [Internet]. <http://isrctn.com/>. Available from: <http://dx.doi.org/10.1186/isrctn26092754>
19. Princeton B, Santhakumar P, Prathap L. Awareness on Preventive Measures taken by Health Care Professionals Attending COVID-19 Patients among Dental Students. *Eur J Dent.* 2020 Dec;14(S 01):S105–9.
20. Mathew MG, Samuel SR, Soni AJ, Roopa KB. Evaluation of adhesion of *Streptococcus mutans*, plaque accumulation on zirconia and stainless steel crowns, and surrounding gingival inflammation in primary molars: randomized controlled trial. *Clin Oral Investig.* 2020 Sep;24(9):3275–80.
21. Sridharan G, Ramani P, Patankar S, Vijayaraghavan R. Evaluation of salivary metabolomics in oral leukoplakia and oral squamous cell carcinoma. *J Oral Pathol Med.* 2019 Apr;48(4):299–306.
22. R H, Hannah R, Ramani P, Ramanathan A, Jancy MR, Gheena S, et al. CYP2 C9 polymorphism among patients with oral squamous cell carcinoma and its role in altering the metabolism of benzo[a]pyrene [Internet]. Vol. 130, *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology.* 2020. p. 306–12. Available from: <http://dx.doi.org/10.1016/j.oooo.2020.06.021>
23. Antony JVM, Ramani P, Ramasubramanian A, Sukumaran G. Particle size penetration rate and effects of smoke and smokeless tobacco products - An invitro analysis. *Heliyon.* 2021 Mar;7(3):e06455.
24. Sarode SC, Gondivkar S, Sarode GS, Gadbail A, Yuwanati M. Hybrid oral potentially malignant disorder: A neglected fact in oral submucous fibrosis. *Oral Oncol.* 2021 Jun 16;105390.
25. Hannah R, Ramani P, WM Tilakaratne, Sukumaran G, Ramasubramanian A, Krishnan RP. Author response for “Critical appraisal of different triggering pathways for the pathobiology of pemphigus vulgaris—A review” [Internet]. Wiley; 2021. Available from: <https://publons.com/publon/47643844>
26. Chandrasekar R, Chandrasekhar S, Sundari KKS, Ravi P. Development and validation of a

formula for objective assessment of cervical vertebral bone age. *Prog Orthod.* 2020 Oct 12;21(1):38.

27. Subramanyam D, Gurunathan D, Gaayathri R, Vishnu Priya V. Comparative evaluation of salivary malondialdehyde levels as a marker of lipid peroxidation in early childhood caries. *Eur J Dent.* 2018 Jan;12(1):67–70.
28. Jeevanandan G, Thomas E. Volumetric analysis of hand, reciprocating and rotary instrumentation techniques in primary molars using spiral computed tomography: An in vitro comparative study. *Eur J Dent.* 2018 Jan;12(1):21–6.
29. Ponnulakshmi R, Shyamaladevi B, Vijayalakshmi P, Selvaraj J. In silico and in vivo analysis to identify the antidiabetic activity of beta sitosterol in adipose tissue of high fat diet and sucrose induced type-2 diabetic experimental rats. *Toxicol Mech Methods.* 2019 May;29(4):276–90.
30. Sundaram R, Nandhakumar E, Haseena Banu H. Hesperidin, a citrus flavonoid ameliorates hyperglycemia by regulating key enzymes of carbohydrate metabolism in streptozotocin-induced diabetic rats. *Toxicol Mech Methods.* 2019 Nov;29(9):644–53.
31. Alsawalha M, Rao CV, Al-Subaie AM, Haque SKM, Veeraraghavan VP, Surapaneni KM. Novel mathematical modelling of Saudi Arabian natural diatomite clay. *Mater Res Express.* 2019 Sep 4;6(10):105531.
32. Yu J, Li M, Zhan D, Shi C, Fang L, Ban C, et al. Inhibitory effects of triterpenoid betulin on inflammatory mediators inducible nitric oxide synthase, cyclooxygenase-2, tumor necrosis factor-alpha, interleukin-6, and proliferating cell nuclear antigen in 1, 2-dimethylhydrazine-induced rat colon carcinogenesis. *Pharmacogn Mag.* 2020;16(72):836.
33. Hema Shree K, Ramani P, Sherlin H, Sukumaran G, Jeyaraj G, Don KR, et al. Saliva as a Diagnostic Tool in Oral Squamous Cell Carcinoma - a Systematic Review with Meta Analysis. *Pathol Oncol Res.* 2019 Apr;25(2):447–53.
34. Zafar A, Sherlin HJ, Jayaraj G, Ramani P, Don KR, Santhanam A. Diagnostic utility of touch imprint cytology for intraoperative assessment of surgical margins and sentinel lymph nodes in oral squamous cell carcinoma patients using four different cytological stains. *Diagn Cytopathol.* 2020 Feb;48(2):101–10.
35. Karunakaran M, Murali P, Palaniappan V, Sivapathasundharam B. Expression and distribution pattern of podoplanin in oral submucous fibrosis with varying degrees of dysplasia – an immunohistochemical study. *J Histotechnol.* 2019 Apr 3;42(2):80–6.
36. Sarode SC, Gondivkar S, Gadbail A, Sarode GS, Yuwanati M. Oral submucous fibrosis and heterogeneity in outcome measures: a critical viewpoint. *Future Oncol.* 2021 Jun;17(17):2123–6.
37. Raj Preeth D, Saravanan S, Shairam M, Selvakumar N, Selestin Raja I, Dhanasekaran A, et al. Bioactive Zinc(II) complex incorporated PCL/gelatin electrospun nanofiber enhanced

bone tissue regeneration. *Eur J Pharm Sci.* 2021 May 1;160:105768.

38. Prithiviraj N, Yang GE, Thangavelu L, Yan J. Anticancer Compounds From Starfish Regenerating Tissues and Their Antioxidant Properties on Human Oral Epidermoid Carcinoma KB Cells. In: PANCREAS. LIPPINCOTT WILLIAMS & WILKINS TWO COMMERCE SQ, 2001 MARKET ST, PHILADELPHIA ...; 2020. p. 155–6.
39. Sonis AL. The prevalence of oral mucosal lesions in United States adults: data from the Third National Health and Nutrition Examination Survey, 1988-1994. *J Evid Based Dent Pract.* 2005 Sep;5(3):166–7.
40. AlBaker AM. The oral health-related quality of life in edentulous patients treated with Conventional complete dentures [Internet]. Vol. 30, *Gerodontology.* 2013. p. 61–6. Available from: <http://dx.doi.org/10.1111/j.1741-2358.2012.00645.x>
41. Ayesh MH. Angular cheilitis induced by iron deficiency anemia. *Cleve Clin J Med.* 2018 Aug;85(8):581–2.
42. Ross JA. Folic-acid deficiency as a cause of angular cheilosis. *Lancet.* 1971 Oct 16;2(7729):875.
43. Oza N, Doshi JJ. Angular cheilitis: A clinical and microbial study. *Indian J Dent Res.* 2017 Nov;28(6):661–5.
44. Lugović-Mihić L. Differential Diagnosis of Cheilitis – How to Classify Cheilitis? [Internet]. Vol. 57, *Acta Clinica Croatica.* 2018. Available from: <http://dx.doi.org/10.20471/acc.2018.57.02.16>
45. Shulman JD. Prevalence of oral mucosal lesions in children and youths in the USA [Internet]. Vol. 15, *International Journal of Paediatric Dentistry.* 2005. p. 89–97. Available from: <http://dx.doi.org/10.1111/j.1365-263x.2005.00632.x>
46. Park KK, Brodell RT, Helms SE. Angular cheilitis, part 2: nutritional, systemic, and drug-related causes and treatment. *Cutis.* 2011 Jul;88(1):27–32.
47. Argadianti AF, Ernawati DS, Hernawan I. The Role of Glycated Collagen as an Angular Cheilitis Predisposing Factor n Diabetics [Internet]. *Proceedings of the 7th International Meeting and the 4th Joint Scientific Meeting in Dentistry.* 2017. Available from: <http://dx.doi.org/10.5220/0007291600370042>
48. Scully C. Angular cheilitis (angular stomatitis) [Internet]. *Oral and Maxillofacial Medicine.* 2013. p. 223–5. Available from: <http://dx.doi.org/10.1016/b978-0-7020-4948-4.00033-7>