Analysis of hemoglobin levels among oral cancer patients - An institutional study

Running Title- Hemoglobin in OSCC patients

ABSTRACT:

Background: Oral squamous cell carcinoma (OSCC) is one of the most common types of cancer worldwide. It is estimated that approximately half of all the tumors affecting the head and neck region commonly affect the oral cavity. Premalignant lesions can manifest as leukoplakia, erythroplakia, keratosis or even oral candidiasis. Hemoglobin (Hb) is a protein contained in the red blood cells of the body and plays an important role in delivery of oxygen to the tissues. A sufficient level of Hemoglobin is required to maintain oxygenation of the tissues. Anemia is defined as a reduction in hemoglobin levels below the lower limit pertaining to a particular age group. Treating anemia by increasing the levels of hemoglobin has proven to increase the quality of life of cancer patients. The aim of the present study is to analyze the Hb level in OSCC patients attending our institution.

Materials and Methods: The present retrospective institutional study was conducted after obtaining ethical clearance from the Institutional Ethical Approval Board to access patient records and data. A total of 5, 00,000 case sheets were analyzed from June 2019 to February 2021. Suitable inclusion and exclusion criteria were applied and case sheets were shortlisted. The data were entered in MS Excel spreadsheet and further statistical analysis was carried out using SPSS. All results were displayed as graphs and pie charts.

Results: 64 cases of OSCC were included in the present study with a male predominance. 45% of the study population had a level between 9-11 mg/dl. 60.3% of the population belonged to the age group of 50 and above.

Conclusion: Anemia in cancer can be precipitated due to various factors. It can be caused or exacerbated by the cancer itself due to immunosuppression or due to chemotherapy. Anemia can also be pre existing due to underlying conditions. It was found that hemoglobin levels are found to be higher in males and higher in ages 50+ when compared to ages 30-40. Low levels of hemoglobin and anemic conditions in oral cancer patients can cause excessive fatigue and can significantly affect quality of life and hence, hemoglobin therapy is widely administered to oral cancer patients.

Key words: Anemia; Hemoglobin; Oral cancer; Squamous cell carcinoma; Quality of life; Novel analysis; Innovation.

INTRODUCTION:

Oral Squamous Cell Carcinoma, is one of the most common types of cancer worldwide. It is estimated that approximately half of all the tumours affecting the head and neck region commonly affect the oral cavity. (1) OSCC is an important health issue with a wide spectrum of etiologies. (2) Common factors predisposing to oral cancer include tobacco use, smoking, betel quid chewing, use of alcohol, viral or fungal infections and there are various causes that cannot be determined. Smokers are more prone to developing these cancers when compared to non-smokers. (3) Premalignant lesions can manifest as leukoplakia, erythroplakia, keratosis or even oral candidiasis. Most common presenting features of oral cancers are painless ulcers, white patches, painful lumps with irregular margins, inability to open the mouth normally. (4)(5)

Hemoglobin (Hb) is the protein that is contained within the red blood cells of the body. Hemoglobin plays an important role in delivery of oxygen to the tissues. A sufficient level of Hemoglobin is required to maintain oxygenation of the tissues. (6) Hemoglobin is considered to be one of the most intriguing topics to study about given its complex roles and essential functions in the human body. (7) Emphasising more on its structure, Iron atoms of the hemoglobin combine with protoporphyrin to form haem groups which help in oxygen transport. (8)(9)(10) Our team has extensive knowledge and research experience that has translated into high quality publications (11-30)

Anemia is a very common finding in cancer patients. Hemoglobin levels in oral cancer can relate to the quality of life of the patient.(31) (32) Anemia is defined as a reduction in hemoglobin levels below the lower limit pertaining to a particular age group.Anemia of chronic disease refers to anemia that occurs alongside chronic infections and inflammations despite of adequate body iron stores. Anemia is seen in chronic dental diseases such as Periodontitis.(33) Anemia can also be inherited such as in Fanconi's anemia and can progressively lead to carcinoma.(34) Presence of anemia elicits a poor prognostic factor, and may also cause a negative effect on quality of life of the patient due to cancer induced fatigue.(35,36) In patients undergoing chemotherapy treatment, the chances of inducing anemia is higher than 90% (37) Treating the anemia, by increasing the levels of hemoglobin has proven to increase quality of life of the cancer patients. (38) The aim of this study was to analyse the hemoglobin levels among oral cancer patients.

MATERIALS AND METHODS:

This study is a retrospective study conducted in a university setting. An ethical approval was obtained from the Institutional Ethical Approval Board to access patient records and data. A total of 5,00,000 case sheets were analysed from June 2019 to February 2021.Suitable inclusion and exclusion criteria were applied and case sheets were shortlisted. All oral cancer patients and

Hemoglobin levels were included. Incomplete records and insufficient data were excluded from the study. Since this study is conducted within a university setting, it has a low external validity and a high internal validity. All data was tabulated using MS Excel. This data was then exported to IBM SPSS Software Version 23 (Chicago) for final statistical analysis. Descriptive statistics and Chi-square testing was done to draw a comparison between the hemoglobin levels. All the data obtained after analysis was represented in the form of graphs and pie charts.

RESULTS:

In total 64 OSCC cases were included in the present study out of which 81.2% were males (n=52) and remaining 12 were females with a definitive male preponderance (M:F::4.3:1). All the results obtained were presented as pie charts and bar graphs.In Figure 1, Hemoglobin levels of the oral cancer patients are depicted. 45% of the population had a level between 9-11 mg/dl. About 60.3% of the population belonged to the age group of 50 and above.

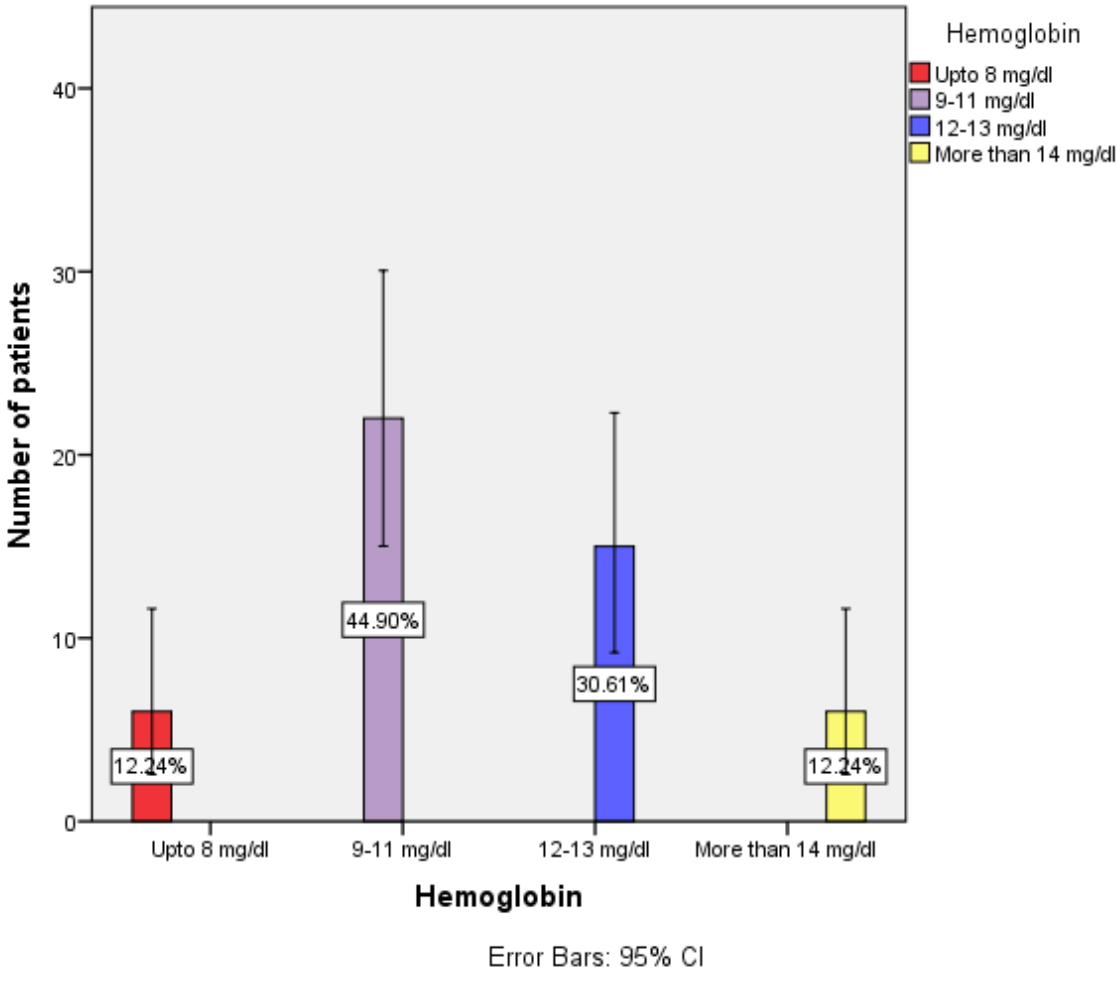

Figure 1 shows a bar chart depicting the Hemoglobin levels of the oral cancer patients. 12.24% of patients had a Hb level upto 8 mg/dl (red), 44.9% had a level of 9-11 mg/dl (purple), 30.61%

had Hb levels between 12-13 mg/dl (blue) and 12.24% had a Hb level higher than 14 mg/dl (yellow).

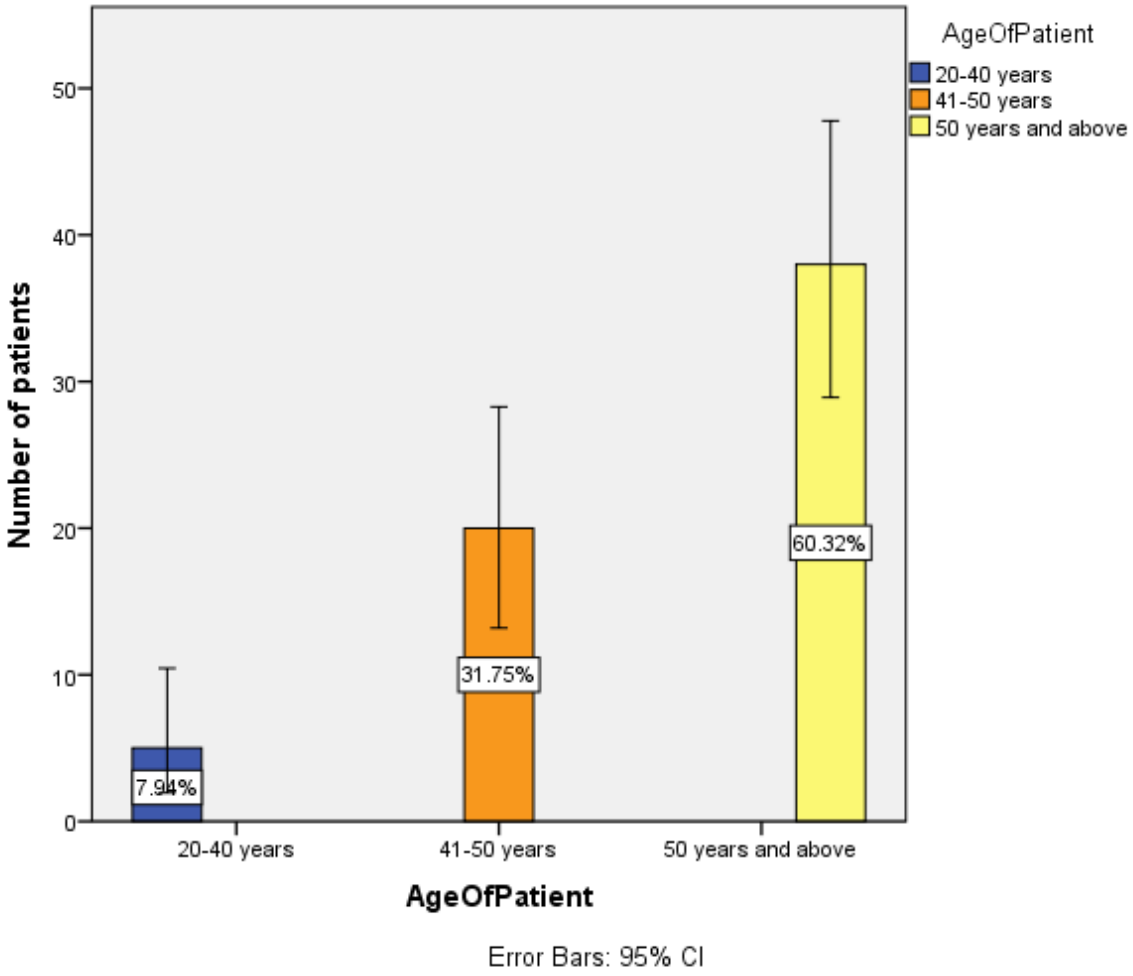

Figure 2 shows a bar chart depicting the age of the oral cancer patients. 7.94% of the population belonged to the age group between 20 to 40 years, 31.75% of the population were between the ages of 41 to 50. A majority of the population (60.32%) belonged to the age group of more than 50 years.

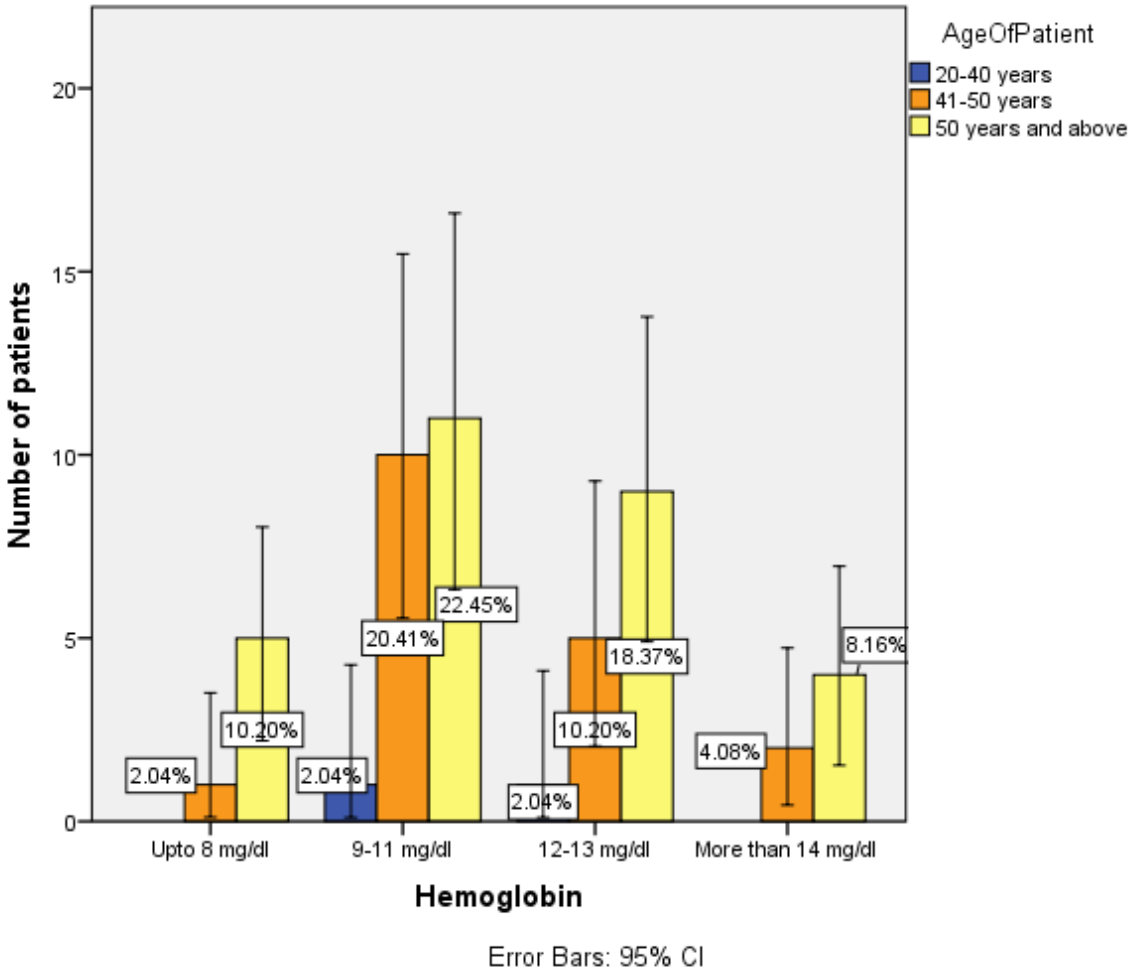

Figure 3 shows a bar graph depicting a comparison between age of the patient and their hemoglobin levels and number of patients. X axis represents Hemoglobin level of the patient and Y axis represents number of the patients. It can be seen that across the age groups, 20-22 % of the population had Hb levels between 9-11 mg/dl. Pearson's Chi-Square testing was done and the value was found to be 2.889 and P value was found to be 0.823 hence, not significant. Orange represents patients aged between 41-50 years. Blue represents patients amongst the age group of 20 to 40 years and Yellow represents the patients more than 50 years of age.

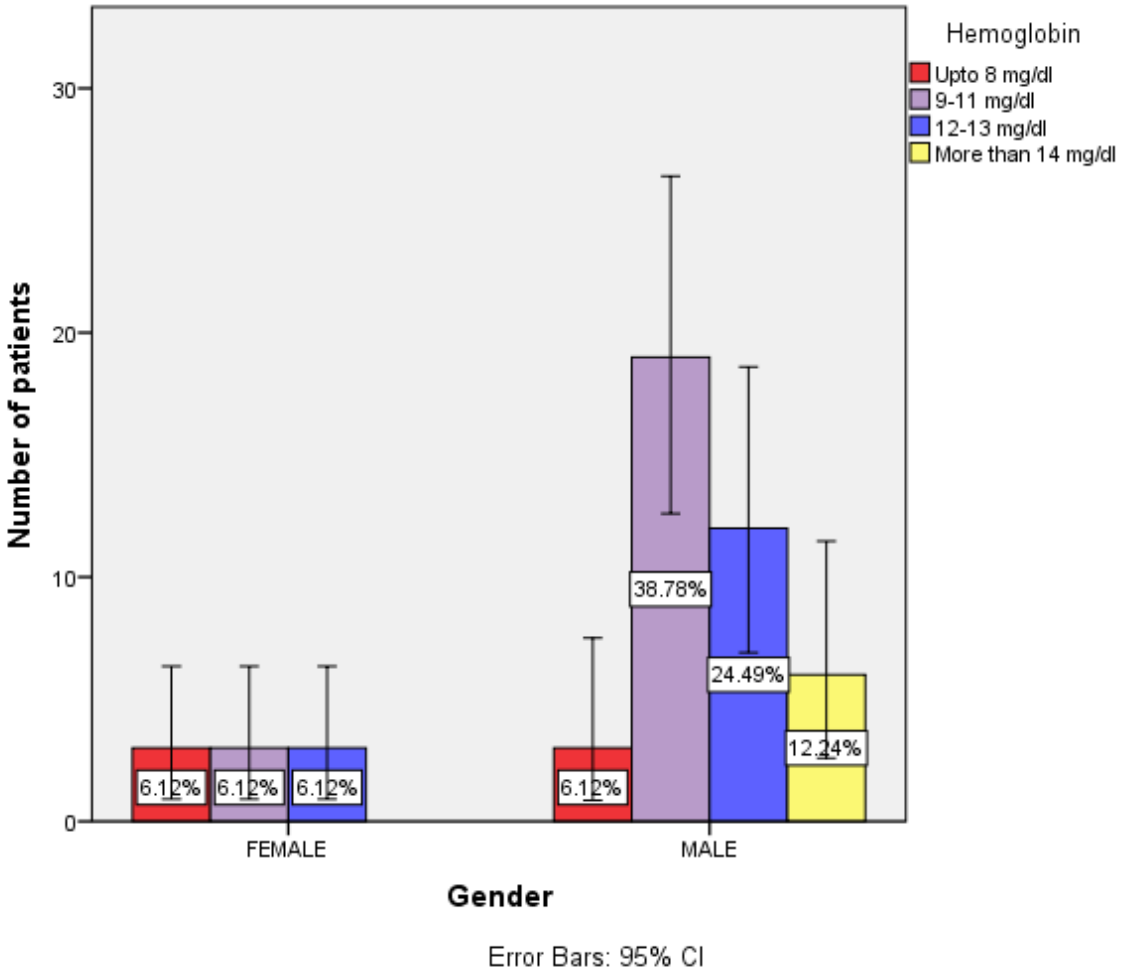

Figure 4 shows bar graphs representing a comparison between gender of the patient and their hemoglobin levels. The X axis represents Gender and the Y axis represents the number of the patients. This graph reveals that among females, none had Hb levels more than 14 mg/dl, while 12.24% of males had Hb levels more than 14 mg/dl. Pearson Chi-Square testing was done and the value was found to be 5.709, P value was 0.127, hence considered not significant. Red represents Hb level upto 8 mg/dl, Purple represents Hb levels between 9-11 mg/dl, Blue represents Hb levels between 12-13 mg/dl and Yellow represents Hb levels more than 14 mg/dl.

DISCUSSION:

Anemia is a very common finding in cancer patients and is a frequent complication of chemotherapy. The intense immunosuppressive treatment in cancer therapy leads to a drop in hemoglobin levels in general. Anemia can be taken up as one of the many adverse prognostic factors in cancer patients.

We found a definitive male predilection which is similar to previous studies.(39) It was found that the maximum number of cases were aged 50 years and above and the majority (45%) had a Hb value between 9-11 mg/dl. In contrast to previous studies, a male predominance was seen. (40) Mean Hb levels in males with OSCC have been found to be 11.25 ± 1.63, which was comparatively higher than Hb values in females. (10.77 ± 1.71)

A study done by Osterborg A et al,(41) showed a direct correlation between quality of life and level of Hemoglobin. It showed that as Hemoglobin levels increased during chemotherapy, quality of life was improved. Transfusion of packed RBCs aims to increase the level of hemoglobin and is commonly used along with cancer therapy so as to avoid anemic conditions leading to fatigue and other complications. (31) Low hemoglobin levels are associated with poorer overall quality of life, greater fatigue and other complications. Some interventions that can be done to reverse fatigue and other anemia interlinked symptoms should be employed so as to have a positive effect on the quality of life of the patient. (42,43)

There are however some inherent limitations of the study. The results of this study cannot be generalised to the whole population as many patients may be lost to other hospitals and private practitioners. However, it does provide a baseline data for further studies. Also other parameters such as MCV, MCHC could not be included in this study.

CONCLUSION:

Anemia in cancer can be precipitated due to various factors. It can be caused or exacerbated by the cancer itself due to immunosuppression or due to chemotherapy. Anemia can also be pre existing due to underlying conditions. Anemia can be considered as an adverse prognostic factor in such patients. A low level of Hemoglobin can directly impair the quality of life of the patient. In this study, an association was drawn between the hemoglobin levels and the cancer patient within the University. From the graphs obtained, it can be concluded that hemoglobin levels are found to be higher in males and higher in ages 50+ when compared to ages 30-40. Low levels of hemoglobin and anemic conditions in oral cancer patients can cause excessive fatigue and can significantly affect quality of life and hence, hemoglobin therapy is widely administered to oral cancer patients.

COMPETING INTERESTS 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. Kademani D. Oral Cancer. Mayo Clin Proc. 82(7):878–87.
2. Sciubba J. Oral Cancer The Importance of Early Diagnosis and Treatment. Am J Clin Dermatol. 22 August, 2012;2:239–51.
3. Brad Neville TD. Oral Cancer and Precancerous Lesions. CA Cancer J Clin. 2002 Aug;52(4):195–215.
4. Oral cancer: Clinical features. Oral Oncol. 2010 Jun 1;46(6):414–7.
5. Shah JP, Johnson NW, Batsakis JG, Batsakis JG. Oral Cancer. Thieme; 2003. 496 p.
6. HEMOGLOBIN AND HEMATOCRIT [Internet]. Vol. 28, Anesthesiology. 1967. p. 763–763. Available from: http://dx.doi.org/10.1097/00000542-196707000-00028
7. Perutz MF. Hemoglobin Structure and Respiratory Transport [Internet]. Vol. 239, Scientific American. 1978. p. 92–125. Available from: http://dx.doi.org/10.1038/scientificamerican1278-92
8. Muirhead H. The Structure of Haemoglobin [Internet]. Naturstoffe. 1996. p. 41–64. Available from: http://dx.doi.org/10.1007/978-3-662-25280-2_2
9. M. F. Perutz, M. G. Rossman, Georg Will. Structure of Haemoglobin. 1960 Feb 13; Available from: http://www.gradadm.ifsc.usp.br/dados/20102/FFI0776-1/Perutz_1960.pdf
10. Ranney HM, Shaklai N, Yguerabide J. HEMOGLOBIN AND THE RED CELL MEMBRANE [Internet]. Biochemical and Clinical Aspects of Hemoglobin Abnormalities. 1978. p. 509–13. Available from: http://dx.doi.org/10.1016/b978-0-12-164350-8.50041-8
11. 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.

12. 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.

13. 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.

14. 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

15. 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 1;7(3):e06455.

16. 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.

17. 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

18. 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.

19. 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.

20. 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.

21. 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.

22. 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.

23. 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.

24. 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.

25. Shree KH, Hema Shree K, Ramani P, Herald Sherlin, Sukumaran G, Jeyaraj G, et al. Saliva as a Diagnostic Tool in Oral Squamous Cell Carcinoma – a Systematic Review with Meta Analysis [Internet]. Vol. 25, Pathology & Oncology Research. 2019. p. 447–53. Available from: http://dx.doi.org/10.1007/s12253-019-00588-2

26. 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.

27. Karunagaran 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 [Internet]. Vol. 42, Journal of Histotechnology. 2019. p. 80–6. Available from: http://dx.doi.org/10.1080/01478885.2019.1594543

28. 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.

29. 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.

30. 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.

31. Dicato M, Plawny L, Diederich M. Anemia in cancer. Ann Oncol. 2010 Oct;21 Suppl 7:vii167–72.

32. Knight K, Wade S, Balducci L. Prevalence and outcomes of anemia in cancer: a systematic review of the literature [Internet]. Vol. 116, The American Journal of Medicine. 2004. p. 11–26. Available from: http://dx.doi.org/10.1016/j.amjmed.2003.12.008

33. Anumolu VNSH, Srikanth A, Paidi K. Evaluation of the relation between anemia and periodontitis by estimation of blood parameters: A cross-sectional study. J Indian Soc Periodontol. 2016 May;20(3):265–72.

34. Auerbach AD. Fanconi anemia. Dermatol Clin. 1995 Jan;13(1):41–9.

35. Caro JJ, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer: a systemic, quantitative review. Cancer. 2001 Jun 15;91(12):2214–21.

36. Caro JJ, Jaime Caro J, Salas M, Ward A, Goss G. Anemia as an independent prognostic factor for survival in patients with cancer [Internet]. Vol. 91, Cancer. 2001. p. 2214–21. Available from: http://dx.doi.org/10.1002/1097-0142(20010615)91:12<2214::aid-cncr1251>3.0.co;2-p

37. Tas F, Eralp Y, Basaran M, Sakar B, Alici S, Argon A, et al. Anemia in oncology practice: relation to diseases and their therapies. Am J Clin Oncol. 2002 Aug;25(4):371–9.

38. Quirt I, Robeson C, Lau CY, Kovacs M, Burdette-Radoux S, Dolan S, et al. Epoetin Alfa Therapy Increases Hemoglobin Levels and Improves Quality of Life in Patients With Cancer-Related Anemia Who Are Not Receiving Chemotherapy and Patients With Anemia Who Are Receiving Chemotherapy [Internet]. Vol. 19, Journal of Clinical Oncology. 2001. p. 4126–34. Available from: http://dx.doi.org/10.1200/jco.2001.19.21.4126

39. Bordoloi B, Tandon A, Jaiswal R, Srivastava A, Singh R, Shafique U. Demographic and clinicopathological profile of oral squamous cell carcinoma patients of North India: A retrospective institutional study [Internet]. Vol. 9, SRM Journal of Research in Dental Sciences. 2018. p. 114. Available from: http://dx.doi.org/10.4103/srmjrds.srmjrds_21_18

40. Haider RZAS. Hematological Presentation of Oral Squamous Cell Carcinoma Patients. EC Dental Science. 2019 Jan 29;18(2):321–5.

41. Osterborg A, Brandberg Y. Relationship between changes in hemoglobin level and quality of life during chemotherapy in anemic cancer patients receiving epoetin alfa therapy. Cancer. 2003 Jun 15;97(12):3125–6; author reply 3126–7.

42. Cella D. Factors influencing quality of life in cancer patients: anemia and fatigue. Semin Oncol. 1998 Jun;25(3 Suppl 7):43–6.

43. Brandberg Y. Relationship between anemia, fatigue, and quality of life in cancer patients [Internet]. Recombinant Human Erythropoietin (rhEPO) in Clinical Oncology. 2002. p. 173–84. Available from: http://dx.doi.org/10.1007/978-3-7091-7658-0_9