Science Publications

Universal Journal of Stomatology, 2022, 1, 554
www.scipublications.org/journal/index.php/ujs
DOI: 10.31586/ujs.2022.554

Research Article

Haematological Alterations among Patients with Oral and Dental Health Problems in the Tripoli Region

Azab Elsayed Azab [1,*], Hanan M. M. Aljefari [2]

[1] Department of Physiology, Faculty of Medicine, Sabratha University, Libya

[2] Department of Medical Engineering, Division of Genetic Engineering, Libyan Academy, Tripoli, Libya

[*] Correspondence: Azab Elsayed Azab (azabelsaied@yahoo.com)

Abstract: Background: Oral health plays an important role in maintaining life functions and quality of life**.** Gingivitis and periodontitis are two forms of periodontal disease that exist on a spectrum ranging from bleeding, erythematous, and inflamed gingival tissue to the loss of attachment and alveolar bone. Dental caries and periodontal diseases are the most common oral ailments and the major causes of tooth loss. **Objectives:** The study aimed to evaluate the haematological alterations among patients with oral and dental health problems in the Tripoli region. **Material and Methods:** The present study was conducted on 200 patients with oral and dental health problems attending six medical centers in Tripoli region from the 01st March 2022 to the 01st June 2022. Also, 100 healthy individuals without any oral and dental health problems or any other diseases were recruited as a control group. This study was approved by the Research and Ethical Committee of the Libyan Academy of graduate studies and medical centers. One ml of venous blood was withdrawn from each participant in the study for the determination of haematological parameters. The data were compared using SPSS Statistics for Windows, Version 26. **Results:** The results showed that red blood corpuscles (RBCs) count, hemoglobin concentration, hematocrit value, MCV, MCH, and MCHC in patients with oral and dental health problems were decreased significantly ($P<0.01$) compared to the control group. White blood cell count, neutrophils%, and platelets count in patients with oral and dental health problems were significantly ($P<0.01$) increased compared to the control group. On the other hand, lymphocytes% and mixed % WBCs were significantly ($P<0.01$) decreased compared to the control group. **Conclusion:** It can be concluded that oral and dental health problems were associated with a significant alterations in haematological parameters. Red blood corpuscles count, hemoglobin concentration, hematocrit value, MCV, MCH, MCHC, lymphocytes%, and mixed % WBCs were decreased significantly and White blood cell count, neutrophils%, and platelets count were significantly increased in patients with oral and dental health problems compared to the control group. Further studies are needed to confirm these results.

Keywords: Oral and dental health problems, Periodontitis, Dental caries, Haematological parameters, Tripoli Region

How to cite this paper:

Elsayed Azab, A., & Aljefari, H. M. M. (2022). Haematological Alterations among Patients with Oral and Dental Health Problems in the Tripoli Region. *Universal Journal of Stomatology*, *1*(1), 12–24. Retrieved from https://www.scipublications.com/journal/index.php/ujs/article/view/554

Received: November 4, 2022
Accepted: December 12, 2022
Published: December 14, 2022

1. Introduction

Periodontal disease is considered one of the most common oral diseases, constituting one of the main public health problems, where about 5 to 20% of the world population suffers from severe generalized periodontitis [1, 2]. Periodontitis results in loss of connective tissue and bone support [3] and is a leading cause of tooth loss around the world [3-5]. It has a multifactorial etiology, with several potential risk factors for the development of the disease, affecting mainly black individuals exposed to low socioeconomic or educational conditions, diabetes, obesity, and smoking [2, 6, 7]. Genetic,

dermatological, haematological, granulomatous, immunosuppressive, and neoplastic disorders can also have periodontal manifestations [3].

Gingivitis and periodontitis are two forms of periodontal disease that exist on a spectrum ranging from bleeding, erythematous, and inflamed gingival tissue to the loss of attachment and alveolar bone [5, 8, 9].

Caries is a polymicrobial disease that results from the breakdown of dental enamel by lactic acid that is created when cariogenic bacteria in the biofilm digest dietary fermentable carbohydrates [5].

Dental caries and periodontal diseases are the most common oral ailments and the major causes of tooth loss. With urbanization on the rise, increasingly westernized food intake [10, 11] and a lack of primary preventive measures in place, could see a rise in dental caries and related ailments. This could burden its already ailing healthcare system [11].

Periodontitis is a chronic insidious infectious disease of mixed bacterial origin and does impact the general health of the individual. Chronic infection has a known effect on the cytokine levels of the body which adversely affects erythropoiesis [12].

Anemia of chronic disease is a common health problem that occurs in patients with acute or chronic activation of immune system and production of inflammatory cytokines, so it is resembling periodontal diseases from this aspect [13].

1.1. Objectives

The study aimed to evaluate the haematological alterations among patients with oral and dental health problems in the Tripoli region.

2. Materials and Methods

The present cross-sectional study was carried out on 200 subjects with oral and dental health problems attending Six medical centers in Tripoli region from the 01st March 2022 to the 01st June 2022, and 100 healthy individuals with healthy gingival, aged from 15 to 80 years. Subjects were selected from among patients who were referred to the clinics of dentistry in the Tripoli region for periodontal treatment and for other dental health reasons.

Ethical approval and patient consent statements were taken from every patient. The study design was reviewed and approved by the Ethical Committee of the Libyan Academy of graduate studies and the medical centers. Oral health examination was carried out in the department of public health dentistry. All the clinical measurements were made using a manual periodontal probe (Williams' periodontal probe) on the gingival area adjacent to the teeth of each participant. The subjects were examined clinically for the presence of plaque, gingival bleeding, clinical attachment level, and probing pocket depth. The following indices were determined: DMFT (decayed, missing, and filled permanent teeth), DMFS (decayed, missing, and filled permanent surfaces), DEFT (decayed, extracted, and filled deciduous teeth), DEFS (decayed, extracted, and filled deciduous surfaces), GI (Gingival Index) [14] and PI (Plaque Index) [15], Deep grooves, and White spots were also recorded by the same dentist.

2.1. Blood sampling and determination of haematological parameters

A blood sample of 3 ml was drawn by venous puncture from each participant. The blood samples were collected in K, EDTA tubes for the haematological examinations. The haematological parameters (RBCs count, Hb, HCT, MCV, MCH, MCHC, WBCs count, differential count of WBCs, and Platelets count) were determined using an automated hematology analyzer Sysmex (K- 4500) machine.

2.2. Statistical Analysis

The data were analyzed using SPSS ver. 26. The Kolmogorov-Smirnov test was used to assess the normality of distribution of continuous variables. The statistical significance of differences between groups was evaluated with the independent t-test. A P-value of <0.05 was considered significant for all statistical test.

3. Results

3.1. Red blood corpuscles count and it indices in control and patients with oral and dental health problems.

Red blood corpuscles (RBCs) count and it indices in control and patients with oral and dental health problems are shown in Table 1 and figures (1-6). RBCs count, hemoglobin concentration, hematocrit value, MCV, MCH, and MCHC in patients with oral and dental health problems were decreased significantly ($P<0.01$), 4.07 ± 0.03, 11.47 ± 0.10, 34.03 ± 0.30, 83.46 ± 0.27, 28.16 ± 0.09 & 33.74 ± 0.07 compared to the control group, (4.72 ± 0.04, 14.42 ± 0.10, 39.82 ± 0.31, 84.45 ± 0.11, 30.59 ± 0.08 & 36.23 ± 0.06), respectively.

Table 1. Red blood corpuscles count and it indices in control and patients with oral and dental health problems.

Groups Parameters	Control Mean±SE	Patients with oral and dental health problems Mean±SE
RBCs (x10⁶//µL)	4.72 ± 0.04	4.07 ± 0.03**
Hb (g/dl)	14.42 ± 0.10	11.47 ± 0.10**
HCT (%)	39.82 ± 0.31	34.03 ± 0.30**
MCV (fL)	84.45 ± 0.11	83.46 ± 0.27**
MCH (pg/cell)	30.59 ± 0.08	28.16 ± 0.09**
MCHC (g/dl)	36.23 ± 0.06	33.74 ± 0.07**

: Significant at (P<0.01) when compared with control group.

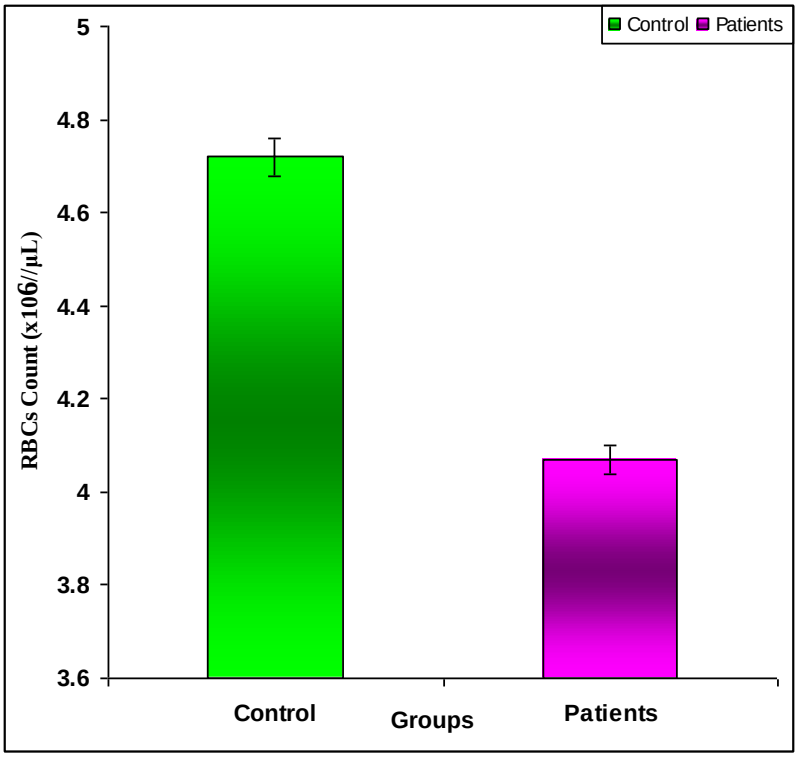

Figure 1. RBCs count in control and patients with oral and dental health problems

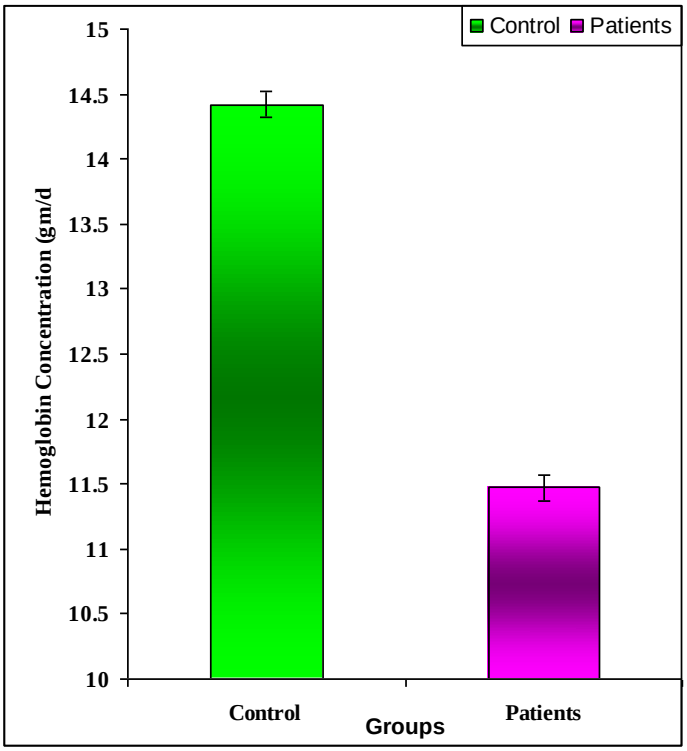

Figure 2. Hemoglobin concentration in control and patients with oral and dental health problems

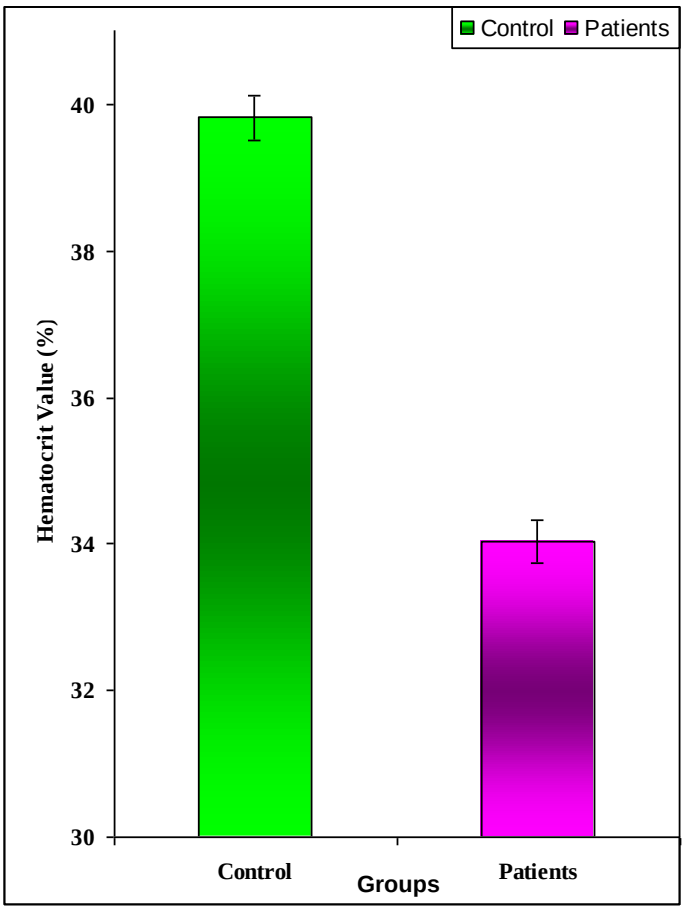

Figure 3. Hematocrit value in control and patients with oral and dental health problems

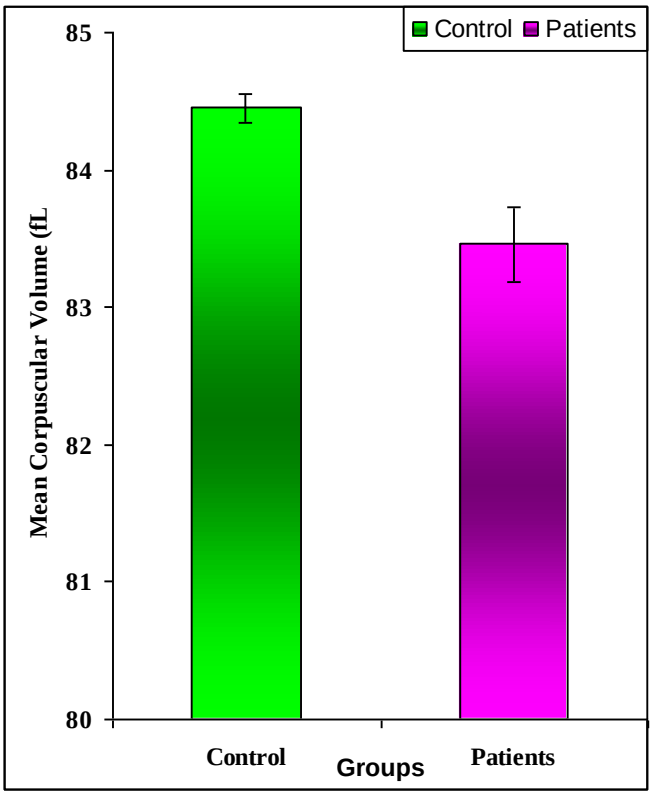

Figure 4. Mean corpuscular volume in control and patients with oral and dental health problems

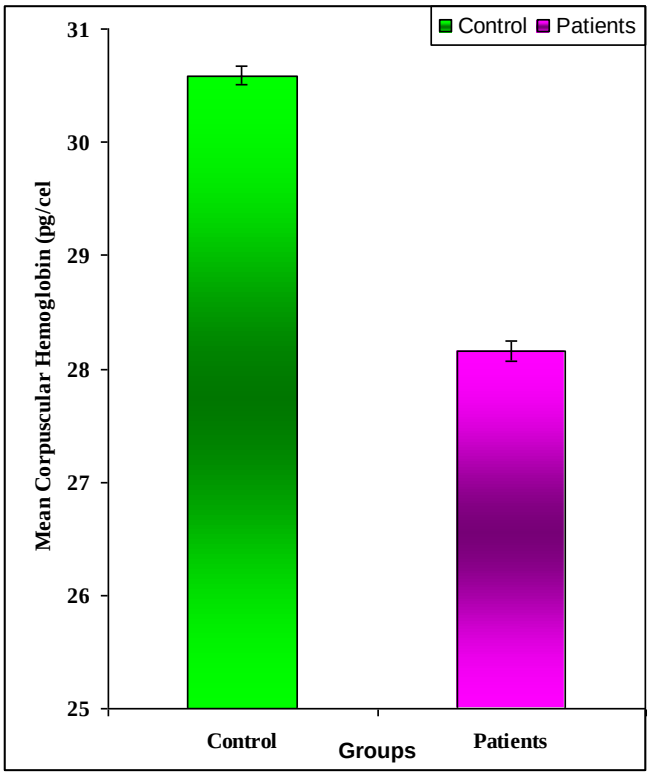

Figure 5. Mean corpuscular hemoglobin in control and patients with oral and dental health problems

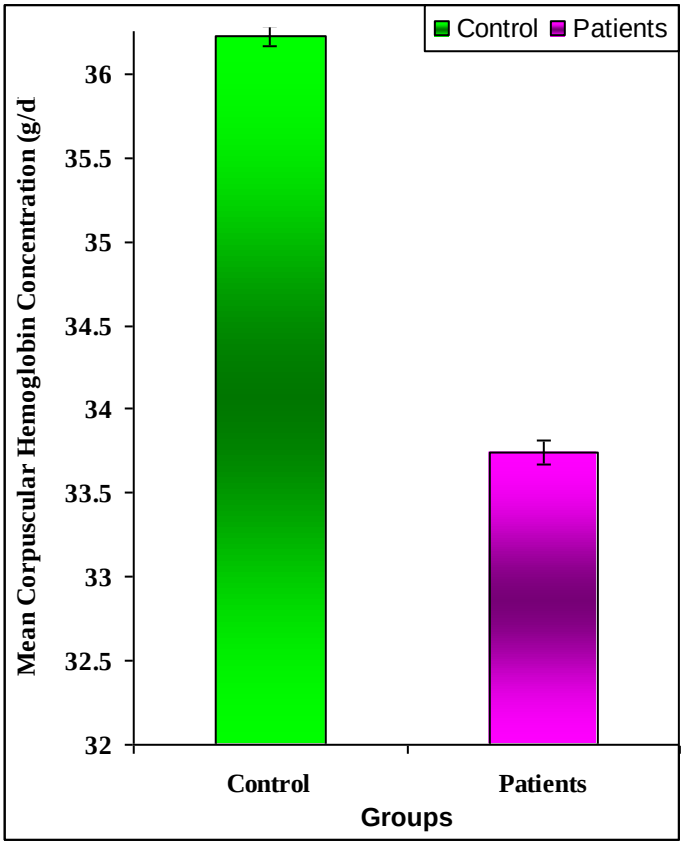

Figure 6. Mean corpuscular hemoglobin concentration in control and patients with oral and dental health problems

3.2. White blood cell count, neutrophils%, lymphocytes%, mixed%, and platelets count in control and patients with oral and dental health problems.

Data in Table 2 and figures (7-11) are shown White blood cell count, neutrophils%, lymphocytes%, mixed%, and platelets count in control and patients with oral and dental health problems. White blood cell count, neutrophils%, and platelets count in patients with oral and dental health problems were significantly ($P<0.01$) increased, 8.09 ± 0.10, 67.58 ± 0.41 & 306.8 ± 5.0 compared to the control group, (6.22 ± 0.12, 56.68 ± 0.56 & 261.7 ± 5.8), respectively. On the other hand, lymphocytes% and mixed% were significantly ($P<0.01$) decreased, 25.94 ± 0.39& 6.58 ± 0.20, compared to the control group, (35.74 ± 0.56& 7.59 ± 0.28), respectively.

Table 2. White blood cell count, neutrophils%, lymphocytes%, mixed%, and platelets count in control and patients with oral and dental health problems.

Groups		
Parameters	**Control Mean±SE**	**Patients with oral and dental health problems Mean±SE**
WBCs (x103//µL)	6.22 ± 0.12	8.09 ± 0.10**
Neutrophils %	56.68 ± 0.56	67.58 ± 0.41**
Lymphocytes %	35.74 ± 0.56	25.94 ± 0.39**
Mixed %	7.59 ± 0.28	6.58 ± 0.20**
PLTs (x103//µL)	261.7 ± 5.8	306.8 ± 5.0**

: Significant at (P<0.01) when compared with control group.

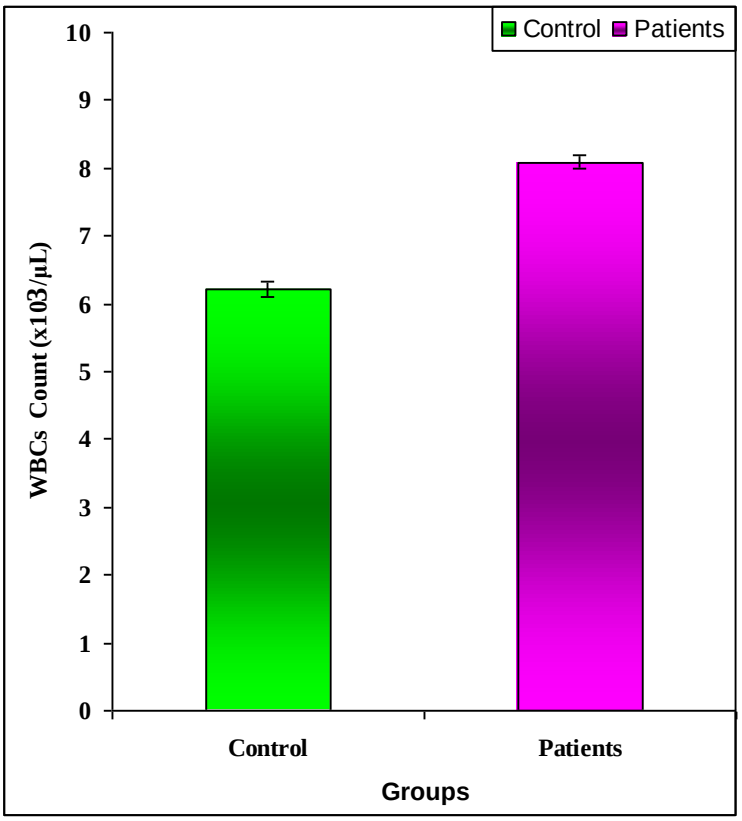

Figure 7. WBCs count in control and patients with oral and dental health problems

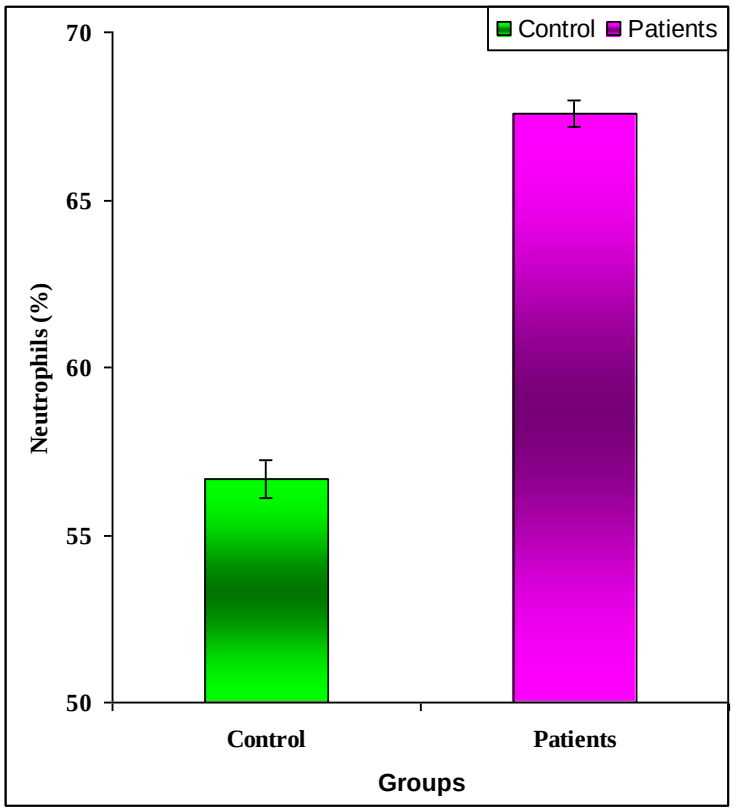

Figure 8. Neutrophils percentage in control and patients with oral and dental health problems

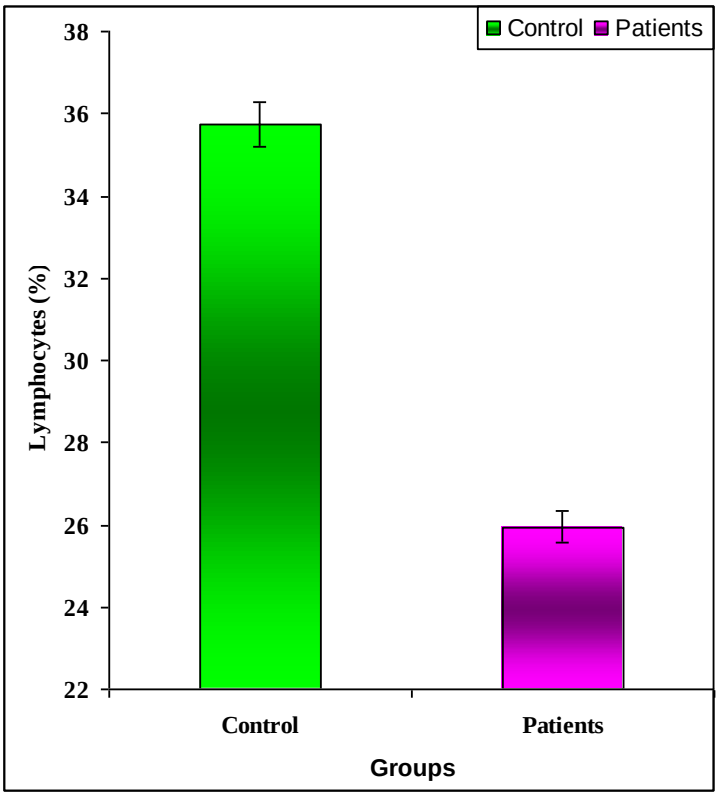

Figure 9. Lymphocytes percentage in control and patients with oral and dental health problems

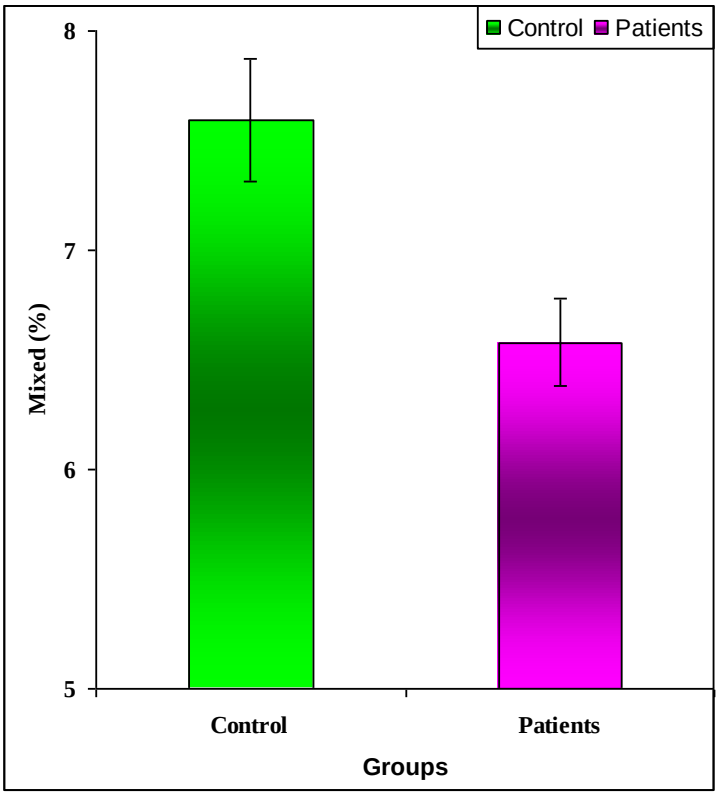

Figure 10. Mixed WBCs percentage in control and patients with oral and dental health problems

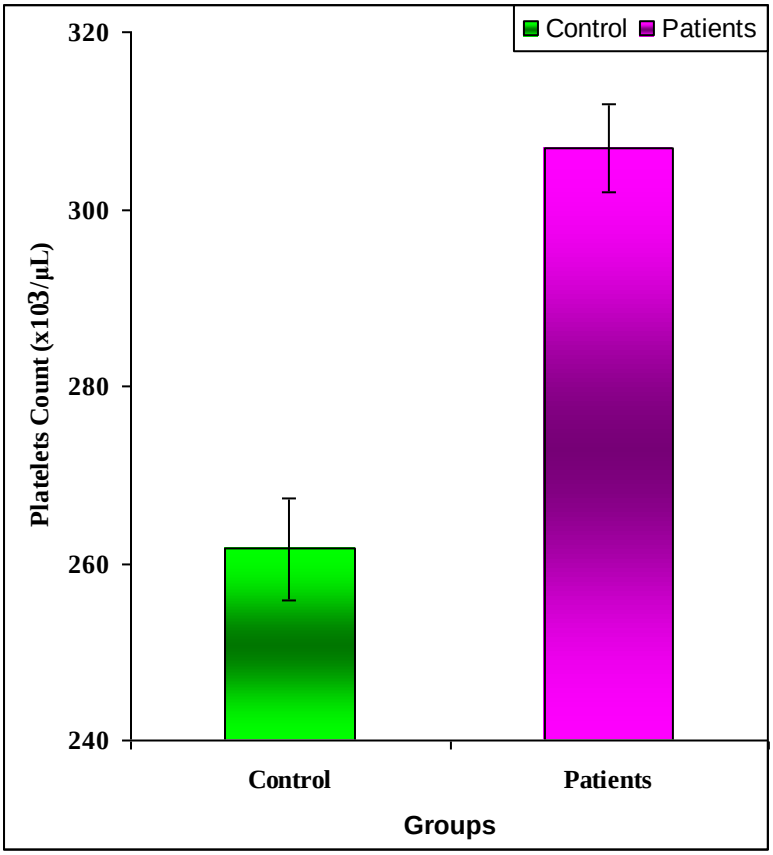

Figure 11. Platelets count in control and patients with oral and dental health problems

4. Discussion

The present study aimed to evaluate the haematological alterations in patients with oral and dental health problems in Tripoli region. Infections, malignant cells, and autoimmune dysregulation all lead to the activation of the immune system and production of inflammatory cytokines (TNF-α, IL-1, and IL-6) which can depress Epo production leading to the development of anemia [16, 17]. Periodontitis is a chronic insidious infectious disease of mixed bacterial origin and does impact the general health of the individual. Chronic infection has a known effect on the cytokine levels of the body which adversely affects erythropoiesis [12].

The results of the present study showed a significant ($P<0.01$) decrease in RBCs count, hemoglobin concentration, hematocrit value, MCV, MCH, and MCHC in patients with oral and dental health problems compared with the control group. These results run parallel with the study of Jenabian *et al.,* [18] who found that a reduction of MCV, MCH, Hb, and Hct in patients with a moderate chronic periodontitis. Several previous studies showed that a significant decrease in Hb and RBCs counts in periodontitis patients when compared to healthy controls [17, 19-26]. Also, Irhayyim, [13] found that a significant decreased in mean values of Hb, MCV, and MCH in patients with chronic periodontitis compared with the control group. These differences may be due to the periodontitis caused by specific types of microorganisms mainly gram negative, anaerobic bacteria with high percentage of spirochetes accumulate in gingival sulcus in the periodontal pocket [13, 27], the actual active sits of connective tissue loss showing have a high percentage of *P.gingivalis, Aggrigatibacter actinomycetemcomitans*, *Campylobacter rectus,* and etc [13, 28]. These microoganisms liberate toxic substances such as lipopolysaccharides, protease, collagenase and other that motivate the innate and adaptive immune system of the host [13,

29]. Antigen presenting cells such as B cells, macrophage, and dendritic cells begin to interact with T cells that lead to differentiation of plasma cells and produce of chronic lesion with beginning the signs and symptoms of inflammation [13, 30]. All these process lead to release of inflammatory cytokines in blood such as TNF-α, IL-6, IL-8 and other from various cells like macrophage, monocytes, and fibroblast. The liberation of these cytokines lead to bone and attachment loss and construes the pathogenesis of periodontal diseases [13, 31, 32].

Previously chronic inflammation or infection may be interpreting the underlying cause of anemia of chronic disease (ACD), and increase some of inflammatory cytokines such as TNF-α, IL-1 are observed in ACD. These cytokines lead to decrease the life span of RBC and impair erythroids development and reduce erythropoietin response to anemia and abnormality of iron store, in addition the increase production of inflammatory cytokines inhabit the maturation and differentiation of erythrocytes [13, 33-37] because the cytokines prevent release the erythropoietin from kidney [13, 18].

Periodontal disease is considered to be an inflammatory disorder that is related to the accumulation of oral microbial biofilm and the host response to this accumulation. The host reaction to gingival microorganisms is characterized in part by increase in the polymorph nuclear leukocyte counts, which is one of the most important steps in host defense. Exaggerated leukocytes and neutrophils of host response are a very important component in the pathogenesis of periodontal disease [25]. Wheeler *et al.*, [38] mentioned that infections increase WBCs and neutrophil counts, and these increases might be linking infections with systemic diseases, including cardiovascular diseases. Beydoun *et al.*, [39] reported that periodontal disease may be directly related to WBCs count and % neutrophils and inversely related to % lymphocytes.

Platelets play a crucial role in managing vascular integrity and regulating hemostasis, and they are involved in the fundamental biological process of chronic inflammation associated with disease pathology, thrombosis, and atherogenesis [40]. Li *et al.*, [41] and Schneider, [42] reported that platelet counts increase in cardiovascular diseases and vascular complications.

The current results showed a significant ($P<0.01$) increase in White blood cell count, neutrophils%, and platelets count and a significant ($P<0.01$) decrease in lymphocytes% and mixed% WBCs in patients with oral and dental health problems compared to the control group. Similar results were obtained by several previous studies that reported a significant increase in WBCs counts in periodontitis patients when compared with healthy controls [17, 23-26, 43-47]. Agnihotram *et al.*, [48] recorded a significant increase in WBCs, neutrophils, and plateletes count in periodontitis patients when compared with healthy subjects. Al-Rasheed [49] reported that a significant increase ($P<0.001$) in WBCs and platelet counts patients with chronic periodontitis compared with the control group. Ustaoglu *et al.*, *[46]* and Botelho *et al.*, *[47]* mentioned that the periodontitis group was found to have a significantlyt higher levels of WBCs and neutrophils count compared to the healthy control group. Also, Gustafsson and Asman [50] reported that a significant increase in peripheral polymorph nuclear leukocytes in periodontitis patients compared with the healthy controls.

The increases in WBC and neutrophil counts reflect the inflammatory response of the body to an infection with a periodontal cause. These could be the result of the enhanced response of total leukocyte and neutrophil counts in peripheral blood, which is in conformity with the basic function of leukocytes in infection and inflammation [25, 47, 51]. The gingival inflammation response is characterized by some dense inflammatory infiltrate rich in leukocytes, which could in turn be dumped into the systemic circulation [47, 52, 53, 54].

Periodontal bacteria could invade the periodontal tissues via the ulcerated epithelium and trigger a systemic response to counteract any harmful effect [47]. The local continuous inflammatory and bacterial interplay could stimulate the bone marrow to produce

chronically larger numbers of inflammatory cells [47, 55]. It is justified by the fact that in early stages of periodontitis, the rate of blood flow is increased due to vasodilation. But subsequently, there is a slowing and stasis of blood stream. With stasis, changes in normal axial flow of the blood in the microcirculation take place. The normal axial flow consists of a central stream of cells comprising leukocytes, and RBCs, and a peripheral cell-free layer of plasma close to the vessel wall. Due to stasis, the central stream of cells widens and the peripheral zone becomes narrower because of plasma loss by exudation. After this margination, the neutrophils of the central column come close to the vessel wall as a result of redistribution [37]. All consequences finally cause an increase in neutrophils and leukocytes [37, 56, 57].

The studies of Wakai *et al.*, [19], Nicu *et al.*, [58], Papapanagiotou *et al.*, [59], and Romandini *et al.*, [60] showed that a significant increase in platelets counts in periodontitis patients compared to healthy individuals and that periodontal treatment leads to decreased in platelets count [49, 61]. This higher platelet count may be explained due to dental plaque bacteria, including the periodontal pathogen *Porphyromonas gingivalis*, which induces platelet activation and aggregation [44, 46].

On the other hand, the study of Kumar *et al.*, [45] showed that non-significant changes in platelets count in chronic periodontitis patients when compared with the healthy group. Also, Ustaoglu *et al.*, *[46]* recorded that a none significant increase in platelet count in periodontitis patients compared to the control group.

5. Conclusion

It can be concluded that oral and dental health problems were associated with significant alterations in haematological parameters. Red blood corpuscles count, hemoglobin concentration, hematocrit value, MCV, MCH, MCHC, lymphocytes%, and mixed % WBCs were decreased significantly and White blood cell count, neutrophils%, and platelets count were significantly increased in patients with oral and dental health problems compared to the control group. Further studies are needed to confirm these results.

References

[1] Batista R. (2010). Study of the Association of Periodontal Conditions and the Thickening of the Carotid Intimal Complex. Federal University of Espirito Santo.

[2] Rosa, J. A. A., dos Santos Fernandez, M., Vieira, I. S., Madi, R. R., de Melo, C. M., & da Cunha Oliveira, C. C(2020). Detection of oral Entamoeba gingivalis and Trichomonas tenax in adult Quilombola population with periodontal disease.-OD-OVTOS-Int. J. Dental Sci., 22(2): 157-164.

[3] Pihlstrom BL, Michalowicz BS, and Johnson NW. (2005). Periodontal diseases. Lancet. 366(9499): 1809-1820.

[4] Alpert PT. (2017). Oral health: the oral-systemic health connection. Home Health Care Manag Pract., 29(1): 56-59.

[5] Kane SF. (2017). The effects of oral health on systemic health. Gen Dent., 65: 30-34.

[6] Mumghamba E. G., Markkanen H. A., and Honkala E. (1995). Risk factors for periodontal diseases in Ilala, Tanzania. J Clin Periodontol.. 22 (5): 347-354.

[7] Beck J. D. (1996). Periodontal implications: older adults. Annals of periodontal., 1 (1): 322-357.

[8] Jin LJ, Lamster IB, Greenspan JS, Pitts NC, Scully C, and Warnakulasuriya S. (2016). Global burden of oral diseases: emerging concepts, management and interplay with systemic health. Oral Dis., 22(7): 609-619.

[9] Petersen OE, and Ogawa H. (2005). Strengthening the prevention of periodontal disease: the WHO approach. J Periodontol., 76(12): 2187-2193.

[10] Huew R, Waterhouse P, Moynihan P, Kometa S, and Maguire A. (2012). Dental caries and its association with diet and dental erosion in Libyan schoolchildren. Int J Paediatr Dent., 22: 68-76.

[11] Peeran, S. W., Altaher, O. B., Peeran, S. A., Alsaid, F. M., Mugrabi, M. H., Ahmed, A. M., and Grain, A. (2014). Oral health in Libya: addressing the future challenges. Libyan J Med., 9(23564): 1- 7.

[12] Parihar S, Sharma NK, Bhatnagar A, Kishore D, Parihar AV, and Rahman F. (2019). Comparison of hematological parameters for signs of anemia among participants with and without chronic periodontitis: A cross-sectional study. J Indian Assoc Public Health Dent., 17(1): 4-7..

[13] Irhayyim NS. (2020). Evaluation of Some Blood Parameters in Anemic Patients in Relation to Periodontal Condition. Indian J Forens Med Toxicol., 14(1): 734-740.

[14] Loe H, and Silness J. (1963). Periodontal disease in pregnancy (I). Prevalence and severity. Acta Odontol Scand, 21:551-553.

[15] Silness J, and Loe H. (1964). Periodontal disease in pregnancy (II). Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 24:747-759.

[16] Pradeep AR, and Anuj S. (2011). Anemia of chronic disease and chronic periodontitis: Does periodontal therapy have an effect on anemic status? J Periodontol., 82: 388 394.

[17] Anumolu VN, Srikanth A, and Paidi K. (2016). Evaluation of the relation between anemia and periodontitis by estimation of blood parameters: A cross-sectional study. J Indian Soc Periodontol., 20: 265-672.

[18] Jenabian N, Sattari FD, Salar N, Bijani A, and Ghasemi N. (2013). The relation between periodontitis and anemia associated parameters. J Dentomaxill Radiol Pathol Surg., 2(3):26-33.

[19] Wakai, K., Kawamura, T., Umemura, O., Hara, Y., Machida, J. I., Anno, T., and Ohno, Y. (1999). Associations of medical status and physical fitness with periodontal disease. J Clin Periodontol., 26(10): 664-672.

[20] Hutter JW, van der Velden U, Varoufaki A, Huffels RA, Hoek FJ, and Loos BG. (2001). Lower numbers of erythrocytes and lower levels of hemoglobin in periodontitis patients compared to control subjects. J Clin Periodontol., 28: 930 936.

[21] Kowolik MJ, Dowsett SA, Rodriguez J, De La Rosa RM, and Eckert GJ. (2001). Systemic neutrophil response resulting from dental plaque accumulation. J Periodontol., 72: 146 151.

[22] Loos BG. (2005). Systemic markers of inflammation in periodontitis. J Periodontol., 76 (11 Suppl): 2106 2115.

[23] Gokhale SR, Sumanth S, and Padhye AM. (2010). Evaluation of blood parameters in patients with chronic periodontitis for signs of anemia. J Periodontol., 81:1202 1206.

[24] Yamamoto T, Tsuneishi M, Furuta M, Ekuni D, Morita M, and Hirata Y. (2011). Relationship between decrease of erythrocyte count and progression of periodontal disease in a rural Japanese population. J Periodontol., 82:106–113.

[25] Pejcic A, Kesic L, Pesic Z, Mirkovic D, and Stojanovic M. (2011). White blood cell count in different stages of chronic periodontitis. Acta Clin Croat., 50:159 167.

[26] Ali S. (2012). The correlation between hemoglobin level and generalized moderate chronic periodontitis. Oral Maxillofac Surg Periodontol., 24: 85 88.

[27] Silva, N., Dutzan, N., Hernandez, M., Dezerega, A., Rivera, O., Aguillon, J. C., ... & Gamonal, J. (2008). Characterization of progressive periodontal lesions in chronic periodontitis patients: levels of chemokines, cytokines, matrix metalloproteinase-13, periodontal pathogens and inflammatory cells. J Clin Periodontol., 35(3): 206-214.

[28] Loomer, P. M. (2004). Microbiological diagnosis testing in the treatment of periodontal disease. J periodontal 2000., 34(1): 49-56.

[29] Graves D. (2008). Cytokines that promote periodontal tissues destruction. J, periodontal., 79:1585-1591.

[30] Gemmell, E., and Seymour, G. J. (2004). Immunoregulatory control of Th1/Th2 cytokine profiles in periodontal disease. J Periodontol 2000, 35(1): 21-41.

[31] Aljohani HA. (2010). Association between hemoglobin level and severity of chronic periodontitis. JKAU: Med SCI., 17(1): 53-64.

[32] Klokkevold PR, Newman MG, and Takei HH. (2015). Carranza's clinical periodontology. Elsevier Saunders,12th edition.

[33] Means JR. (2003). Recent developments in the anemia of chronic disease. Current Hematol Report., 2(2): 116-121.

[34] Havemose-Poulsen, A., Westergaard, J., Stoltze, K., Skjødt, H., Danneskiold-Samsøe, B., Locht, H., and Holmstrup, P. (2006). Periodontal and hematological characteristics associated with aggressive periodontitis, juvenile idiopathic arthritis, and rheumatoid arthritis. Journal of periodontology, 77(2), 280-288.

[35] Matsumura, I., and Kanakura, Y. (2008). Pathogenesis of anemia of chronic disease. Nihon Rinsho. Japanese J Clinical Med., 66(3): 535-539.

[36] Preshaw PM, and Taylor JJ. (2012). Periodontal pathogenesis. In Newman MG, Takaei HH, Klokkevold PR, Carranzas FA, editor. Carranzas clinical periodontology,11th ed. Pliladephia Sanders Elseviers: PP. 194-216.

[37] Kolte RA, Kolte AP, and Deshpande NM. (2014). Assessment and comparison of anemia of chronic disease in healthy subjects and chronic periodontitis patients: A clinical and hematological study. J Indian Soc Periodontol., 18: 183 186.

[38] Wheeler JG, Mussolino ME, Gillum RF, and Danesh J. (2004). Associations between differential leucocyte count and incident coronary heart disease: 1764 incident cases from seven prospective studies of 30,374 individuals. Eur Heart J., 25(15): 1287-1292.

[39] Beydoun, H. A., Hossain, S., Beydoun, M. A., Weiss, J., Zonderman, A. B., and Eid, S. M. (2020). Periodontal disease, sleep duration, and white blood cell markers in the 2009 to 2014 National Health and Nutrition Examination Surveys. J periodontol., 91(5): 582-595

[40] Thomas MR, and Storey RF. (2015). The role of platelets in inflammation. Thromb Haemost., 114(3): 449-458.

[41] Li N, Hu H, Lindqvist M, Wikstr̨om-Jonsson E, Goodall AH, and Hjemdahl P. (2000). Platelet-leukocyte cross talk in whole blood. Arterioscler Thromb Vasc Biol., 20(12): 2702-2708.

[42] Schneider DJ. (2009). Factors contributing to increased platelet reactivity in people with diabetes. Diabetes Care., 32(4): 525-527.

[43] Shi, D., Meng, H., Xu, L., Zhang, L., Chen, Z., Feng, X., Lu, R., Sun, X., and Ren, X. (2008). Systemic inflammation markers in patients with aggressive periodontitis: a pilot study. J. Periodontol. 79 (12): 2340–2346.

[44] Monteiro, A.M., Jardini, M.A., Alves, S., Giampaoli, V., Aubin, E.C., Neto, A.M., and Gidlund, M. (2009). Cardiovascular disease parameters in periodontitis. J. Periodontol. 80 (3): 378–388.

[45] Kumar, B. P., Khaitan, T., Ramaswamy, P., Sreenivasulu, P., Uday, G., and Velugubantla, R. G. (2014). Association of chronic periodontitis with white blood cell and platelet count–A case control study. J Clin Exp Dent., 6(3): e214-217.
[46] Ustaoglu, G., Erdal, E., and İnanır, M. (2020). Does periodontitis affect mean platelet volume (MPV) and plateletcrit (PCT) levels in healthy adults?. Rev Assoc Med Brasileira, 66: 133-138.
[47] Botelho, J., Machado, V., Hussain, S. B., Zehra, S. A., Proença, L., Orlandi, M., and D'Aiuto, F. (2021). Periodontitis and circulating blood cell profiles: a systematic review and meta-analysis. Exper Hematol., 93: 1-13.
[48] Agnihotram, G., Singh, T. R., Pamidimarri, G., Jacob, L., and Rani, S.. (2010). Study of clinical parameters in chronic periodontitis. Int J Appl Biol Pharm Technol., 1: 1202–1207.
[49] Al-Rasheed, A. (2012). Elevation of white blood cells and platelet counts in patients having chronic periodontitis. Saudi Dent J., 24(1): 17-21.
[50] Gustafsson, A., and Asman, B., (1996). Increased release of free oxygen radicals from peripheral neutrophils in adult periodontitis after Fc delta-receptor stimulation. J. Clin. Periodontol., 23 (1): 38–44.
[51] Rudin SR. (2003). Laboratory tests and their significance in Walter Hall. Crit Decs Periodontol., 8:4-6.
[52] Ryder MI. (2010). Comparison of neutrophil functions in aggressive and chronic periodontitis. Periodontol 2000., 53: 124–137.
[53] Aboodi GM, Goldberg MB, and Glogauer M. (2011). Refractory periodontitis population characterized by a hyperactive oral neutrophil phenotype. J Periodontol., 82: 726–733.
[54] Hirschfeld J. (2014). Dynamic interactions of neutrophils and biofilms. J Oral Microbiol., 6:1-10.
[55] Belkaid Y, and Hand TW. (2014). Role of the microbiota in immunity and inflammation. Cell., 157:121-141.
[56] Nibali L, D'Aiuto F, Griffiths G, Patel K, Suvan J, and Tonetti MS. (2007). Severe periodontitis is associated with systemic inflammation and a dysmetabolic status: A case control study. J Clin Periodontol., 34: 931–937.
[57] Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, and De Nardin E. (2001). Periodontal infections contribute to elevated systemic C-eactive protein level. J Periodontol., 72: 1221–1227.
[58] Nicu EA, Van der Velden U, Nieuwland R, Everts V, and Loos BG. (2009). Elevated platelet and leukocyte response to oral bacteria in periodontitis. J Thromb Haemost., 7(1):162-170.
[59] Papapanagiotou, D., Nicu, E., Bizzarro, S., Gerdes, V., Meijers, J., Nieuwland, R., van der Velden, U., and Loos, B.G. (2009). Periodontitis is associated with platelet activation. Atherosclerosis, 202 (2): 605–611.
[60] Romandini M, Lafor A, Romandini P, Baima G, and Cordaro M. (2018). Periodontitis and platelet count: a new potential link with cardiovascular and other systemic inflammatory diseases. J Clin Periodontol., 45:1299–1310.
[61] Christan, C., Dietrich, T., Ha gewald, S., Kage, A., and Bernimoulin, J., (2002). White blood cell count in generalized aggressive periodontitis after non-surgical therapy. J. Clin. Periodontol., 29 (3): 201–206.