Doctoral School of Medicine

RESEARCH ON PERIODONTAL PATHOLOGY IN PATIENTS WITH DIABETES MELLITUS

SUMMARY

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CONTENT

JUSTIFICATION FOR TOPIC CHOICE

I have chosen this topic based on the hypothesis that periodontal tissue can be the site of a series of diseases that pose a particular problem because of the influence they can have on the systemic pathology.It has been scientifically proven that the clinical course of the disease may be influenced by genetic factors, which could also result in increased susceptibility to infection even if inflammatory periodontal disease is induced by plaque bacteria. Chronic inflammatory burden has been considered as a plausible biological process linking periodontal disease to systemic disorders, but the link between general and periodontal diseases has not been definitively elucidated. Diabetes clearly heightens the risk of periodontal disease, and plausible biological mechanisms have been abundantly demonstrated.Less clear is the impact of periodontal disease on the glycaemic control of diabetes and the mechanisms by which it occurs. It is possible that periodontal diseases may serve as initiators or propagators of insulin resistance in a similar way to obesity, thus worsening glycemic control. Certainly, further studies are needed to clarify this aspect of the relationship between periodontal disease and diabetes.

INTRODUCTION

Periodontal disease is currently the most common chronic inflammatory disease. Periodontitis has a multifactorial pathogenesis, and it occurs because of the interaction between bacterial and environmental factors, as well as the immunological and genetic ones. Host response plays the central role in the pathogenesis of periodontitis despite the need for bacterial stimulation necessary for the onset of periodontal disease.(1,2)

The response to periodontal pathogens is determined by the nature and control of both the innate and acquired immune response. In recent decades, studies in the literature have linked the periodontal disease to an increased risk of systemic complications. Periodontal infections and diabetes are closely associated and widespread. Obesity and insulin resistance may also play a role in this relationship.Inflammation is a critical player in the association, and its importance is just coming to light. Diabetes clearly increases the risk of periodontal disease, and plausible biological mechanisms have been abundantly demonstrated. Less clear is the impact of periodontal disease on glycaemic control of diabetes and the mechanisms by which it occurs. It is possible that periodontal diseases may serve as initiators or propagators of insulin resistance in a similar way to obesity, thus worsening glycemic control. Further research is needed to clarify this aspect of the relationship between periodontal disease and diabetes.(4)

In this paper we have tried to highlight the periodontal disease-diabetes relationship.The relationship between periodontal disease and diabetes has been studied since the 1920s - 1930s, when it was revealed that periodontal disease can be induced by diabetes through specific changes in the gum tissue produced under its influence.In severe periodontal disease diabetes mellitus is an important risk factor.

1. DENTAL CARIES

1.1 Ethiopatogenic factors

Studies in the literature support the idea that the etiopathogenic factors involved in dental caries are multiple, and they must act simultaneously to trigger the onset of the caries process.(1)

1.2 The microbial ecosystem of plaque and the dental caries

Miller added dental caries to the category of bacteria-dependent conditions.(3,4,5)

1.3 Pathogenicity of bacterial plaque

The main contributory factor to tooth decay is bacterial plaque, and its action consists of:

- the accumulation of a large number of micro-organisms, mostly acidogenic, on a small surface area;
- the ability of these microorganisms to ferment a wide range of carbohydrates, in particular *Streptococcus mutans*, thereby rapidly and massively producing a significant amount of acid*;*
- the ability to produce acid even in the absence of a substantial intake of carbohydrates from the diet by using levan;
- maintaining the pH of the bacterial plaque below the critical threshold of 5.5 for a long time.(16-25)

2. PERIODOTAL DISEASE

2.1 Definition and prevalence

Periodontitis is considered to be the most prevalent inflammatory disease worldwide, affecting nearly 50% of the adult population and 60% of the elderly population.(27)

Latest US epidemiological data confirm high prevalence of periodontitis in over 47% of adults. It is assumed that 7-13% of the adult population will develop severe forms of the disease. It is currently estimated that severe periodontitis affects 5-20% of any population and

mild to moderate periodontitis is a problem of most adults. The generalised form of severe periodontitis is thought to affect 10% of the population.(28,29)

2.2 Etiopathogenesis

The pathogenesis of periodontitis is multifactorial, resulting from a complex interaction between bacterial accumulation in the subgingival biofilm, host immune response, genetic and environmental factors. Host response has been shown to be a key factor in the clinical expression of periodontitis, 20% of which is due to bacterial variation, 50% is attributed to genetic variation and more than 20% to tobacco users, stress, and other systemic diseases.(34)

2.3Anatomopathological classification of periodontal disease

2.3.1 Initial stage

It is characterized by acute exudative changes, without being clinically evident, and has a duration of 2-4 days. It represents an acute and irreversible inflammatory response to periodontopathogenic bacteria, translated by dilation of the gingival vessels and the appearance of exudate, containing IgG, complement, fibrin and PMN antibodies. (79,80)

2.3.2 Stage of onset or early lesions

It is characterized by the predominance of T lymphocytes, when the disease becomes clinically manifest, over a period of 4-7 days. Activated monocytes and macrophages secrete pro-inflammatory cytokines such as IL-1, TNF, IL-4 and IL-6 that induce lymphocyte proliferation, and T helper 1 lymphocytes secrete TNF-α, TNF-β and TNF-γ. B lymphocytes and plasma cells secrete antibodies. The course of the disease is determined at this stage, when the local immune response can effectively produce healing.(80-86)

2.3.3 The stage of settled of developed lesions

It appears at 2-3 weeks, and it is characterized by the predominance of plasma cells, which synthesize IgG antibodies. T-lymphocytes proliferate within deep tissue, with alveolar bone damage and bone resorption occurring.(80-86)

2.3.4 Destructive stage of advanced lesions

It is characterized by the destruction of the gingival epithelium and bone matrix, which determines the depth of the periodontal pocket. The lymphocytic and macrophage infiltrate extends apically, with large amounts of cytokines produced, especially TNF-α and IL-1. (79-87)

3. DIABETES MELLITUS

3.1 Definition

Diabetes mellitus through the presence of chronic hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. Several pathogenic processes are involved in the development of diabetes.(101,102,103,104)

3.2 Epidemiology

Type 1 diabetes is among the most common chronic diseases found in childhood. According to the American Diabetes Association, this form is present in 5-10% of patients with diabetes. Peak incidence occurs during puberty, around age 10-12 in girls and age 12-14 in boys. The incidence of type 1 diabetes has increased worldwide in the last decades of the 20th century. Since 1950, a linear increase has been noticed in Scandinavia, the UK, and the US.

Estimations referring to diabetes for 2019 show an increasing prevalence according to age. Similar trends are projected for 2030 and 2045. (105,106)

4. ORAL HEALTH AND DIABETES

Diabetes adversely affects all the soft and hard tissues surrounding the teeth. Compared to their peers without diabetes, people with diabetes, especially those with sub-optimal glucose control, have more oral consequences. Severity of diabetes and severity of periodontitis are associated. The final result of untreated periodontal disease is tooth loss. The absence or mobility of teeth causes both social and psychological distress and poses quality of life issues on patients. (118,119)

4.1 Periodontal disease and diabetes mellitus

Studies show that the oral health of diabetic patients with poor control can worsen faster than in other patients and that they do not respond effectively to conventional therapy. (122,123)

4.2 The effects of diabetes on the periodontium

Although some authors found no significant association between diabetes and gingival

inflammation, the prevalence and severity of gingivitis was found to be higher in people with diabetes. These studies suggest that the presence of diabetes is often, but not always, associated with increased gum inflammation. In addition, the level of glycemic control may play a role in the gingival response to plaque in people with diabetes. (125)

4.3 Mechanisms by which diabetes can influence periodontal disease

Although bacteria are required for periodontal disease, there are few differences in the subgingival microflora between diabetic and non-diabetic patients with periodontitis, although some early studies reported higher proportions of Capnocytophaga species in those with diabetes. The apparent lack of significant differences between potential pathogens suggests that alterations in the host immunoinflammatory response may have a major influence on the increased prevalence and severity of periodontal destruction seen in diabetes. (120,121,122,123)

4.4 Mechanisms by which periodontal disease can influence diabetes

Studies suggest that patients with periodontitis, particularly those colonized by gram-negative organisms such as P. gingivalis, Tannerella forsythensis and Prevotella intermedia, have significant serum markers of inflammation such as C-reactive protein (CRP), IL-6 and fibrinogen as compared to subjects without periodontitis. Systemic dissemination of these organisms or their products may induce bacteremia or endotoxemia, prompting an elevated inflammatory state and stimulating increased levels of serum inflammatory markers. (137,138)

5. THE IMPORTANCE OF RADIOLOGICAL EXAMINATION IN THE DIAGNOSIS OF PERIODONTAL DISEASES

Following the clinical examination of the cephalic extremity and of the oral cavity, the doctor establishes the presumptive diagnosis, which may become a diagnosis of certainty after complementary X-ray examinations have been carried out.Panoramic radiography or orthopantomography is one of the complementary methods of choice in the complementary diagnosis of any disease of the stomatognathic system. (149,150)

Examination of the image on a correctly performed panoramic radiograph involves highlighting features that fall outside the normal range and may be considered pathological.

6. THE INFLUENCE OF BIOCHEMICAL MEDIATORS IN PARODOTAL INFLAMMATION

Within the immune system, cytokines such as interleukins (ILs), interferons (IFNs) and tumor necrosis factor (TNF) play a key role as signaling proteins that mediate innate and acquired immune responses. Aberrant cytokine expression or dysregulation of cytokine activity has been associated with the development of an impressive variety of human diseases. The main cytokines identified in periodontal disease include interleukin IL-1, IL-1β, IL-6, IL-8, IL-10 and TNF, which influence the activity of other cells in the immune response. (167,168,169)

6.1.1 Interleukin (IL)1β

In periodontal disease, IL-1 is one of the most active stimulators of osteoclastic activity. Proinflammatory cytokines, such as interleukin-1β, play an important role in the initiation and regulation of immune responses in periodontium. It has been proven that IL-1 can stimulate bone resorption and has therefore been implicated in the pathogenesis of inflammation-induced bone resorption. (172,173,174,175)

6.1.2 Inteleukin (IL) 4

In periodontal tissue, lack of IL-4 can cause macrophage accumulation, increased expression of CD14 and increased production of IL-1β, TNF-α and prostaglandin E2 (PGE2) in monocytes, resulting in bone resorption. (176,177,178)

6.1.3 Interleukin (IL) 6

Several studies have showed dramatically increase of IL-6 levels in inflammatory periodontal lesions, and this IL is also considered to be a useful indicator or diagnostic marker for advanced periodontitis. Increased IL-6 levels in peripheral blood are most likely due to increased local IL-6 production in inflamed tissue in periodontitis patients, which supports that IL-6 values in gingival fluid can serve as a reference for diagnosing disease activity or progression of periodontal lesions. (179,180,181)

6.1.4 Interleukin (IL) 8

IL-8 expression is increased in affected periodontal tissues and studies show that a high level of IL-8 has been detected in the crevicular fluid of patients with periodontitis. (182,183,184)

6.1.5 Interleukin (IL) 10

Interleukin 10 is an anti-inflammatory cytokine, known as an inhibitory factor of cytokine synthesis. IL-10 expression is minimal in unstimulated tissues and appears to require stimulation by endo- and exotoxins. (184,185)

6.1.6 Tumor necrosis factor alfa (TNF-α)

The latest studies demonstrate that TNF plays an important role in mediating polysaccharide-induced bone loss. IL-1 and TNF inhibitors applied in combination significantly reduce osteoclast activity and bacterial-induced bone loss in periodontal disease. (197,198,199)

7. LOCAL AND SYSTEMIC TREATMENT IN PERIODONTITIS

Periodontal disease requires appropriate treatment due to its complex nature.The earlier it is applied, in the early stages of the disease, the greater the chance of success. The treatment must include multiple procedures characteristic to the disease process, and it must aim to promote progress towards healing.

Once started, the treatment should be carried out at regular intervals, without interruptions that may slow the progress towards healing.

Simple removal of local factors is insufficient and results in an apparent clinical cure. Microulcer removal by biostimulation procedures should complement mechanical treatment.Treatment must be complex and complete, carried out multiprocedurally and must be more diversified the more advanced the disease is.

The general health of the periodontal patient also influences the treatment of periodontal disease and must be considered. Consultation and collaboration with the specialist doctor is therefore mandatory.

The main condition for success towards improvement or cure is that the treatment must be individualised for each case. (202,203)

PERSONAL RESEARCH

1. Working hypothesis

The working hypothesis for the present research was based on the clinical observation that patients with diabetes present characteristic odonto periodontal pathologies. The general objective of the thesis was based on this finding, and we set out to study markers of chronic inflammation in patients with periodontal disease. We were also interested in highlighting these changes in the course of periodontal disease.

The current research is founded on the premise that acute and chronic diseases originating in the marginal periodontium pose a particular problem in the general pathology of the entire human body.The clinical progression of periodontal disease may be influenced by genetically acquired factors leading to modified susceptibility to infection, even if plaque-induced inflammatory periodontal disease is caused by bacteria.

Diabetes can have a negative effect on the incidence and progression of periodontal disease, and in the diabetes-periodontal equation we can see a reciprocity.

Subsequent purposes:

- obtaining data on dental pathology;
- obtaining epidemiological data on periodontal disease;
- assessment of the severity of periodontal disease at different stages;
- comparison of plasma marker concentrations at different stages of periodontal disease;
- correlations between plasma markers and clinical indicators related to periodontal disease progression;

2. Study material

The study material used in the present research to assess the influence of diabetes mellitus on periodontal pathology comprises two distinct groups of patients. A total of 420 people were enrolled in the study, divided into two groups as follows:

1. A group of 210 subjects, presenting with periodontal pathology and diabetes mellitus, who presented to the dental clinic ambulatory and the University Dental Centre between March 2018 and August 2020;
2. The second group is the control group, also consisting of 210 subjects with periodontal pathology but without diabetes mellitus.

A series of inclusion and exclusion criteria were developed for inclusion in the study.

2.1.Structure of the research group

The research group, composed of 210 subjects, can be structured according to a number of criteria as follows:

a) according to age: (subjects are aged 26-65)

- age groups 26-30 years: 10 subjects – 5%
  31-40 years: 25 subjects – 12%
  41-50 years: 58 subjects – 28%
  51-60 years: 76 subjects – 36%
  61-65 years: 41 subjects – 16%

b) according to gender: 105 men – 50%
105 women – 50%

2.2 Structure of control group

The control group, composed of 210 subjects, can be structured according to several criteria as follows:

a) according to age: (subjects are aged 26-65 ani)

- age groups - 26-30 years: 8 subjects – 4%
  - 31-40 years: 33 subjects – 16%
  - 41-50 years: 49 subjects – 23%
  - 51-60 years: 80 subjects –38%
  - 61-65 years: 40 subjects – 19%

b) according to gender: 105 men – 50%
105 women – 50%

The previously presented batch structure was applied in the first 3 research studies. For study 4 of this thesis, we used a research group of 33 subjects with dental disease and diabetes and a homogeneous control group of 33 subjects with dental disease but without diabetes. Subjects included in this study met the inclusion and exclusion criteria applied in the other studies. We also applied the distribution of subjects by age group similar to previous studies. All subjects were well informed and gave their consent for inclusion in this study.

3. Working methodology

The working methodology includes the identification of periodontal pathology in patients with diabetes. The subjects of our study were analysed in the clinical context and assessed using specific methodologies which include the analysis of their oral health status.

3.1 Research methods used in the study

The research methods that were applied in the current study and will be described in the following pages are:

1. symptoms and syndromes questionnaire
2. clinical examination of the oral cavity
3. radiological examination on orthopantomography
4. determination of plasma cytokine concentration
5. statistical processing of the obtained data

STUDY 1: IDENTIFICATION OF POTENTIAL RISK FACTORS IN THE ONSET AND PROGRESSION OF PERIODONTAL PATHOLOGY

Introduction

Periodontitis is a multifactorial disease influenced by various risk factors. Old age causes functional changes in the immune system, increasing susceptibility to chronic disease. Gender, lifestyle, and environmental factors are associated with the development and progression of periodontal disease. The influence of these risk factors on periodontal disease is a research concern, as the progression and treatment of periodontal disease may be influenced by the presence of these factors.

Work hypothesis

The aim of this study is to obtain demographic data from the subjects included in the study as well as data on certain risk factors that may determine the progression of periodontal disease.

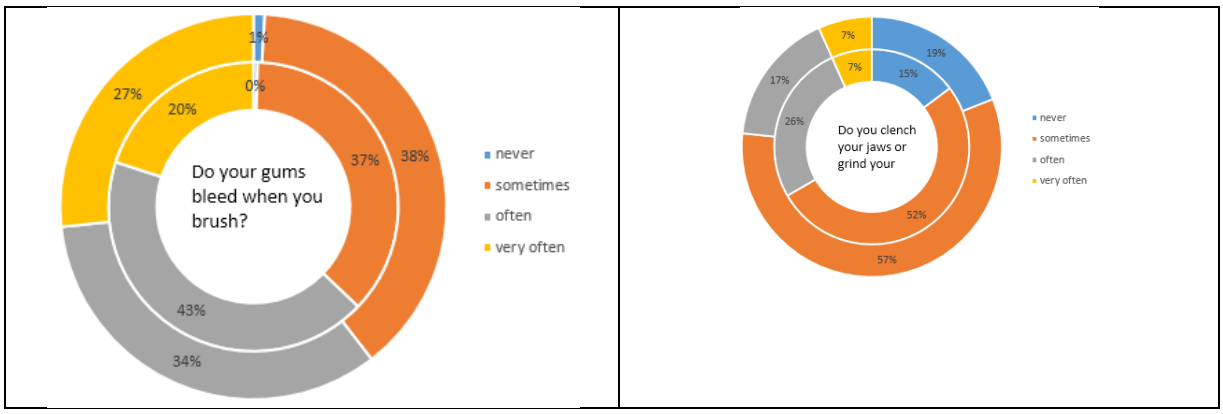
This study started from the idea that it may be possible to slow down the progression of periodontal disease by early implementation of prophylaxis after identification of possible risk factors.

Material and method

A group of 210 subjects with periodontal pathology who presented to the dental surgery and the University Dental Centre between March 2018 and August 2019 was studied;
All patients were informed about the conduct of the study and gave their consent for inclusion.

Results

Following the statistical processing of the data collected after the application of the questionnaire, we obtained results that are statistically significant. This working method is described in detail in chapter "*3.1.1 Method of applying the symptoms and syndromes questionnaire*" and presented in Annex 1. The interpretation of this method may have a certain degree of subjectivity because it depends to a large extent on the willingness and attention with which the subjects taken in the study answered the questions in the questionnaire. SPSS (Statistical Program for Social Science) version 25 was used for the statistical processing, which is described in detail in chapter "*3.1.6 Statistical data processing method*". The questionnaire used in the study was divided into two sets of questions. The first set of questions (I 1-48) refers to general data on the health status of the 210 subjects included in the study and the second set of questions in the questionnaire (II 1-21) refers to data on the oral and dental health status of the subjects included in the study. The obtained results are presented in the following charts:



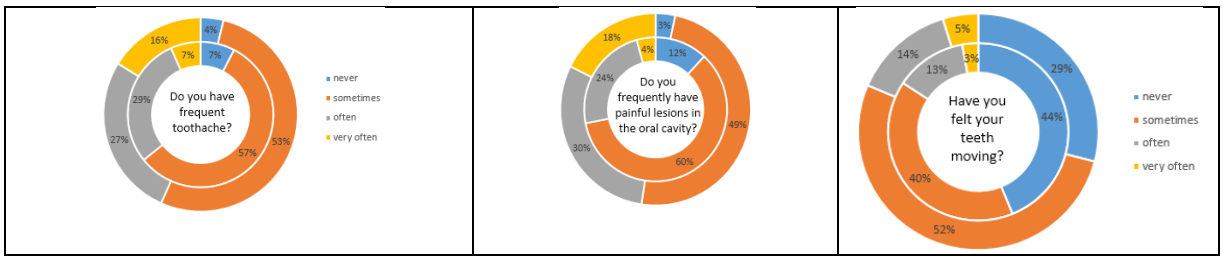


Figure no 1-Data analysis of oral health by answering questions II 1-6 (group C or research group, group M or control group)

The data analysis revealed that gingival bleeding is "Often" present in about half of the subjects of the research group and only "Sometimes" present in patients of the control group.Also, more than half of the subjects in the research group say that they "Sometimes" have jaw clenching compared to fewer patients in group M who say the same. Dental pain is present "sometimes" in more than half of the subjects in the research group and in the control group. Similar results were obtained for the presence of painful lesions in the oral cavity, where a higher percentage of subjects in the research group said they "sometimes" had painful lesions in the oral cavity.

It is interesting to note that more than half of the subjects of the research group declare that they have tooth mobility compared to less than half of the subjects of the control group who declare this.

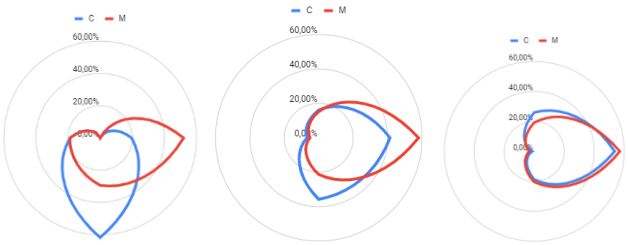


Figure no. 2- Data analysis of oral health by answering questions II 6-8 (group C or research group, group M or control group)

Analysis of these data shows that patients in both groups have approximately the same degree of oral hygiene and use oral hygiene aids extremely rarely.

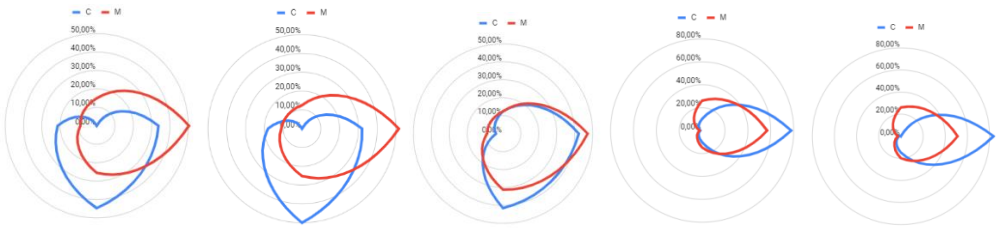


Figure no.3 - Data analysis of oral health by answering questions II 9-13 (group C or research group, group M or control group)

We can conclude from the data analysis that the addressability to dental services is low, the results being similar for both the control group and the research group. None of the patients in either group had undergone dental or periodontal treatment in the previous 12 months, which was also an *exclusion criterion* from the study. The vast majority of patients in both the control and witness group claim to have had no orthodontic treatment and no sore spots on the facial skin.

Most patients in the research group had prolonged bleeding after dental extractions or other surgery.Patients in both groups say they only go to the dentist when pain occurs. 73.81% of the patients in the research group consider that their dental problems have worsened in recent years compared to 57.62% of the patients in the control group who consider that their dental problems have not worsened.

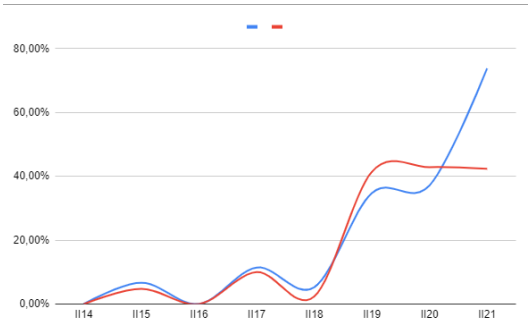


Figure no. 4 – Graphical analysis of oral health data by answering questions II 14-21 (group C or research group, group M or control group)

4.5 Discuţii

Studies in the literature have shown that certain dental conditions can be associated with the presence of diabetes and support the idea that periodontal disease is the main cause of tooth loss in patients with diabetic disease.(70)

In this study we try to highlight the importance of knowing the general status and the importance of the existence of local risk factors (mucobacterial plaque, tartar, bone resorption) that can determine or influence both the activity of diabetes mellitus and the activity of periodontal pathology.

It is important to point out that most of the subjects in the research group show changes in smell and taste, compared to the control group of subjects with periodontal disease but without diabetes mellitus where the vast majority do not show altered taste and smell. This finding is similar to that demonstrated by Gibson et al. where he observed that 20.7%

patients with altered taste but was not in line with the study by Quirino et al. where 36.5% patients displayed the symptom.

Xerostomia is frequently present in diabetes mellitus, it is also present in most of the subjects in the research group who have very low saliva quantity, sensation of dry mouth or throat and irritated throat, which explains the increased frequency of dental caries. This finding was similar to Ship's studies, who demonstrated that diabetics had low salivary flow, but this finding was at contradictory to the studies of Quirino et al. (68.6%) where they demonstrated an increased incidence of hyposalivation in diabetics, while Miralles et al. suggested that there was no difference in salivary flow between diabetics and healthy subjects.

Compared to the control group without diabetes, the subjects of the research group report that they are sometimes anxious, restless, nervous and have moments of depression, difficulty concentrating, forgetfulness, and lack of energy, symptoms that affect their quality of life and decrease their work performance.In most patients with diabetes, dental problems have worsened in recent years, and they often have bleeding gums and painful lesions in the oral cavity. As for dental mobility, it is present in a higher percentage in subjects with diabetes compared to those without diabetic disease, which is also supported by literature data.(75)

4.6 Conclusions

From this study we can conclude that the addressability to dental services is low, the results being similar in both the control group and the research group, as the patients admitted they only go to the dentist when pain occurs. It was found that patients in both groups have approximately the same degree of oral hygiene and use oral hygiene products extremely rarely.Diabetic patients develop symptoms that affect their quality of life, and regular visits to the dental office for checkups can prevent oral cavity complications from developing.The dental practitioner has the duty and responsibility to know the patient and the complications of diabetes, as well as to provide a complete and comprehensive treatment. Poor hygiene leads to the development of bacterial flora forming supra- and subgingival plaque and promoting the development of dental calculus. In the oral environment, the association of local irritations with bacterial plaque and the imbalances produced by diabetic disease intervene in the progression of periodontal disease and carious pathology. Research in this area should be encouraged.

STUDY 2 - THE IMPORTANCE OF CLINICAL AND RADIOLOGICAL PARAMETERS AS INDICATORS IN THE APPEARANCE AND PROGRESSION OF PERIODONTAL DISEASE

Introduction

In order to establish a complete and comprehensive diagnosis, the subjects were clinically examined in a specialist dental clinic. During the clinical examination we followed general criteria but also specific evaluation criteria which were recorded in a dental examination form customized to the present study. The number on the examination form corresponds to the questionnaire number and refers to the same patient so that, when the data obtained are processed statistically, appropriate correlations can be made.

Working hypothesis

The aim of this study is to establish a complete and comprehensive diagnosis. Establishing prophylaxis and slowing the progression of periodontal disease can be achieved by identifying possible risk factors.

Material and method

The patient groups described numerically and structurally in study 1 were used for the present study. The same study inclusion and exclusion criteria were followed, all patients were informed and gave their consent for inclusion in the study.Panoramic radiographs were taken of all subjects who are the subject of the study material in the current research. These X-rays were taken with the same machine so that they could be compared with each other. All patients gave their consent for inclusion in the study.

Results

To present the results of the data analysis, indicators of central tendency such as mean (mean), standard deviation (SD), median (median), interquartile range (25th - 75th percentiles), minimum value (min) and maximum value (max) were used for quantitative data and number of cases and percentages for qualitative data. For the comparative analysis of the two groups (control group - C and witness group - M) the Student T test or Mann-Whitney U test were used for the quantitative variables, respectively the Chi-Square or Fischer tests for the qualitative variables. Excel and SPSS software tools were used for data preprocessing and

analysis, and following statistical processing of the collected data, after clinical and radiological examination of the subjects, we obtained results that are statistically significant.

We obtained statistical differences between the two groups of subjects in terms of gingival bleeding, the presence of bacterial plaque and tartar in the frontal and molar group, both in the cervical third, middle third and incisally or occlusally. The clinical variables described above are missing in more than half of the witness group, whereas in the control group very few subjects were identified as not having these risk factors for periodontal damage. The subjects of the research group show a much higher percentage of gingival recession and tooth mobility in both the frontal and lateral groups. The clinical examination shows a grade 2 to 3 mobility in the research group compared to the control group where no subject shows grade 3 mobility, the vast majority showing grade 1 dental mobility. The analysis of the data on the number of periodontal pockets and their depth revealed statistically significant differences between the two studied groups.

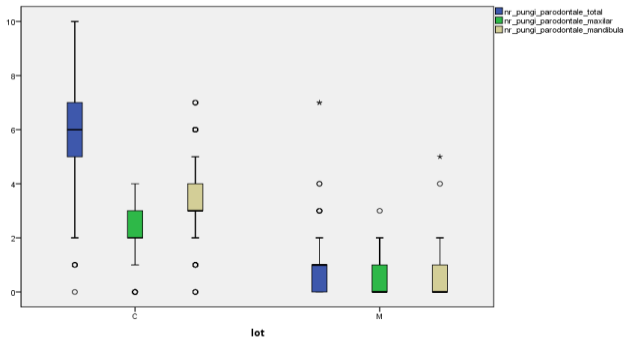


Figure no. 5 - Graphical analysis of the variable "number of periodontal pockets total, maxillary and mandibular" for the two groups (group C or research group, group M or control group)

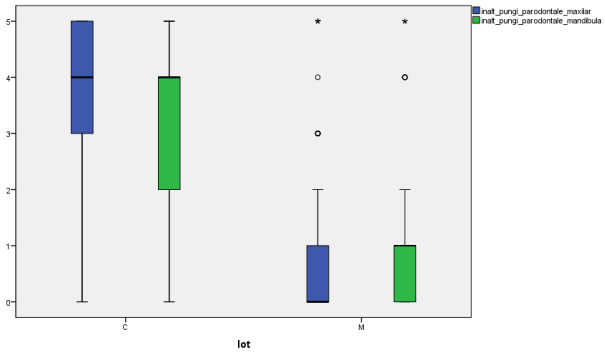


Figure no. 6– Graphical analysis of the variable „depth pungi of periodontal pockets maxillary and mandibular" for the two groups (group C or research group, group M or control group)

Following the statistical analysis of the mandibular bone thickness data, statistically significant changes were detected in the 36th, 46th and midline molars respectively (19.18±7.15 lot C vs. 30.04±10.47 lot M, right; 23.45±9.46 lot C vs. 29.65±10.60 lot M left; 18.96±5.72 lot C vs. 31.97±9.76 lot M midline). (p=0.000) We also observed that jawbone thickness at the level of the first molar on both the left and right sides is significantly lower in

the research group compared to the control group (st: 8.98±4.32 vs. 16.63±4.48, p=0.000, dr: 9.50±3.18 vs. 18.48±2.83, p=0.000). Changes are also observed in the nasal spine where the maxillary bone is significantly lower in the research group compared to the control group. (p=0.000)

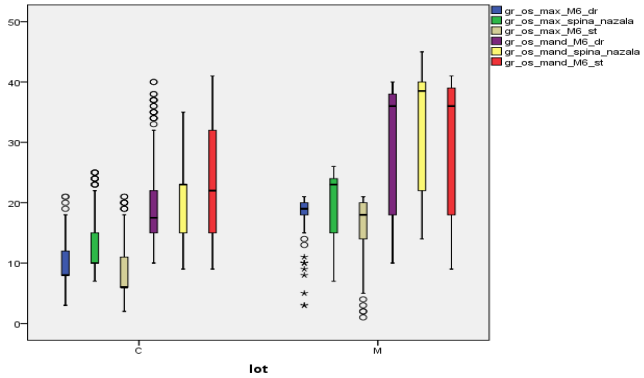


Figure no. 7- Graphical analysis of the variable "maxillary and mandibular bone thickness M6 left, right as well as at the level of the nasal spine and midline" for the two groups (group C or group to be investigated, group M or control group

In the study we also obtained statistically insignificant differences in the number of treated and untreated carious processes, number of coronal fillings, classes of maxillary and mandibular edentulousness prosthetic and non-prosthetic.

Figure no. 8- Descriptive analysis of the variable "edentulousness class, maxilla and mandible" for the two groups (group C or research group, group M or control group)

Discussions

In the present study we tried to highlight the effects of diabetes on oral health, based on the idea that periodontal disease is a complication of diabetes caused by the presence of general factors, but also local factors, in particular the presence of bacterial plaque. We took into account clinical and radiological indicators, and we focused on periodontal parameters that showed certain peculiarities, much more aggressive in patients diagnosed with diabetes

and periodontal disease compared to the group of subjects with periodontal disease but without diabetes.

The factors favouring the development of periodontal disease in patients with diabetes are mainly the presence of bacterial plaque and dental calculus. Gingival bleeding is the first clinical sign assessing the extent of gum inflammation.In the present study, we found statistically significant differences between the two groups in the presence of risk factors for periodontal disease, namely gingival inflammation, evidenced by the presence of gingival bleeding, mucobacterial plaque and tartar, both in the cervical third, middle third and incisally or occlusally in the lateral teeth.They also showed increased attachment loss, with high values of gingival recession size and frequency. Most subjects in the research group had deep periodontal pockets, diffuse bone resorption and resorption of interdental septa both frontally and laterally. This explains the increased dental mobility present in the patients of the study group, the majority of whom had grade 2, 3 mobility. It is observed that bone damage is much more pronounced in the subjects of the research group compared to the control group. The subjects of the research group show marked mobility, deep periodontal pockets and marked diffuse bone resorption compared to the control group where patients' lack of dental mobility at the molar level was evident in more than half of the control group, and 92.86% of the subjects of the control group do not show resorption of interdental septa.

Conclusions

We can conclude that subjects with diabetes have a lower interest in maintaining oral health, present risk factors for periodontal disease (gingival inflammation, plaque-mucobacterial, tartar) both in the incisor group and in the molars in a much higher percentage compared to the control group, thus explaining the local bone damage, much more pronounced in this group.

STUDY 3 - CORRELATIONS BETWEEN THE RESULTS OBTAINED BY THE QUESTIONNAIRE METHOD AND THE CLINICO-RADIOLOGICAL EXAMINATION

Introduction

To establish a complete and comprehensive diagnosis, the subjects were clinically examined in a specialist dental clinic. During the clinical examination we followed general criteria but also specific evaluation criteria which were recorded in a dental examination form individualized to the present study. The number on the examination form corresponds to the

questionnaire number and refers to the same patient so that, when the data obtained are processed statistically, appropriate correlations can be made.

6.2 Working hypothesis

In order to carry out the present study, we have chosen to make correlations between the answers with the most significant results obtained from the questionnaire applied in study 1 and the clinical and radiological variables assessed in study 2, with the most statistically significant results.

Material and method

The material used in the present study, in order to make correlations between the results obtained in the questionnaire application method and the method of clinical and radiological evaluation of the oral cavity, includes the groups of patients that were also involved in the two studies mentioned above.To carry out the statistical correlations in this study, we used the SPSS (Statistical Program for Social Science) software, version 25.0, which provides facilities for both data analysis and graphical representation, as described in detail in chapter "*3.1.6 Statistical Data Analysis*".

Results analysis

The statistical analysis of the correlation between the two variables, gingival bleeding, and health status, shows that of those who consider their current health status to be very good or good, in the case of the control group, more than half of them have gingival bleeding to the touch or spontaneous bleeding. Those who consider their current state of health to be bad are only patients from the control group and more than half of them have spontaneous gingival bleeding.

The statistical correlation between health status and bacterial plaque in the incisors showed that in the research group the vast majority of subjects (73.9%) had mucobacterial plaque in the cervical third. 13% of the subjects of the control group had muco bacterial plaque at the middle and incisal third. Of those who consider themselves to be in good health half of the research group have mucobacterial plaque.

The statistical correlation of the two variables, health status and molar tartar level, shows that within the research group those who consider their current health status to be very good, 21.7% have dental calculus in both the cervical and middle third and only 8.7% are free of molar tartar. Also, following the statistical correlation of the degree of dental mobility at the

incisor level and the health status in the research group, those who consider that they have a very good or good current health status show degree 2 mobility at the incisor level compared to the subjects of the control group have a very good or good health status, they do not show dental mobility at the incisor level. Of the research group subjects who considered they have a bad state of health, most showed grade 3 mobility at the level of the incisiors.

The control group subjects who claim to have a good state of health had a mean periodontal pocket depth at molar probing of 4.06±1.39 standard deviation. In terms of gingival retraction, there are significant differences between the two groups at both molar and incisor level: the control group shows an average gingival retraction of 2.30 mm at incisor level and 2.04 mm at molar level, while the witness group shows an average gingival retraction of 0.73 mm at incisor level and 0.58 mm at molar level.

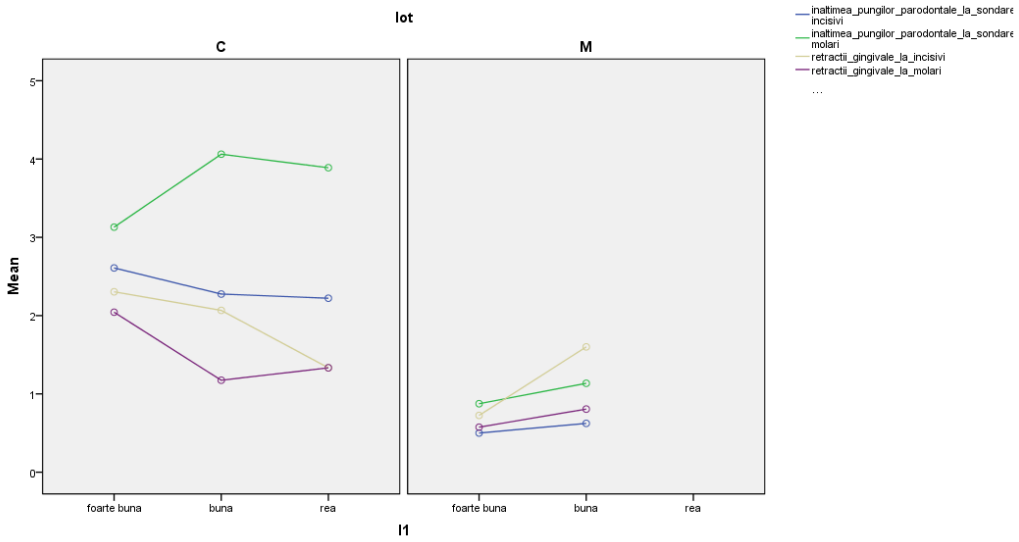


Figure no 9 – Graphical analysis of periodontal pocket depth when probing at incisor and molar level correlated with health status and gingival recession at incisor and molar level correlated with health status for the two groups (group C or research group, group M or control group)

We obtained a significant positive correlation between the degree of tooth mobility in incisors and molars and changes in odour (i6 - Do you feel that things don't smell the same anymore?).Also a significant positive correlation was observed between the degree of dental mobility in incisors, molars, mucobacterial plaque, tartar in molars and moments of depression, impatience / agitation (i28, i29). Likewise, there is a direct correlation between the degree of mobility in incisors and the degree of mobility in molars, respectively between tartar in incisors and mucobacterial plaque in incisors, tartar in molars and bacterial plaque in molars.

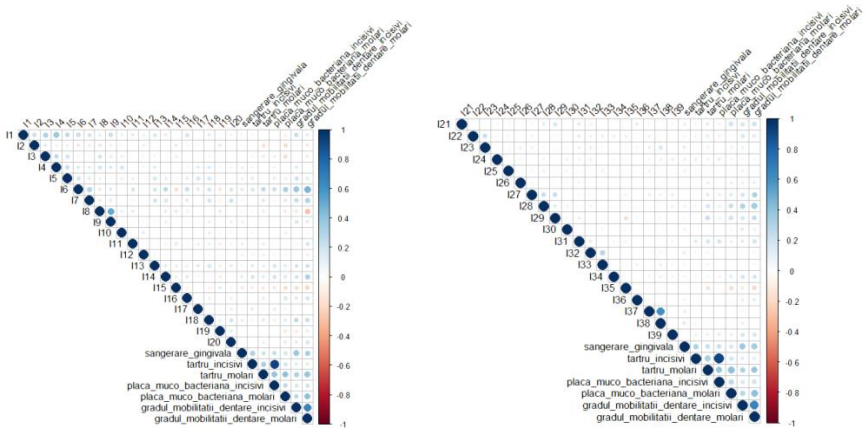


Figure no 10 – Graphical analysis of the correlation between general health variables (i1-i20; i21-i39) and actual oral-dental variables

A significant positive correlation was observed between the practice of going to the family doctor or dentist for check-ups and the level of tartar and mucobacterial plaque in molars and the degree of dental mobility in incisors and molars.

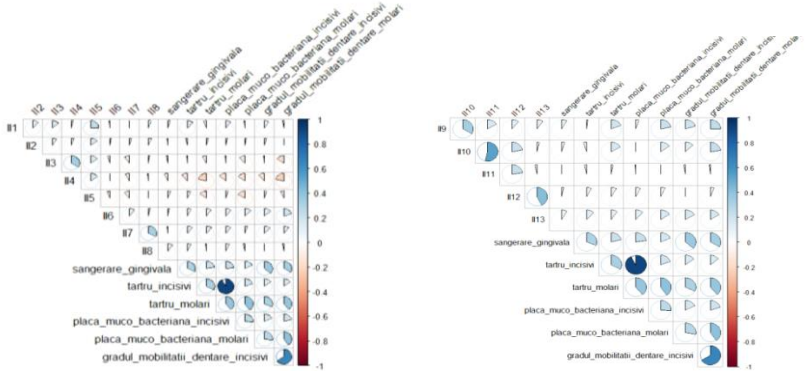


Figure no 11 –Graphical analysis of the correlation between variables related to oro-dental health status (II2-II8 and II9-II13) and variables related to actual oro-dental status

Discussions

Diabetes mellitus is one of the major chronic health problems facing the world today and the most common endocrine and metabolic disorder. It ranks 7th among the leading causes of death. Studies show that 50% of diabetic patients are usually undiagnosed. The incidence seems to be rising rapidly these days, and the ratio of patients with type I to type II diabetes is 1:3. It has been shown that several oral manifestations occur in diabetic patients.

In our study, following the correlation between health status and clinical variables, we found that among those within the control group who consider their current health status to be very good or good, more than half have spontaneous or upon touch gingival bleeding, as well as bacterial plaque in the incisors up to the cervical third and in the molars up to the middle

third. These patients also have tartar up to the level of the middle third in both incisors and molars. Plaque and tartar are risk factors that can influence the progression of periodontal disease.

Our study highlights the degree of dental mobility at the incisor level according to the state of health as follows: 87% of the research group of those who consider that they have a very good current state of health show degree 2 mobility at the incisor level compared to the subjects of the control group where 70% of those who consider that they have a very good state of health and do not show dental mobility at the incisor level.60.7% of the subjects of the research group who consider themselves to be in good health have a degree 2 mobility in the incisors compared to the subjects of the control group who consider themselves to be in good health, where 37.1% have no mobility in the incisor group. In the case of the subjects of the research group who consider that they have a bad health, 77.8% present drage 3 mobility at the level of incisors. The study also highlights the height of the periodontal pockets and gingival recession according to the assessment of the health status evaluated at the time of the questionnaire, as follows: the subjects of the control group who claim to have a good current health status have a higher average height of the periodontal pockets at the survey compared to the control group as well as a more pronounced gingival recession. The study shows a significant positive correlation between the practice of going to the family doctor or dentist for check-ups and the level of tartar and mucobacterial plaque in molars and the degree of tooth mobility in incisors and molars.

6.6 Conclusions

The present study concludes that the subjects of the research group, subjects with diabetes mellitus and periodontal disease, although they consider themselves to be in very good health, show much more pronounced periodontal pathology compared to the control group, consisting of subjects with periodontal disease but without diabetes mellitus.

Decision trees were used to analyse which are the main discriminating factors between the two groups. In the context of considering all variables in both questionnaires, the following discriminating factors were identified: sinus mucosal inflammation, bone resorption, degree of dental mobility in molars, nasal spinal bone thickness, resorption of interdental septa. Thus, a large proportion of the control patients have inflammation of the sinus mucosa and asymmetric bone resorption and nasal spine bone thickness below 39 mm, while a large proportion of the control patients have no inflammation of the sinus mucosa and the degree of dental mobility in molars is below grade 3.

STUDY 4- THE IMPORTANCE OF IMMUNOLOGICAL MARKERS ANALYSIS IN THE PROGRESSION OF PERIODONTAL PATHOLOGY

Introduction

Extensive research in recent decades has demonstrated that cytokines play important roles in tissue homeostasis. In addition, it has been shown that increased cytokine production can lead to disease and tissue destruction. Of further interest is that cytokines play important roles in inflammatory responses and are also prominent regulators of tissue homeostasis.Monitoring cytokine expression in inflamed periodontal tissues could be an objective way of assessing periodontal disease activity.

Working hypothesis

The working hypothesis for this study had as starting point the clinicat observation that diabetic patients may present a series of specific periodontal conditions. Early diagnosis and treatment can be achieved by identifying plasma immunological markers in periodontal disease, depending on the stage of the disease. To avoid complications, the diagnosis of periodontal disease must be established in the early stages in patients with diabetes, with the aim of developing prophylactic measures or even early initiation of therapy.

Material and method

A group of 66 subjects with periodontal pathology who presented to the dental surgery and the University Dental Centre between March 2019 and August 2020 was studied. We investigated the evaluation of clinical indicators characteristic of generalized periodontal disease as well as the evaluation of immunological markers IL1β, IL4, IL8 and TNFα. To verify the accuracy of some hypotheses, statistical interferences in this study, we used SPSS software (Statistical Program for Social Science), version 25.0, as this program provides facilities for both data analysis and graphical representation.All patients gave their consent for inclusion in the study.

Results analysis

We have made the distribution by environment of origin, and it appears that of the total number of subjects 48.5% come from rural areas and 51.5% from urban areas. The distribution of the groups is thus homogeneous and without statistically significant differences

(p> 0.005). Of the 66 subjects included in the study, 33 are female subjects and 33 are male subjects. The gender distribution between subjects with periodontal disease and diabetes mellitus and subjects with periodontal disease but without diabetes mellitus does not differ significantly, which is why differences obtained in the assessment of clinical indicators cannot be attributed to differences between the two genders. Analysis of the age of the subjects shows that the average age is about 53 years with a minimum age of 33 years and a maximum age of 66 years. The distribution by age group shows that 42.4% of the subjects are patients over 61 years of age. The 41-50 age group comprises 24.2% of the total number of subjects, and the 51-60 and 30-40 age groups comprise a similar percentage of subjects, respectively 18.2% for the 51-60 age group and 15.2% for the 30-40 age category.

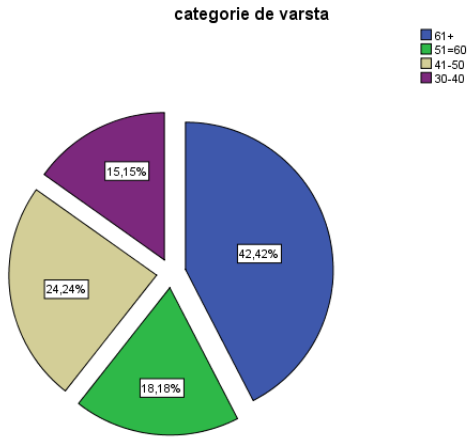


Figure no.12- Distribution of subjects according to age

Statistical analysis of the data on the distribution of patients by stage of disease shows that 36.4% of the subjects in the study have an early stage of periodontal disease, 30.3% have a moderate stage, and 28.8% of the subjects have an advanced stage of periodontal disease. Only 4.5% of all subjects included in the study have good oral hygiene and are considered healthy patients.

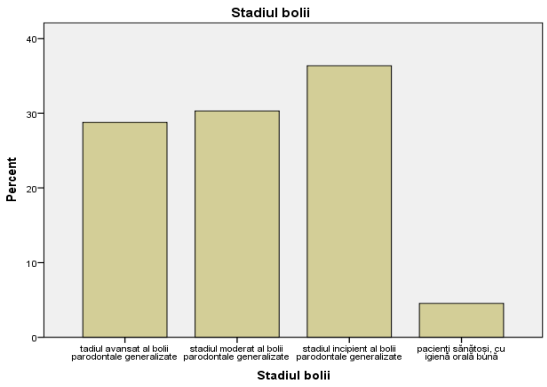


Figure no 13- Distribution of subjects according to disease stage

We applied independent samples t-tests in the study and obtained statistically significant differences between the two groups for all clinical variables included in the study and for the analyzed immunological markers.We obtained changes in immunological markers according to the stage of periodontal disease. Highly statistically significant differences between incipient and moderate disease stage are shown for interleukin 1β.Also, in the level of interleukin 4 it is observed that the mean values are lower in the early stage than in the moderate stage (p=0.000).We also observed highly statistically significant differences in interleukin 8 and TNFα levels between the two stages of generalized periodontal disease. For both early-stage interleukin 8 and early stage TNFα the mean values are lower than for moderate stage. (p=0.000)

Table 1- differences between the incipient and moderate disease stage

	Disease stage	N	Mean	Std. Deviation	Std. ErrorMean
Interleukin 1β (values)	Stage two	24	10,46	5,756	1,175
	Stage three	20	21,80	7,509	1,679
IL 4	Stage two	24	25,88	5,535	1,130
	Stage three	20	34,10	7,833	1,752
IL8	Stage two	24	49,42	7,330	1,496
	Stage three	20	58,90	2,673	,598
TNFα	Stage two	24	30,63	6,233	1,272
	Stage three	20	45,75	6,950	1,554

Tabel 2– differences between the incipient and moderate stage of disease

	Levene's Test for Equality of Variances		t-test for Equality of Means			
	F	Sig.	t	df	Sig. (2-tailed)	MeanDifference
Interleukin 1β (valori)	5,265	,027	-5,670	42	,000	-11,342
			-5,535	35,192	,000	-11,342
IL 4	10,148	,003	-4,071	42	,000	-8,225
			-3,946	33,333	,000	-8,225
IL8	24,191	,000	-5,481	42	,000	-9,483
			-5,886	30,003	,000	-9,483
TNFα	,581	,450	-7,607	42	,000	-15,125
			-7,531	38,659	,000	-15,125

We obtained statistically significant differences in the analysis of immunological markers between early and advanced periodontal disease in all variables except interleukin 4 (p>0.05).We observed that in early-stage interleukin 1β, interleukin 8 and TNF α have much lower mean values than in advanced stage.(p=0.000). We can conclude that the value of these immunological factors increases with the progression of periodontal disease.

Table 3 – differences between early and advanced stage disease

	Disease stage	N	Mean	Std. Deviation	Std. ErrorMean
Interleukin 1β (values)	Stage two	24	10,46	5,756	1,175
	Stage for	19	29,21	11,497	2,638
IL 4	Stage two	24	25,88	5,535	1,130
	Stage for	19	26,89	4,557	1,045
IL8	Stage two	24	49,42	7,330	1,496
	Stage for	19	70,21	11,736	2,692
TNFα	Stage two	24	30,63	6,233	1,272
	Stage for	19	57,47	8,514	1,953

Table4– differences between the incipient and advanced stage of disease

	Levene's Test for Equality of Variances		t-test for Equality of Means			
	F	Sig.	t	df	Sig. (2-tailed)	MeanDifference
Interleukin 1β (valori)	12,184	,001	-6,977	41	,000	-18,752
			-6,495	25,079	,000	-18,752
IL 4	,008	,930	-,647	41	,521	-1,020
			-,662	40,918	,511	-1,020
IL8	6,325	,016	-7,114	41	,000	-20,794
			-6,751	28,693	,000	-20,794
TNFα	2,865	,098	-11,940	41	,000	-26,849
			-11,518	32,007	,000	-26,849

We were interested to see if there were significant correlations between the immunological markers studied in both the research and control groups. For this purpose, we used the parametric test to calculate the Pearson correlation coefficient.

1. RESEACRH GROUP

Table5– correlation of immunological marker data in research group subjects

		Interleukina 1β (valori)	IL 4	IL8	TNFα
Interleukin 1β (values)	Pearson Correlation	1	-,924**	,924**	,946**
	Sig. (2-tailed)		,000	,000	,000
	N	33	33	33	33
IL 4	Pearson Correlation	-,924**	1	-,850**	-,951**
	Sig. (2-tailed)	,000		,000	,000
	N	33	33	33	33

IL8	Pearson Correlation	,924**	-,850**	1	,889**
	Sig. (2-tailed)	,000	,000		,000
	N	33	33	33	33
TNFα	Pearson Correlation	,946**	-,951**	,889**	1
	Sig. (2-tailed)	,000	,000	,000	
	N	33	33	33	33

** The correlation is significant if p is less than 0.01

When analyzing data from subjects with periodontal disease and diabetes, we obtained positive, statistically significant correlations (p=0.000) between interleukin 1β and interleukin 8 and TNFα. The Pearson correlation coefficient shows that we have a high, direct correlation between the two and that they vary in the same direction, both increasing.The subjects of the research group show statistically significant negative correlations.(p=0.000)The negative correlation coefficients obtained show that we have an inversely proportional increase, with the correlated variables changing in the opposite direction.

2. WITNESS GROUP

Table 6 – correlation of immunological marker in subjects within the witness group

		Interleukin 1β (values)	IL 4	IL8	TNFα
Interleukin 1β (values)	Pearson Correlation	1	-,775**	,884**	,854**
	Sig. (2-tailed)		,000	,000	,000
	N	33	33	33	33
IL 4	Pearson Correlation	-,775**	1	-,802**	-,887**
	Sig. (2-tailed)	,000		,000	,000
	N	33	33	33	33
IL8	Pearson Correlation	,884**	-,802**	1	,742**
	Sig. (2-tailed)	,000	,000		,000
	N	33	33	33	33
TNFα	Pearson Correlation	,854**	-,887**	,742**	1
	Sig. (2-tailed)	,000	,000	,000	
	N	33	33	33	33

** The correlation is significant if p is less than 0.01

In subjects with periodontal disease but without diabetes in the control group, we obtained positive, statistically significant correlations (p=0.000).Increased IL1β in subjects with periodontal disease causes an increase in IL8 and TNFα, likewise increased IL8 and TNFα causes an increase in IL1β. We obtained negative correlations from which we can conclude that an increase in IL4 causes a decrease in IL1β, IL8 and TNFα, respectively, with the correlated variables changing in the opposite direction. These correlations suggest that, both in patients with periodontal disease and diabetes mellitus and in subjects with periodontal disease but without diabetes mellitus, the interdependence between the cytokines studied is common

Our study aimed to evaluate the levels of immunological markers in relation to the stages of disease, thus demonstrating a significant increase in interleukin 1β, 8 and TNFα in the two, three and for stages, indicating an increase in the average level of these cytokines with the progression of periodontal disease.

Discussions

It has been shown that periodontal disease can cause a chronic inflammatory response and that the bacteria present in periodontitis can cause an increase in biochemical markers of inflammation in patients' peripheral blood, which is why chronic systemic inflammation caused by periodontal pathology can be a risk factor for multiple diseases. In the present study we included a total of 66 subjects, all of whom were informed about the study and agreed to data processing by giving written consent. Subjects were selected according to the inclusion and exclusion criteria used in previous studies. The distribution of groups was thus homogeneous and without statistically significant differences ($p > 0.005$). Of the 66 subjects included in the study, 33 are female subjects and 33 are male subjects. The gender distribution between subjects with periodontal disease and diabetes mellitus and subjects with periodontal disease but without diabetes mellitus did not differ significantly, which is why differences obtained in the assessment of clinical indicators cannot be attributed to differences between the two genders.

We obtained statistically significant differences between the two groups in all variables included in the study. For data analysis we used the t-test, which showed us how significant the differences were between the two groups of patients included in this study.

We aimed in this study to highlight biochemical markers of inflammation during periodontal disease. Following statistical analysis of the data, we obtained statistical differences in interleukin 1β levels between the two groups. Following statistical analysis of the data, we obtained statistical differences in interleukin 1β levels between the two groups. IL4 has been shown to play a central role in the pathogenesis of periodontal disease and to be closely related to periodontal tissue health IL 4 was studied at the plasma level to reveal changes in its levels in the progression of periodontal disease. Some studies in the literature have shown no change in average levels of this cytokine in patients with periodontal disease compared to healthy patients. In the present study, we observed statistical differences between the two groups when analysing the data on interleukin 4 values.

Fokema et al. and others in the literature have demonstrated increased plasma levels of IL8 in subjects with periodontal disease. Several studies in literature show that although periodontal disease is associated with increased concentrations of this cytokine in the

crevicular fluid, the effects of the disease have been minimal on plasma interleukin levels. In the present study, there was a statistical difference in the mean plasma interleukin 8 levels between the two groups.

TNFα is known to induce bone resorption, similar to interleukin 1β, by activating osteoclasts. Studies in literature have shown that TNFα shows increased levels in the crevicular fluid and periodontal tissues of patients with periodontal disease and that it plays a very important role in alveolar bone resorption and periodontal tissue destruction, being a proinflammatory cytokine. Because periodontal disease is associated with increased TNFα, it is generally believed that TNFα is one of the mediators of the local bone destruction seen in this chronic disease. It has been demonstrated that plasma TNFα showed significantly increased levels in subjects with periodontal disease, which correlated with loss of gingival attachment and periodontal pocket depth, suggesting a correlation between TNFα levels and periodontal disease progression.(192) Our study shows a statistical difference between the two groups in the level of the cytokine TNFα.

Periodontitis is common in older subjects, and this is supported by the fact that aging causes structural and functional changes in the immune system, thus increasing susceptibility to chronic diseases. However, ageing can only cause periodontal disease if periodontal inflammation is present at the same time. The prevalence and severity of periodontal disease in old age is simply the effect of prolonged exposure to microbial aggression. Our study showed for the age groups 30-40 and 51-60 statistically significant changes in the level of interleukin 8 where an increase of this cytokine with advancing age was evident.

It is known that periodontal disease is more common in the older population than in younger people. It is assumed that the disease will become more common in the future among older people, as many of these people retain their teeth well into old age. The present study shows an increase in the stage of the disease and worsening of the disease with advancing age.

Our study aimed to evaluate the levels of immunological markers in relation to the stages of disease, thus demonstrating a significant increase in interleukin 1β, 8 and TNFα in the two, three, and for stages, which indicates an increase in the average level of these cytokines with the progression of periodontal disease.

We were interested to see if there were significant correlations between the immunological markers studied in both the research and control groups. For this purpose, we used the parametric test to calculate the Pearson correlation coefficient. The correlation of the average of immunological markers in the present study shows us, according to the stage of the disease, that in the two stage of generalized periodontal disease, we obtained positive, statistically significant correlations($p<0.01$), in all studied variables. The positive Pearson

correlation coefficient between IL1β and IL4, IL1β and IL8 , IL1β and TNFα and vice versa shows that we have a direct correlation between these variables, all varying in the same increasing direction. We also obtained positive correlations between IL4 with IL8, IL4 with TNFα and between IL8 and TNFα, all these variables vary in the same direction, so an increase in one of them causes an increase in the other. We obtained no negative correlation coefficient, which means that all variables taken in the study increase, none of them decreases at this stage of the disease. The mean disease stage for the research group was M = 3.21 (p = 0.000). This average supports literature data showing that subjects with diabetes have more advanced stages of periodontal disease compared to subjects with periodontal disease but without diabetes.

Literature data show that TNFα acts in a similar way to IL1β by inducing bone and cartilage resorption through osteoclast activation. Both variables have an increased level in the research group; this explains why the average disease stage is higher compared to the witness group. The presence of TNF stimulates osteoclast formation.(193)

Conclusions

The onset of periodontal disease women occurs at older stages, while males have younger ages of onset of periodontal disease. We found an increased aggressiveness of periodontal disease with advancing age. The data obtained in the present study show an association between plasma levels of these cytokines and progression of periodontal disease. An increase in cytokines 1β, 8 and TNFα has been shown with disease progression, resulting in a systemic proinflammatory status. Further studies and correlation with other cytokines are needed to validate their importance as a biomarker in periodontal disease.In conclusion, we can still support the involvement of immunological markers in the pathogenesis of periodontal disease.

GENERAL CONCLUSIONS

1. The frequency of oral manifestations in diabetic patients was significantly high, demonstrating a relationship between gingival and periodontal disease and diabetes mellitus.
2. Periodontal disease is not necessarily a natural consequence of ageing, but rather a result of changes in the immune system over the course of a lifetime under the influence of a combination of predisposing and risk factors.
3. Interleukin 1β and IL 8 show an increase in their concentration in the progression of periodontal disease stages, suggesting the existence of a systemic proinflammatory status, influenced by the severity of the disease.
4. Interleukin TNFα is important in the serological diagnosis of periodontal disease, serving as a systemic inflammatory marker of the presence and progression of periodontal disease.
5. Diabetes mellitus contributes to cytokine imbalance with increased generation of pro-inflammatory cytokines, especially IL-1β and TNF-α which have negative effects on alveolar bone.
6. Patients with diabetes should make major efforts to prevent periodontal disease.
7. Periodontal treatment in people with diabetes has the potential to improve glycemic control and overall health indicators, as periodontal-based diseases are associated with increased levels of inflammatory cells and mediators in the systemic circulation.
8. Prevention of periodontal disease should be an integral part of diabetes control.
9. Studies on larger and more homogeneous groups of patients, as well as correlations with different cytokines, are needed to confirm some of the conclusions of this work.

RESEARCH DEVELOPMENT PERSPECTIVES

Our proposal focuses on the development of programs to promote the maintenance of a healthy oral cavity in patients with diabetes because it is well known that the predisposition to oral infections in patients with diabetes is much higher compared to clinically healthy subjects, and results in the development of dental caries and ultimately tooth loss. There are numerous studies explaining chronic oral complications in patients with diabetes and their negative effects on glycaemic control. Prevention of these complications, especially in patients with diabetes, is important because of the possible undesirable effects they can have on glycaemic control with repercussions on the patient's quality of life.

We consider the present research as a basis for future medical research that may develop the topic of oral health impairment under the influence of changes in carbohydrate metabolism.

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