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by
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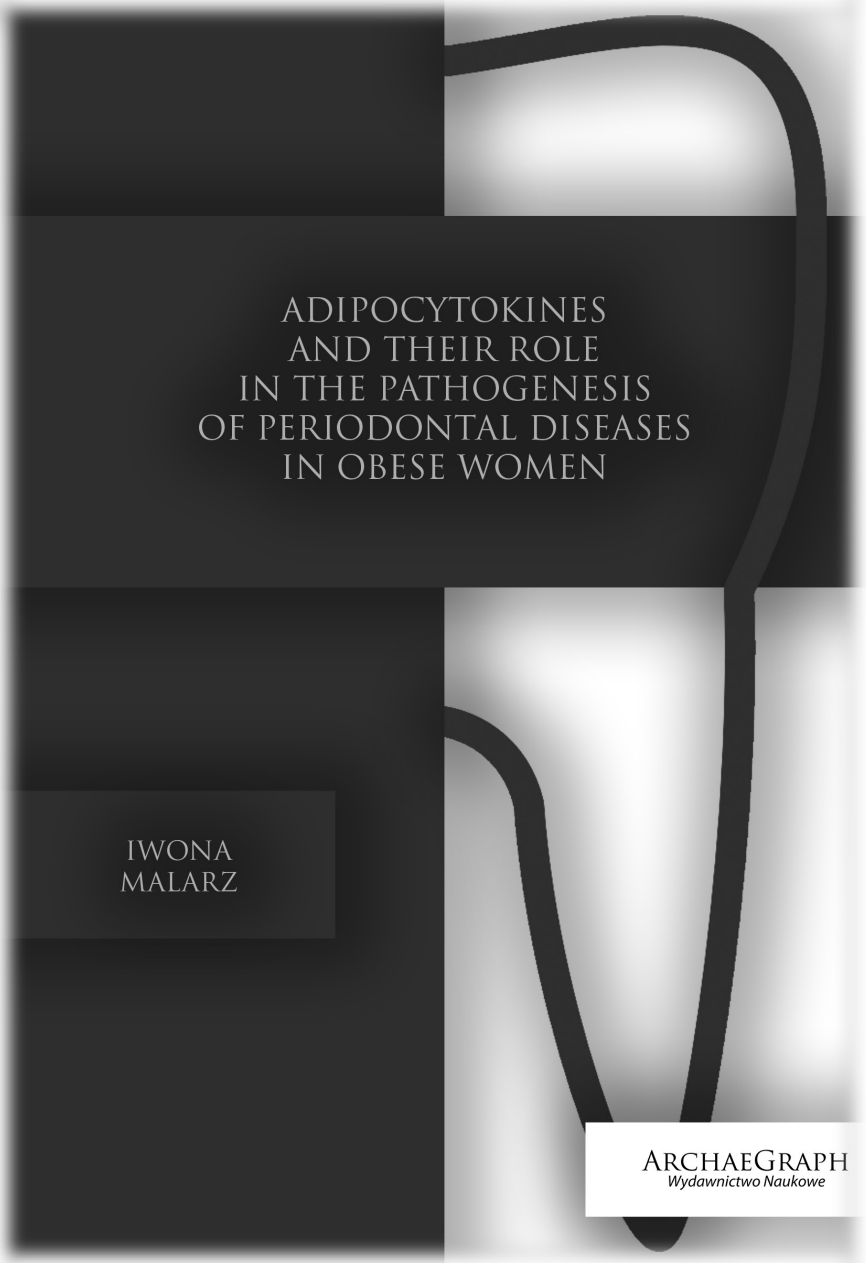

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INTRODUCTION

In Poland, in the middle-aged patient population, periodontal diseases are classified as social diseases. Only 1% of the population, according to the Community Periodontal Index of Treatment Needs (CPITN), has no periodontal symptoms and more than 16% has advanced periodontitis. Only 1% of adults in Poland does not require prophylactic and therapeutic measures, around 12% need oral hygiene instructions and plaque removal instructions. In addition to oral hygiene instructions, 23% also require supragingival scaling, and 40 % require subgingival scaling. In 16% of patients, the need for comprehensive treatment of chronic periodontitis is observed. This data comes from epidemiological studies carried out under the supervision of Professor Jańczuk in 1987, from Niigata database of 1990, from research in 1998 and 2002 and from the 2009 National Consulate Report presented in the article of Górska et al. in 2012 [1].

Numerous reports of recent years have shown a close relationship between periodontal diseases and metabolic syndrome [2, 3, 4, 5]. Periodontal inflammation, according to most authors, is a consequence of the action of periodontal pathogens such as Prevotella gingivalis, Prevotella intermedia, Tannerella forsythia or Actinobacillus [6].

However, some authors argue that the bacterial biofilm is insufficient for the development of pathology in the periodontium.

Independent risk factors such as obesity or arterial hypertension may aggravate inflammatory changes in periodontium. Their relationship with teeth loss and periodontal diseases was documented in numerous epidemiological studies [2, 3, 4, 5]. It has been shown that the risk of chronic periodontitis in patients with metabolic syndrome is twice as common as in healthy individuals. Many studies show a significant correlation between these two conditions [7, 8, 9]. Periodontal diseases and their severity in the metabolic syndrome and cardiovascular diseases are closely associated with the presence of pro-inflammatory markers, such as TNF-α, C-reactive protein and IL-6, in blood [10]. Periodontitis is a known risk factor for cardiovascular diseases which have been pointed out to have a strong relationship with inflammatory and metabolic markers, such as glycaemia and triglyceridemia, identified in blood [11]. According to current clinical trends, periodontitis is regarded as an important factor that favours the incidence rate of arteriosclerosis, coronary artery disease and cerebral vascular accidents. Bacteriological studies have shown the presence of the same bacterial strains in periodontal inflammation and in atheroma [12]. A causal connection between diabetes and periodontitis is also suggested. Periodontal diseases are referred to as "the sixth complication of diabetes"[13].

Abdominal obesity is a fundamental diagnostic criterion of metabolic syndrome, among cardiovascular diseases risk factors such as carbohydrate and lipid metabolism disorders and arterial hypertension.

In the pathogenesis of the metabolic syndrome, in addition to insulin resistance, dyslipidaemia, inflammatory process and arteriosclerosis, great significance is assigned

to the endocrine function of the visceral adipose tissue, releasing adipocytokines directly into the portal circulation. Adipokines are bioactive molecules involved in the action of insulin, energy expenditure and in inflammatory and regenerative processes. With visfatin and leptin stimulating the synthesis of pro-inflammatory and proteolytic molecules, a decrease in adiponectin levels and a rise in visfatin and leptin levels in obese individuals increase the risk of periodontitis and cause difficulties in healing [14]. Others, studying patients with periodontitis, showed an increase in vascular endothelial growth factor (VEGF) and TNF-α in gingival crevicular fluid and blood serum, and noticed a decrease in their level after the conservative treatment. During the coexistence of periodontitis and coronary artery disease, a higher VEGF concentration in gingival crevicular fluid, and a lower VEGF concentration in serum were observed [15]. Pradeep et. al. observed that VEGF levels in serum and in gingival crevicular fluid increased with the aggravation of periodontal inflammation [16]. On the other hand, Tabari et. al. recorded higher levels of pro-inflammatory adipocytokine, namely visfatin, in the saliva of patients with periodontitis compared to the healthy group [17]. A group of researchers, namely, Purwar et al. and Meharvade et al. recorded lower salivary and GCF leptin levels and higher serum leptin levels in individuals with periodontitis compared to healthy subjects [18,19]. Meta-analyses regarding serum leptin and adiponectin levels have recently emerged. Most of the studies have shown leptin increase and adiponectin decrease in patients with chronic periodontitis, in the absence of significant changes in post-treatment levels. Patients with no systemic disease

were examined [20]. In another meta-analysis, most researchers recorded an increase or decrease in GCF concentrations of leptin, adiponectin, IL-6, CRP and TNF-α as compared to the level of these factors in systemic circulation in the process of periodontal inflammation [21].

Oral hygiene is essential in prophylaxis of periodontal diseases. It is supported by properly performed dental higienisation treatments of the oral cavity. Ailments resulting from improper dental higienisation cause periodontitis manifested by swelling, redness, bleeding and degenerative changes.

Periodontal Disease as a Disease Entity

Periodontal Diseases are defined as chronic inflammation of tissues surrounding teeth, that is, the tissues that serve as tooth support in sockets and which form a morphological and functional unit together with the teeth that conditions correct operation of the masticatory organ. The following belong to periodontal structures: gums, periodontium, cementum and alveolar process bone [22].

The largest group of diseases includes gingivitis and periodontitis, which are caused as a result of imbalance between micro-organism of the film present on the surfaces of teeth and gums affecting periodontal tissues, and defensive mechanisms of the host. These, in turn, are modified by various risk factors, such as systemic diseases, e.g. diabetes, obesity, hormonal disorders, blood diseases or conditions of autoimmunologic nature and environmental factors, such as improper hygiene of oral cavity, smoking and stress.

Chronic periodontitis is usually characterised by insidious and long-lasting course. Periodontitis is preceded by gingivitis which may not always lead to development of periodontitis. Development of periodontitis depends on individual defensive capability of the host [23]. First symptoms are slight and many times underestimated by patients: oedema, reddening of gums and their periodical bleeding. Frequently, patients are not aware that these

may be symptoms of a onset of the periodontal disease. In the light of current studies, general knowledge of our society about ethiology, symptoms and consequences of periodontitis (such as premature loss of teeth and effect on overall body condition) is highly insufficient. Unfortunately, the early symptoms of periodontopathy are sometimes neglected during a routine dental examination.

Due to the aforementioned reasons, chronic periodontitis is usually diagnosed late and requires complex treatment, which is frequently long, expensive, and not always fully effective. The consequence of periodontitis, which often lasts many years, with characteristic periods of exacerbation and longer periods of remission, is progressing destruction of structures that hold a tooth in its alveolus, which leads to tooth mobility and impaired chewing function with further consequences for an overall health condition [24].

In the light of recent research, factors affecting host's susceptibility are divided into those that we have no impact on - i.e. the so-called determinants and real risk factors, modifying host's response. The following consists determinants of periodontal diseases: age, sex, socioeconomic status and genetic factor. Real etiological factors and risk factors of periodontal diseases, such as microorganisms (biofilm), nicotine addiction, stress, osteoporosis, diabetes and general diseases connected with immunodeficiency may be eliminated. Therefore, disease development is a resultant of the interaction between the afore-mentioned factors, and it also may be modified by the genetically conditioned anatomical and histological structure of periodontium and immunological and inflammatory response of the host [25, 26]. Prevalence of periodontopathy,

particularly in people over 40, and the frequently associated premature teeth loss and systemic effects make it be rated as one of social diseases.

BACKGROUND AND OBJECTIVES OF THE WORK

Obese women constitute an increasing percentage of patients in dental surgeries. Conducting periodic dental hygienization and oral hygiene instruction does not fully prevent the occurrence of periodontal diseases. Many authors of publications indicate that obesity is a risk factor for cardiovascular system diseases and metabolic disorders of carbohydrate and lipid metabolism which coexist or may be implicated by periodontal diseases. These observations prompted me to conduct a study in a group of obese female patients.

The aims of my study were:

1. The assessment of the coexistence of the metabolic syndrome factors and periodontal inflammation, measured by SBI index, in the study group of obese female patients.

2. Determining the influence of several factors of the metabolic syndrome on the increase of the periodontal inflammation index (SBI).

3. Determining the influence of the prognostic value of adipokines in blood on the formation of inflammation in the oral cavity in obese female patients.

4. Finding prognostic markers for periodontal inflammation in peripheral blood tests as an element of dental prophylaxis.

MATERIAL AND METHODOLOGY

Selection of the Study Group

The research project was carried out in the private dental practice of Iwona Malarz, DMD, in Kraków. Blood samples were collected for examination at the collection point and transported to the Central Laboratory „Diagnostyka" in Kraków, where some biochemical tests were performed. Material samples were also delivered to the Department of Physiology SUM in Zabrze for biochemical analysis of adipocytokines. The participants of the study were obese women (n = 90) who came to the dental surgery and met the study inclusion criteria. The research project was approved by the Bioethical Committee of the Medical University of Silesia, number 0022KB1/14/13.

Dental Examination

The state oral cavity was assessed in a dental surgery under the light of a dental lamp with the use of a diagnostic kit: a mirror, a probe and a periodontal probe. The study was conducted by one person. Dental indices (SBI, GI, PlI) were tested twice - before and 3 months after dental hygienization procedures. The collected data were entered into the patients' medical history and into the Microsoft Office Excel spreadsheet for archiving.

Prevalence of Dental Caries

The incidence of dental caries was measured by the DMF (PUW) index.

This number represents the sum of teeth affected by caries, where D (P) means the number of teeth with active primary or secondary caries: M (U) - teeth missing or removed due to caries, and F (W) - filled teeth [27].

Oral Hygiene Index

The Plaque Index (PlI) by Silness and Löe [28] was used to measure the state of oral hygiene. The plaque index assesses the thickness of plaque localised around the neck of the tooth on the four surfaces. Dental plaque was measured at the gingival margin of teeth 16, 11, 24, 36, 31, 44. In case of the absence of teeth 24 and/or 44, the plaque thickness was measured at the gingival margin of teeth 26 and/or 46, respectively. Plaque thickness was measured on a four-point Pl.I scale: The evaluation criteria were as follows: 0 - no plaque; 1 - a thin film of plaque adheres to the gingival margin and neck of the tooth, detected with a probe, but not visible to the naked eye; 2 - moderate plaque accumulation at the gingival margin and/or on the tooth surface and within the gingival pocket visible to the naked eye; 3 - abundant plaque accumulation. The values obtained from all tooth surfaces were summed up and divided by 4 to obtain the Pl.I, assuming the following values: Pl.I = 0.0-0.6 - proper oral hygiene; Pl.I = 0.7-1.8 - average oral hygiene; Pl.I = 1.9-3.0 - poor oral hygiene.

The Condition of Periodontal Soft Tissues

The condition of periodontal soft tissues was assessed using two indices: the Gingival Index (GI) by Löe and Silness [28]

and the Sulcus Bleeding Index (SBI) by Mühlemann and Son [29]. The gingival crevice bleeding index (SBI) was determined after inserting a periodontal probe into the gingival crevice without applying pressure on the bottom of the sulcus.

The Gingival Index was measured at the gingival margin of teeth 16, 11, 24, 36, 31, 44. In case of the absence of teeth 24 and/or 44, the gingival condition was measured at the gingival margin of teeth 26 and/or 46, respectively. The assessment was made in accordance with the four-point scale of gingival condition: 0 - healthy gingiva, light pink colour; 1 - mild inflammation, slight colour change, and slight changes in tissue structure, no bleeding on probing; 2 - moderate inflammation: redness, oedema, glazing and hypertrophy, bleeding on pressure or probing; 3 - severe inflammation: significant redness and gingival oedema, ulceration, tendency to spontaneous bleeding. After adding the scores and dividing them by 4, the value of the GI index for each tooth was obtained. The index value in the range 0.1-1.0 indicates mild gingivitis, in the range 1.1-2.0 moderate gingivitis and in the range 2.1-3.0 severe gingivitis.

The gingival index SBI allows capturing the early stages of gingivitis. This examination was performed on the same teeth the GI index was measured on. The examination consisted in gently probing the gingival cleft, observing the colour and structure of the gingiva, and then qualifying it to one of the categories on a six-point scale: 0 - healthy looking gingiva, no bleeding on probing; 1 - apparently healthy gingiva, but bleeding on probing; 2 - colour change, bleeding on probing; 3 - slight change in shape, colour change, bleeding on probing; 4 - significant change in shape, colour change, bleeding on probing; 5 - marked swelling, colour change, bleeding on probing, possible gingival ulceration. All patients were given dental hygienization treatment and were provided with oral hygiene instructions.

Three months after the dental hygienization treatment, the PlI, GI and SBI were measured again.

Anthropometric and Clinical Data

The physical examination included the measurement of body weight, height, blood pressure, waist circumference, and BMI. The occurrence of metabolic syndrome factors was defined based on the recommendations of the International Diabetes Federation (IDF) (2005). Abdominal obesity defined as waist circumference for the Europeans, waist circumference > 94 cm for men and > 80 cm for women, and 2 of the other 4 criteria: blood pressure > 130/85 mmHg or use of antihypertensive drugs; blood triglyceride concentration > 1.7 mmol/L (150 mg / dL); HDL cholesterol concentration < 1.3 mmol/L (50 mg/dL) in women; fasting glucose level > 5.6 mmol/L (100 mg/dL) or the use of oral medications. The waist circumference was measured by the same person. Blood pressure was measured while patients were in sitting position after a 5-minute period of rest in accordance with the recommendations of the American Heart Association and Seventh Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure and the average of three independent measurements was taken. To calculate body mass index (BMI), the subjects were measured and weighed. BMI was calculated by dividing body weight in kilograms (kg) by height in meters squared (m2). The examination included the measurement of body weight and stature (standing height). The examination was performed in the morning between 8 and 10 a.m.

Laboratory Testings

Blood from the basilic vein, in the amount of 4 ml, was drawn on an empty stomach, after 12-hour fasting and 24 hours without taking any medications, on the day of the dental examination, between 8 and 10 a.m. at the collection point and transferred to "Diagnostyka" Laboratory Sp. z o.o. After centrifugation, the serum was frozen in several separate tubes and placed at -20 C. The samples were then transported, in appropriate containers, to the laboratory of the Department of Physiology SUM in Zabrze and placed at -80 C until the assay was done. Measurements were taken in doublets and simultaneously. CRP and glucose were determined using the Abbott Test method in the „Diagnostyka" laboratory. Serum adipokine concentrations were measured using the enzyme-linked immunosorbent assay method (ELISA) of the Department of Physiology in Zabrze with the use of commercial kits. The concentration of adipokines was read based on the absorbance value, which is directly proportional to their serum concentration. An UQuant reader was used for the measurements. The commercial kits used to determine adipokines, omentin, insulin and lipid profiles: eNAMPT/visfatin BioVentor kit; HGF Abnova Corp HGF (Human) ELISA kit; VEGF Cell Sciences VEGF, Human ELISA kit; leptin RayBio Human Leptin ELISA kit; enzyme immunoassay (EIA) using Calbiotech Inc ELISA kit microplates. The lipid profile was determined by spectrophotometric method using Biochem kits. Insulin resistance (IR) was assessed by the homeostatic model (HOMA). The insulin resistance index value was obtained by multiplying the fasting insulin concentration (mU/L) and the fasting glucose concentration (mmol/L) divided by 22.5. A value was considered abnormal when it was greater than 1.5. [30]. LDL cholesterol was calculated according to Friedewald.

The Methodology of Statistical Calculations

The data of 90 subjects of this research underwent statistical evaluation. In the statistical analysis, the level of significance (type I error) $p \leq 0.05$ was assumed. The statistical calculations were performed using licensed statistical packages:

Statistica v. 7.1 PL by StatSoft and MedCalc Statistical Software v.14.10.2 (MedCalc Software bvba, Ostend, Belgium).

Obesity and periodontal disease

Nowadays, obesity constitutes a global problem, which is confirmed by statistics in many countries. At present, the situation becomes more and more dramatic, the proof being steady growth in the number of obese people all over the world [31, 32]. The percentage of obese persons in Poland increased considerably during the last decade. The latest reports show that 61% men and 50% women in Poland are overweight or obese [33, 34].

Increased rates are observed both among children and adults [2, 35]. The World Health Organisation estimates that 39% adults globally are overweight, and more than 500 million are obese. It is likely that this number will double by 2030. Therefore, obesity is already referred to as the pandemonium of the 21st century [36]. The percentage of obese persons in Poland also increased considerably during the last decade. Research conducted by Instytut Żywności i Żywienia *[Food and Nutrition Institute]* indicates that over 60% men and almost half the women in Poland are overweight or obese. The same problem refers to every third school-age boy and every fifth girl.

Negative influence of incorrect eating habits on the general health has been studied for many years. One should remember that obesity is not only a risk factor in case of such disorders, as cardiovascular diseases, type 2 diabetes or arterial hypertension, but it is also very important in etiopathogenesis of oral cavity diseases, such as

tooth decay and periodontal diseases [37]. Recently, there have been more and more scientific reports on the positive correlation between abdominal obesity and periodontal disease in adults [2,38].

Despite many studies, the exact mechanism of the effect obesity has on the occurrence and intensity of periodontopathic changes is still not fully known. At present, the role and significance of selected hormones, salivary proteins and inflammatory mediators of gum pocket fluid are emphasised as specific biomarkers of pathological processes in the host's body (1). Due to the scale of periodontopathy and obesity occurrence in the society, it becomes necessary to seek new opportunities enabling to perform large-scale screening tests, for which blood, saliva and and gum pocket fluid could be used. Early diagnosis and implementation of therapy covering obese persons would make it possible to hinder development of diseases accompanying overweight and obesity, including periodontopathy.

Table 1. Specification of studies on correlation between obesity and periodontitis.

Martinez-Herrera et al. [39]	Periodontitis occurred more frequently in obese participants and the risk of obesity in obese participants is six folds bigger than in case of slim participants.
Nascimento et al., Suvan et al., and Khader et al. [40, 8, 41]	Abdominal obesity had direct effect on unfavourable results in periodontium.

Suvan et al. [8]	Obese participants had considerably higher average depths of pocket probing after non-surgical treatment of periodontium than obese persons.
Khader et al. [41]	Over 50% of obese participants had periodontium diseases.
Jimenz et al. [42]	A significant correlation between obesity and periodontium diseases.
Kangas et al. [43]	Patients with the biggest waist size or waist to height ratio had the likelihood of gum pocket occurrence higher by 40-60%.
Zimmermann et al. & Kose et al. [44, 45]	Obese participants had higher TNF-α wlevel, when compared with participants with normal weight.
Kose et al. [45]	Considerably higher IL-6 level among obese persons, when compared with non-obese ones.
Zimmermann et al. [44]	The highest leptin concentration was in obese persons.
Buduneli et al. [46]	Leptin and IL-6 were higher in obese persons than in non-obese persons.
Thanakun et al. [47]	Overweight and obese participants leptin had higher levels of and CRP.
Maciel et al. [48]	Obese participants had significantly higher pathogenic factors concerning periodontium than the control group.
D'Aiuto et al. [49]	Severe periodontitis was independently related to intensified oxidative stress.

Atabay et al. [50]	Increased level of oxidative stress caused by obesity may be the reason of periodontium deterioration and disease severity.
Suresh et al. [51]	Obese participants with periodontitis had higher oxidative stress.

Source: elaborated on the basis of own study.

Incorrect eating habits have negative influence on the general health condition. Obesity constitutes a risk factor for such diseases as, for example, cardiovascular diseases or type 2 diabetes, but it is also significant for etiopathogenesis of oral cavity diseases. The role obesity plays in oral cavity diseases and its mechanisms become more and more often the subject of interest of researchers all over the world. The first description of the correlation between obesity and periodontal disease appeared in 1977, when Perlstein and Bissada discovered that resorption of alveolar process is significantly greater in obese rats, when compared with rats of normal weight [52]. Since then, many studies have been conducted in order to examine these correlations. However, it was only in 1998 that the correlation between obesity and periodontitis was also observed in humans [53]. Since then, the correlation between obesity and periodontitis has been confirmed in many ethnic populations and some meta-analyses [54, 55, 8].

According to numerous scientific reports, obesity and periodontitis constitute two chronic inflammatory diseases of similar etiopathogenesis. Mechanisms of their interaction is poorly known or understood at present. Nevertheless, it is known that obesity is the underlying reason of

numerous harmful biological consequences, which may be linked to periodontal diseases pathogenesis. It is suggested that obesity disturbs the capacity of immunological system to adequately react to an attack of periodontopathogenic micro-organisms, such as *Porphyromonas gingivalis*, thus increasing the risk of periodontitis [56, 57, 58]. However, adipocytokins are the ones that play important role in increasing the risk of occurrence and progression of periodontal diseases. It is also very highly likely that there are individual differences in cytokine expression and reactions towards their action, which affect susceptibility to diseases, intensity of changes and consequences for health. The studies suggest that chronic periodontitis may lead to increased inflammation and have influence on the level of adipokines in serum and inflammatory mediators [59].

The research shows that unfavourable effect obesity has on periodontal tissues is caused by direct impact of inflammatory cytokines, mainly such as IL-1, IL-6, TNF-alpha, leptin, adiponectin, resistin or PAI-1 (plasminogen activation inhibitor). Tumour necrosis factor (TNF-alpha) constitutes one of many pro-inflammatory cytokines, secreted either by visceral fat tissue, or pathologically changed periodontal tissues. According to Lundina et al., when secreted by fat tissue, it may exacerbate the scope of damages done to periodontal tissues. The study conducted in young adults showed that TNF-alpha level in gingival fluid has got a positive correlation in patients with BMI > 40 kg/m^2. Such positive correlation in obese patients without periodontal diseases suggests that TNF-alpha originates from fat tissue, which is in line with the hypothesis claiming that obesity constitutes an inflammatory disease. This suggests that TNF-alpha in young adults with great

amount of fat tissues will cause deterioration of periodontal tissues, despite that fact that they did not suffer from periodontal diseases at a young age [60].

Increased concentrations of TNF-alpha and interleukin 6 is determined in obese persons. Moreover, the level of the said cytokines decreases along with body mass loss [61]. High concentration of TNF-alpha may exacerbate symptoms of periodontal disease through stimulation of fibroblasts which enhance synthesis of deteriorating enzymes and stimulate osteoclasts responsible for bone resorption [62]. Interleukin 6 constitutes a cytokine with prothrombotic action, through increasing concentrations of fibrinogen, plasminogen activation inhibitor-1 (PAI-1) and C-reactive protein (CRP). Secreted in bigger amounts by visceral fat tissue, it is connected with increased risk of cardiovascular disorders and type 2 diabetes [63].

PAI-1 (plasminogen activation inhibitor-1), is a protein belonging to coagulation system, which takes part in pathogenesis of obesity and periodontal disease. It is generated by liver and endothelial cells, the production being controlled by lipids and TNF-alpha. The studies show that obese people have increased PAI-1 levels. Its role consists in induction of blood agglutination and, thus, increasing the risk of ischemic heart disease. In obese subjects, it may also reduce blood flow through periodontal blood vessels, leading to development of periodontal disease. According to Akman et al., the level of PAI-1 in plasma plays a significant role in the correlation between periodontal disease and obesity [64].

Leptin is the best known substance excreted by fat tissue. It acts through leptin receptors located mainly in hypothalamus. When the leptin bonds with receptors in

the hypothalamus, neurons cease to generate a neurotransmitter - neuropeptide Y, which acts as appetite stimulator. This way, the hormone reduces appetite and stimulates the sympathetic system. It stimulates the immunological system and increase production of cytokines and phagocytosis through macrophages. Lately, it has also been stated that it participates in the mechanism of bone formation. The studies prove that leptin is present either in healthy gums or those slightly changed by inflammatory processes. Its concentration decreases with the increased pocket depth (PD). Moreover, Purwar et al. proved that concentration of leptin in saliva in slim patients with periodontitis turned out to be considerably lower than in slim persons with healthy periodontium. The authors state that non-surgical periodontological treatment improves the condition of periodontal tissues in chronic periodontitis patients, as well as it reduces leptin levels in plasma and increases its concentration in saliva [65]. Johnson and Serio evaluated levels of leptin, growth factor involving endothelial cells lining the blood vessels, and IL-6 within healthy and inflamed gingival tissues [66]. They noticed that the levels decrease with the progress of gum disease. Karthikeyan et al. evaluated a correlation between leptin levels in gingival tissues and blood serum - they stated that the more advanced the periodontal disease involves the lower levels of leptin within gingival tissues and, at the same time, the its levels are higher in blood serum [67].

Thus, leptin may play a significant role in the development of periodontitis. The latest studies showed that intensity of periodontitis depends on the correlation between leptin content in blood serum and its local concentration [66, 67].

Ghrelin constitutes one of the most important hormones linked to obesity, responsible for the energy balance control, stimulating appetite, responsible for the need to receive food. In 70% ghrelin is secreted by stomach, and the latest studies have showed that it is also produced and secreted by salivary glands. Benedix et al. observed higher ghrelin levels in the saliva of both slim and obese persons than in their blood serum. Moreover, considerably lower levels of ghrelin were observed in slim persons on an empty stomach, when compared with obese patients, whereas, the levels of salivary ghrelin remained stable [68].

The levels of salivary ghrelin decreased only after a normalised meal. Bin-Bin U et al. showed a positive correlation between salivary ghrelin and serum ghrelin levels and BMI, suggesting that the salivary ghrelin level may constitute an alternative to determine its levels in serum in anticipating obesity in patients [69]. Literature of recent years does not report any correlation between ghrelin and its potential effect on periodontium condition. Nevertheless, it is presupposed that ghrelin may play a role of a peculiar obesity bio-marker, the presence of which may be detected in diagnostic material, such as saliva.

Though originally separated in fat tissue, resistin is also produced by immunological system tissues and hence it was linked with an activation of inflammatory processes. The pro-inflammatory features of resistin consists in stimulating secretion of TNF-alpha and IL-6, and thus reducing anti-inflammatory effects of adiponectin. It was also showed that periodontitis is associated with its increased levels in blood serum. Apart from the afore-mentioned pro-inflammatory adipokines, fat tissue also secretes anti-inflammatory factors, such as adiponectin. Adiponectin

influences a series of metabolic processes, particularly glucose and fat acids conversion in the liver. It shows anti-inflammatory (IR) [70, 71].

Systemic lower concentration of adiponectin in blood plasma was stated in obese subjects, when compared with those with regular body mass index. Moreover, the latest studies show lower levels of adiponectin in serum in patients with diagnosed periodontitis [44, 72-76]. From the the current studies it results that periodontitis mainly influence resistins and adiponectin circulating in the blood, and, in tur, obesity and periodontal disease increase levels of leptin and IL-6, which have pro-inflammatory effect. These correlations suggest that both diseases, positively combined, have inflammatory effect.

In 2005, a new adipokine, termed visfatin, was identified [77]. It is identified as a pre-B-cell colony-enhancing factor, which is involved in the early development of growth factor and cytokines and plays a role in energy metabolism. Visfatin is a 52-kDa protein that increases pre-B-cell colony release from lymphocytes and improves B-lymphocytes maturation [78]. In addition, the production of interleukin-1 beta (IL-1 β), tumour necrosis factor alpha (TNF-α) and IL-6-induced by visfatin has also been reported during infection and inflammation [79]. Visfatin is also known as nicotinamide phosphoribosyltransferase (NAMPT), an enzyme that inhibits the biosynthesis of nicotinamide adenine dinucleotide (NAD)[80]. Visfatin is secreted by visceral adipose tissue and macrophages. Moreover, it is isolated from several tissues, such as white blood cells, lymphocytes, muscle, dendritic cells, and bone marrow [81]. Therefore, it is considered an adipokine that is available in inflammatory cells and inflammatory

conditions - the expression of visfatin increases in acute and chronic inflammatory conditions [82].

Despite reports on the role of visfatin as a marker in periodontal diseases [83]only a few studies have been conducted in this field. In one of the studies [84], a correlation between visfatin and the progress of periodontal disease was found. This study evaluated the relationship between the serum and GCF concentrations of visfatin and periodontal diseases and it was eventually concluded that concentration of visfatin in the serum and GCF increased gradually among patients suffering a range of gum diseases from gingivitis to periodontitis. Furthermore, the concentration of visfatin was higher in patients with periodontal disease and type 2 diabetes (T2DM) compared to patients with the periodontal disease but without T2DM. Tabari et al. [17] reported that a relationship existed between salivary visfatin and chronic periodontitis in which salivary visfatin concentration increased during periodontal infection. Another study [85] found that salivary visfatin levels were significantly higher in patients with gingivitis and periodontitis in comparison with healthy subjects.

Omentin, the adipocytokine secretory protein, is mainly secreted in visceral adipose tissue (VAT). Omentin is encoded by two genes, omentin-1 and omentin-2, and the dominant isoform in human plasma is omentin-1 [86]. Omentin increases the sensitivity of adipocytes to insulin, and increasing obesity and insulin resistance have been correlated with lower levels of omentin [87]. Moreover, patients with coronary artery disease and rheumatoid arthritis have reduced omentin levels [88, 89]. In addition, omentin suppresses the ERK/NF-κB pathway to promote vasodilation in blood vessels of rats and diminishes the

expression of adhesion molecules triggered by TNF-α in endothelial cells [90, 91].

Omentin is an adipocytokine identified as a modulator of insulin activity [86]. An in vitro study showed that omentin enhanced insulin-stimulated glucose uptake in adipocytes [92]. Omentin has an anti-inflammatory role in vascular endothelial cells by preventing TNF-α-induced COX-2 expression [93]. In addition, C reactive protein- and TNF-α-induced NF-κB activation was reduced by omentin-1 in human endothelial cells [94]. However, the involvement of omentin in periodontitis or the effect of nonsurgical periodontal treatment on omentin levels have not been investigated so far.

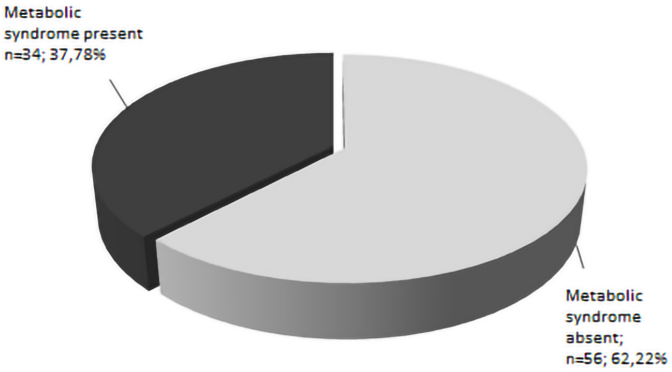
HGF and VEGF correlate well with the features of the metabolic syndrome, and in periodontal diseases we observe their increase in serum. [95, 96, 97]. HGF is an angiogenic, regenerative, cytoprotective factor and increases more in gingivitis than in periodontitis. [98].

SUBJECTS, RESULTS AND DISCUSSION

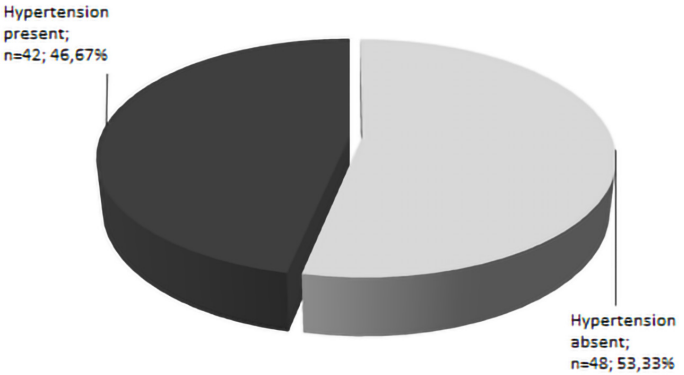
Diagrams A. to E. presents the characteristics of the group of 90 obese women examined in terms of the prevalence of components of the metabolic syndrome.

Diag. A - the prevalence of metabolic syndrome and its components in 90 examined obese women; B - the prevalence of arterial hypertension; C - the prevalence of abnormal blood glucose levels or diabetes; D - the prevalence of abnormal cholesterol level; E - the prevalence of hypertriglyceridemia

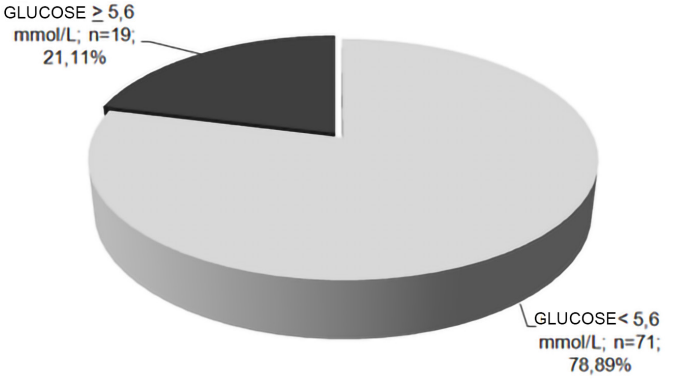
A. Metabolic syndrome present; n=34; 37.78%, Metabolic syndrome absent; n=56; 62.22%



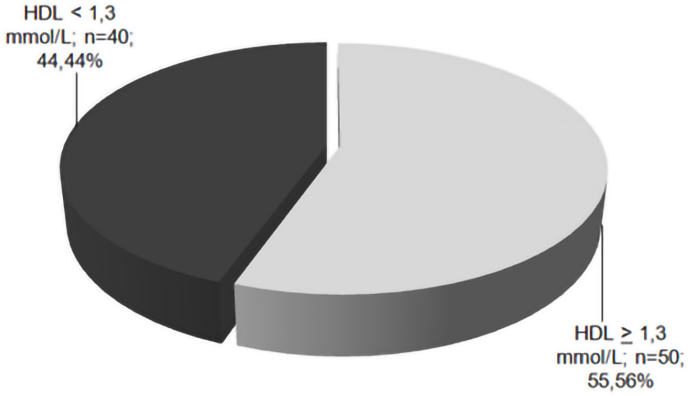
B. Hypertension present; n=42; 46.67%, Hypertension absent; n=48; 53.33%



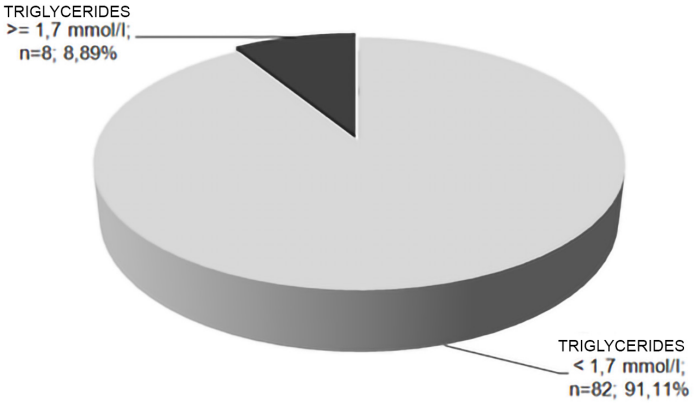
C. Glucose ≥ 5.6 mmol/L; n=19; 21.11%, Glucose < 5.6 mmol/L; n=71; 78.89%



D. HDL ≥ 1.3 mmol/L; n=50; 55.56%, HDL < 1.3 mmol/L; n=40; 44.44%



E. Triglycerides ≥ 1.7 mmol/L; n=8; 8.89%, Triglycerides < 1.7 mmol/L; n=82; 91.11%



As shown in Diagrams (A. to E.), the prevalence of 3, 4 or 5 components of metabolic syndrome (A) in the group of 90 examined obese women was found in 34 patients (37.78%). The percentage of patients with arterial hypertension (B) in the study group was found in 44.67%, i.e. in 42 subjects. Abnormal blood glucose levels or diabetes (C) (treated with Glucophage) was present in 21.11%, i.e. in 19 subjects. Abnormal HDL cholesterol levels (D) was observed in 40.44%, i.e. in 40 subjects while hypertriglyceridemia (E) was found in 8.89%, i.e. in 8 subjects.

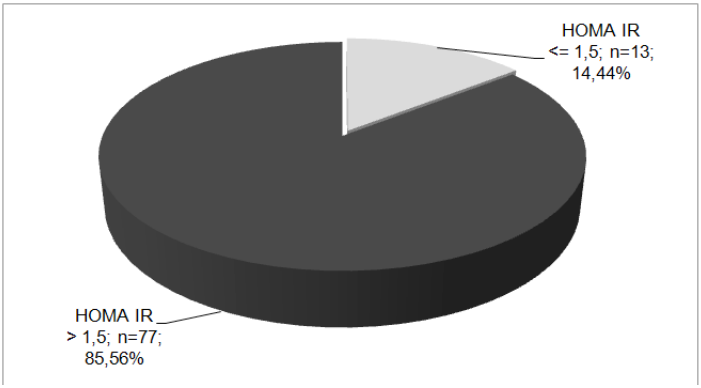
In this study, the subjects were obese female patients, aged 35-49. This wide age range may influence the profiles of cytokines and adipocytokines, as it has already been found in other studies [99, 100] - especially as periodontitis has a higher prevalence in women than in men [101]. Gender affects the profile of cytokines and adipocytokines, with men usually having lower leptin/adiponectin ratio in comparison to women [102, 103].

On the basis of the obtained study results, it was found that insulin resistance (Diag. F) occurred in 77 examined women, which constituted 85,56%. In contrast, abnormal total cholesterol level (Diag. G) occurred in 23 examined women, which constituted 25,56%.

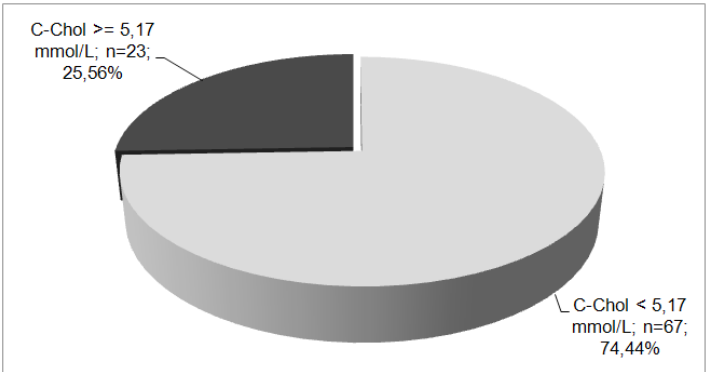
Goodpaster et al. [104] also demonstrated the relationship between the amount of visceral adipose tissue, insulin resistance and the occurrence of type 2 diabetes. Alexander et al. in their studies [105] showed that insulin resistance syndrome is most frequently diagnosed in the highest body weight group. This result was independent of the presence of diabetes.

Diagrams F. & G. Characteristics of the group of 90 obese women under study in terms of the frequency of abnormal values: A - insulin resistance index HOMA IR ; B - total cholesterol (C-Chol)

F. HOMA IR > 1.5; n=77; 85.56%, HOMA IR ≤ 1.5; n=13; 14.44%



G. TC ≥ 5.17; n=23; 25.56%, TC < 5.17; n=67; 74.44%



As is apparent from the data presented in Table 2. (A) and Figure 1. (A, B, C) the values of plaque index (Pl.I), gingival index (GI) and sulcus bleeding index (SBI) were statistically significantly reduced after scaling and root planing at $p < 0{,}0001$ level, compared to their value before scaling and root planing. Table 2.(B) presents

Adipokine concentration in the studied women and Table 2. (C) gingival indicators before and after hygienisation.

The analysis of the data showed the average reduction of PI, GI and SBI, which was in line with the research of Christgau, Patricia et al., Ricardo FA et al. and Kiran et al. Rodrigues et al. and Kiran et al. reported in their studies that PI was reduced by 30-34% and GI was reduced by 19-25% [106-110].

Among studies assessing the impact of scaling and root planing (SRP) on the clinical and biochemical response to SRP in obese patients, six [61, 111-115] stated that obesity does not have a negative modifying impact on SRP outcome. On the other hand, three articles [116, 117, 118] suggested that obesity has a negative impact on the non-surgical periodontal therapy outcomes. Therefore, the impact of obesity on the response to non-surgical periodontal therapy remains uncertain to date.

Table 2. (A). characteristics of a group of 90 obese women in terms of clinical and biochemical parameters

Parameter	**All obese female patients: n = 90 Mean (Median) (Min - Max) [$Q_{25\%}$ - Q_{75}%] ***
Age (years)	41.7 (42.0) (35 - 49) [38 - 45]
BMI (kg/m^2)	39.0 (38.7) (33.9 - 44.3) [37.6 - 40.3]
WC (cm)	112.6 (112.0) (105 - 125) [109 - 116]
RRs (mmHg)	132.9 (130.0) (110 - 160) [120 - 150]

RRr (mmHg)	84.4 (85.0) (60 – 100) [75 – 95]
CHOL (mmol/L)	4.7 (4.4) (3.2 - 6.6) [4.1 - 5.2]
HDL (mmol/L)	1.54 (1.44) (0.73 - 3.30) [1.05 - 1.80]
TG (mmol/L)	1.22 (1.27) (0.66 -1.84) [0.94 -1.41]
LDL (mmol/L)	2.48 (2.28) (1.03 - 4.93) [1.93 - 2.84]
Glucose (mmol/L)	(5.11) (4.0 - 11.3) [5.1 - 5.4]
Insulin (IU/ mL)	14.8 (12.9) (2.1 - 54.9) [8.1 - 17.6]
HOMA-IR	3.60 (2.92) (0.61 - 13.18) [1.81 - 4.14]
CRP (ng/mL)	5.4 (3.9) (0.4 - 32.4) [2.7 - 5.2]

*BMI - body mass index; WC - waist circumference; RRs - systolic blood pressure; RRr - diastolic blood pressure; CHOL - total cholesterol; HDL - high-density lipoproteins; TG - triglycerides; LDL - low-density lipoproteins; HOMA-IR insulin resistance coefficient; CRP - acute phase protein, * Q - quartile*

Table 2 (B) Adipokine concentration in the studied women.

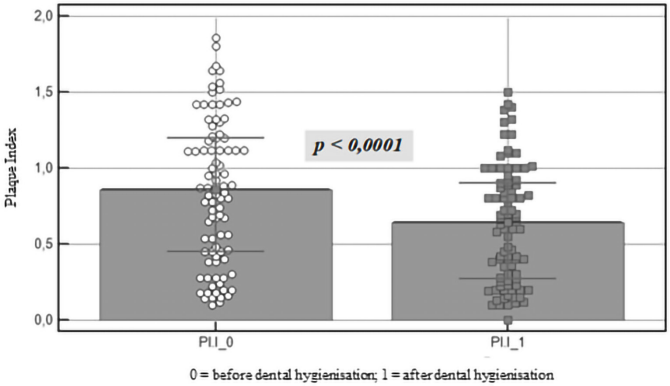
Parameter	mean, (median)	(min – max) [Q25% - Q75%]
Visfatin [ng /mL] n = 81	34,91 (32,56);	(3,2-80,54) [25,86-44,70]
Omentin [ng /mL] n = 55	637,68 (618,42);	(278,0-1401,84) [328,74-905,41]
Leptin [ng/mL] n=89	13,22 (13,08);	(5,65-19,80) [9,13-17,04]
VEGF2 [pg/mL] n=82	138,58 (105,0);	(49,02-340,0) [62,05-192,2]
HGF pg/mL} n=82	431,07 (367,50);	(128,18-1462,0) [282,5-454,71]

Table 2. (C). Characteristics of the group of 90 obese women surveyed in terms of oral hygiene indicators (Pl.I) and the condition of the gums (GI and SBI) before and after hygienization with statistical analysis

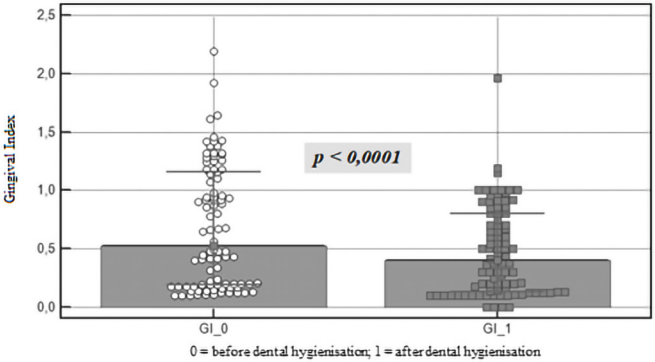
Clinical indicator	All obese female patients before dental hygienisation: n = 90 Mean (Median) (Min - Max) [$Q_{25\%}$ - $Q_{75\%}$]	All obese female patients after dental hygienisation: n = 90 Mean (Median) (Min - Max) [$Q_{25\%}$ - $Q_{75\%}$]	*The Wilcoxon signed-rank test result:*
Pl.I (plaque index)	0.85 (0.86) (0.10-1.86) [0.45 - 1.22]	0.63 (0.64) (0.00 - 1.50) [0.27 - 0.90]	*p < 0.0001*
GI (gingival index)	0.69 (0.53) (0.10 - 2.19) [0.19 - 1.16]	0.47 (0.40) (0.00 - 1.96) [0.13-0.80]	*p < 0.0001*
SBI: (sulcus bleeding index)	0.97 (0.81) (0.08-2.17) [0.34 - 1.70]	0.76 (0.61) (0.00 - 1.96) [0.21 - 1.34]	*p < 0.0001*

Figure 1. (A, B, C). Median and quartiles Q25% and Q75% of the values of A - oral hygiene indicators (Pl.I) and B and C - gingival condition (GI and SBI) in a group of 90 obese women before and after hygienisation

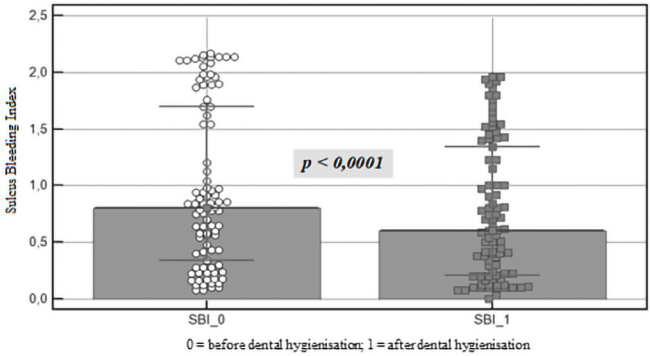
A.



B.



C.



As it can be concluded from the data presented in Table 3 and Figure 2 (A, B, C, D) and Figure 3 (A, B, C, D, E), prior to conventional periodontal therapy, a statistically significant positive correlation was shown between the sulcus bleeding index (SBI) and: body mass index (BMI), waist circumference (WC), the ratio of systolic blood pressure (RRs) and diastolic blood pressure (RRr), the concentration of cholesterol (C-Chol), the concentration of glucose and insulin, insulin resistance coefficient (HOMA-IR) and all metabolic syndrome features. However, prior to conventional periodontal therapy, no statistically significant correlation between the SBI and the age of female patients, or the concentration of CRP, triglycerides and HDL was found.

A stronger correlation has been observed between periodontitis and anthropometric measures of visceral fat accumulation than between periodontitis and the concentration of CRP, triglycerides and HDL. In point of fact, in one of the studies a significant relationship between periodontal disease and WC, without correlation to BMI

was reported [119]. This is consistent with the fact that abdominal adipose tissue secretes a variety of adipocytokines, which induce inflammatory processes and oxidative stress disorders, causing a chronic activation of the acute phase response and the development of insulin resistance (IR). In the same way, in some studies a direct relationship between periodontitis and overweight was identified [42, 120, 121].

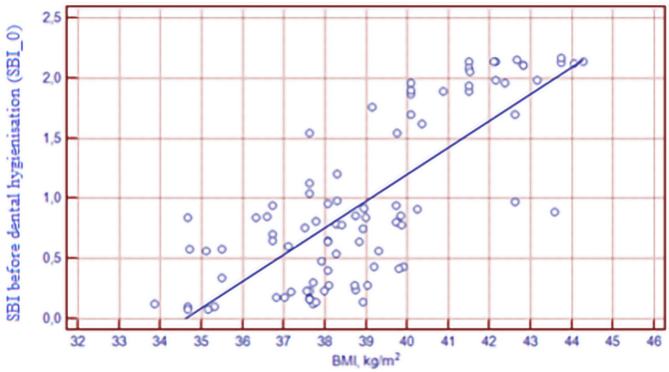
Table 3. Correlation coefficients between sulcus bleeding index (SBI) before dental hygienisation and clinical and biochemical parameters in the researched group of 90 obese women (n = 90).

PARAMETER	n	R (Spearman)	p-value	R (Pearson)	p-value
Age	90	0.053	0.614	0.061	0.571
BMI	90	0.740	**<0.0001**	0.767	**<0.0001**
WC	90	0.567	**<0.0001**	0.585	**<0.0001**
RRs	90	0.489	**<0.0001**	0.506	**<0.0001**
RRr	90	0.521	**<0.0001**	0.510	**<0.0001**
CHOL	90	0.545	**<0.0001**	0.645	**<0.0001**
TG	90	-0.054	0.613	-0.1032	0.336
HDL	90	-0.169	0.110	-0.190	0.860
Glucose	90	0.462	**<0.0001**	0.482	**<0.0001**
Insulin	90	0.553	**<0.0001**	0.448	**<0.0001**
HOMA-IR	90	0.594	**<0.0001**	0.465	**<0.0001**
CRP	90	0.137	0.197	0.141	0.394
The sum of metabolic syndrome characteristics	90	0.667	**<0.0001**	0.638	**<0.001**

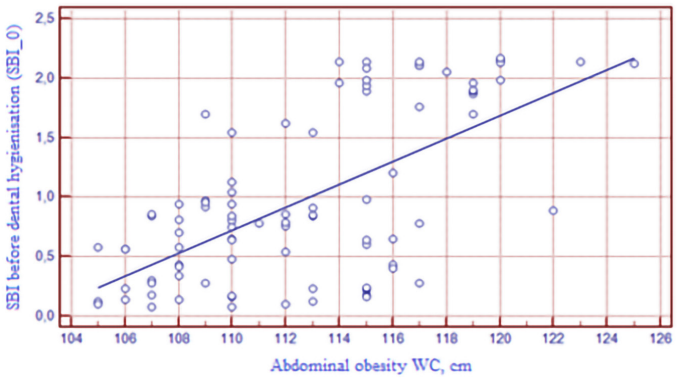
◀ *BMI - body mass index; WC - waist circumference; RRs - systolic blood pressure; RRr - diastolic blood pressure; CHOL - total cholesterol; HDL - high-density lipoproteins; TG - triglycerides; LDL - low-density lipoproteins; HOMA-IR insulin resistance coefficient; CRP - acute phase protein*

Figure 2. (A, B, C, D): Correlations between the SBI gingival bleeding index before hygienisation; body mass index BMI (A); WC waist circumference (B); RRs (C) and diastolic pressure RRr (D).

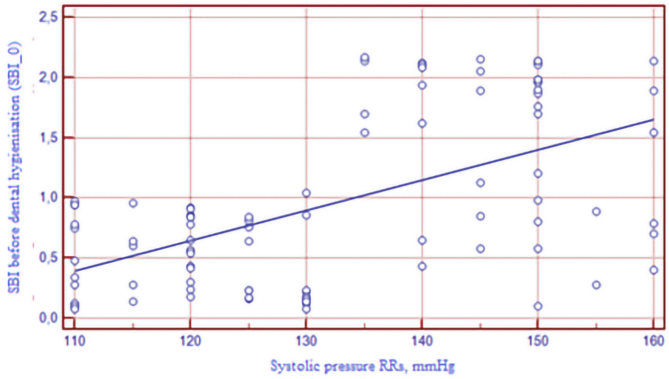
A



B.



C.


SBI before dental hygienisation (SBI_0)
2,5
2,0
1,5
1,0
0,5
0,0
110
120
130
140
150
160
Systolic pressure RRs, mmHg

D.

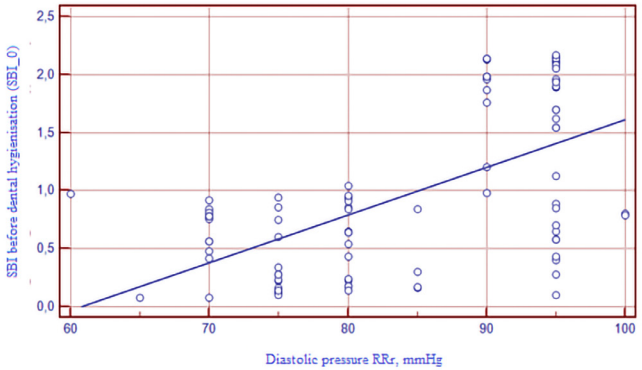
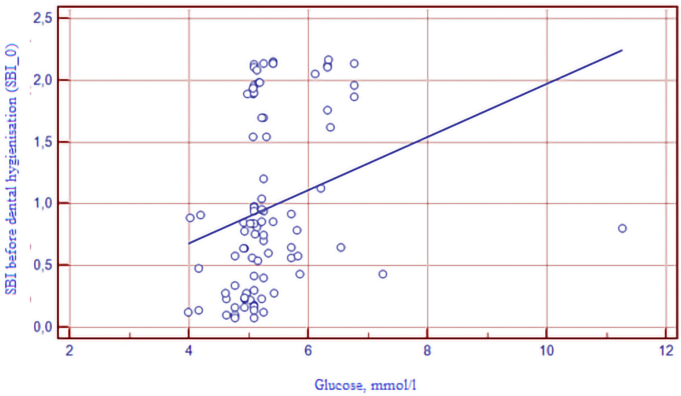
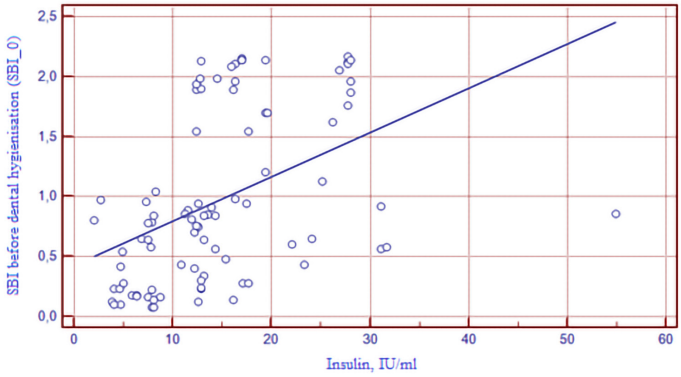

SBI before dental hygienisation (SBI_0)
2,5
2,0
1,5
1,0
0,5
0,0
60
70
80
90
100
Diastolic pressure RRr, mmHg

Figure 3 (A, B, C, D, E). Correlations between the SBI gingival bleeding index before hygienisation and: glucose concentration (A); insulin (B); HOMA-IR (C) insulin resistance index; cholesterol concentration (C) and the sum of metabolic syndrome factors (E).

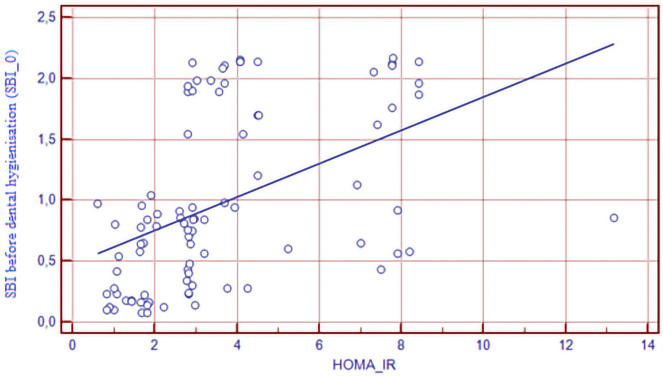
A.



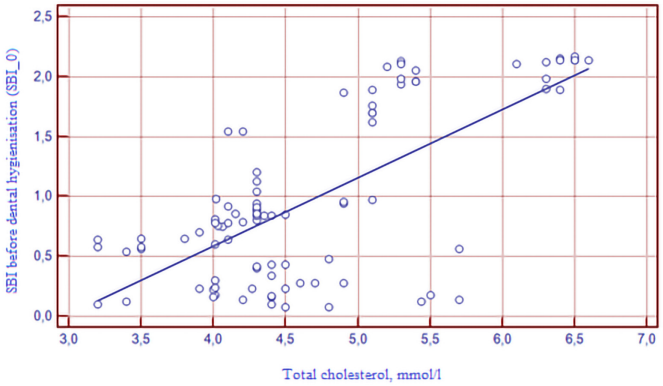
B.



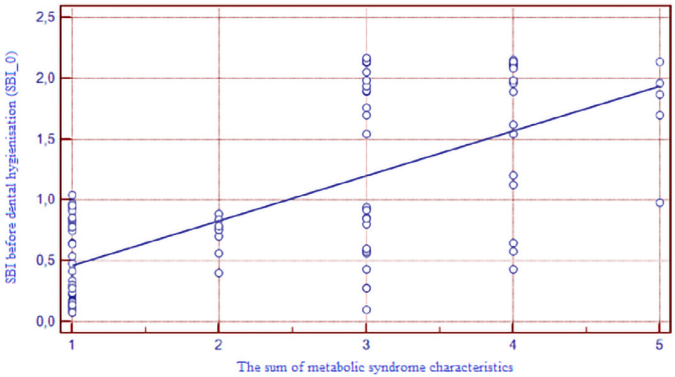
C.


SBI before dental hygienisation (SBI_0)
2,5
2,0
1,5
1,0
0,5
0,0
0
2
4
6
8
10
12
14
HOMA_IR

D.


SBI before dental hygienisation (SBI_0)
2,5
2,0
1,5
1,0
0,5
0,0
3,0
3,5
4,0
4,5
5,0
5,5
6,0
6,5
7,0
Total cholesterol, mmol/l

E.



As is apparent from the data presented in Table 4, among adipokines: visfatin, omentin, leptin and VEGF2 and HGF, only the growth factors, namely VEGF2 and HGF significantly correlated with the value of sulcus bleeding index (SBI) prior to conventional periodontal therapy. Vascular endothelial growth factor (VEGF), a 45-kd homodimeric pro-inflammatory glycoprotein that causes vascular permeability and angiogenesis, plays an important role in the development of chronic inflammatory disease [122]. It seems that this protein is involved in the onset and progression of gingivitis and parodontitis, mainly by promoting vascular network expansion generally observed in inflammation. In particular, its overexpression at the periodontium level has been found in patients with diabetes and periodontitis [123]. Studies [124,125] on molecular mechanism involved in the pathogenesis of diabetes suggest that VEGF plays an important role in microangiopathy and increases angiogenic response. Therefore, in diabetic

patients, important microvascular complications such as ischaemia, angiogenesis, multiple organ permeability and changes in blood glucose levels may be associated with VEGF. VEGF may be one of the factors associated with the aetiology of periodontitis in the early stages [126] and is involved in gingivitis progression in periodontal disease [127].

The role of HGF in periodontitis was reported after the reports of connective tissue attachment loss thus suggesting that HGF may be involved in epithelial invasion through its role as a scatter factor (SF). Ohshima et al. [128] in their study on the role of HGF system in epithelial invasion, suggested that synergistic expression of HGF in connective tissue and hepatocyte growth factor activator (HGFA) expression in epithelium may contribute to disease progression in periodontitis.

In the light of those publication, it seems likely that HGF and VEGF play their roles in periodontal disease.

Table 4. The values of correlation coefficients between SBI before dental hygienisation and adipokines in blood serum in the group of 90 obese women.

Parameter	Number of subjects (n)	R (Spearman)	p-value	R (Pearson)	p-value
Visfatin	81	0.020	0.854	0.187	0.217
Omentin	55	0.051	0.711	-0.076	0.619
Leptin	89	0.013	0.967	-0.015	0.307
VEGF2	82	0.529	**<0.0001**	0.305	**0.040**
HGF	82	0.563	**<0.0001**	0.468	**<0.0001**

VEGF2 - vascular endothelial growth factor; HGF - hepatocyte growth factor

As results from the data presented in Table 5, having analysed MODEL A, it was stated that the following factors significantly increase Sulcus Bleeding Index (SBI) before hygienization: number of metabolic syndrome factors (METABOL), value of the body mass index (BMI) and concentration values of total cholesterol (C-Chol). Whereas, as results from the data presented in Table 6, having analysed MODEL B, it was stated that the following factors significantly increase Sulcus Bleeding Index (SBI) before hygienization: value of systolic pressure sRR, value of insulin resistance ratio HOMA-IR, value of the body mass index BMI and level of total cholesterol concentration (C-Chol) .

Condition caused by untreated periodontitis leads to the occurrence of a systemic inflammatory phenotype, linked to some other disease / systemic disorders, including cardiovascular diseases [129], obesity [130], insulin resistance [131] and metabolic syndrome (MS) [132, 133, 134, 135]. Periodontitis was diagnosed on the basis of periodontium examination in seventeen scientific papers [41, 47, 136-150].

Table 5. The final assessment of the influence of the independent variables adopted in MODEL A on the dependent variable: SBI before dental hygienisation

MODEL A: Dependent variable: SBI before dental hygienisation (SBI_0)						
R = 0.8824 R^2= 0.7787; **p <0.0001**; Std. Error of Estimation: 0.3403						
Independent variable	**BETA**	**BETA st. error**	**B**	**B st. error**	**t(85)**	**p-value**
Intercept			-5.3372	0.6436	-8.2926	**0.0000**
METABOL	0.3875	0.0586	0.2063	0.0312	6.6178	**0.0000**
BMI	0.4337	0.0695	0.1245	0.0200	6.2362	**0.0000**
CHOL	0.2505	0.0678	0.2061	0.0558	3.6934	**0.0004**

Model A scheme.

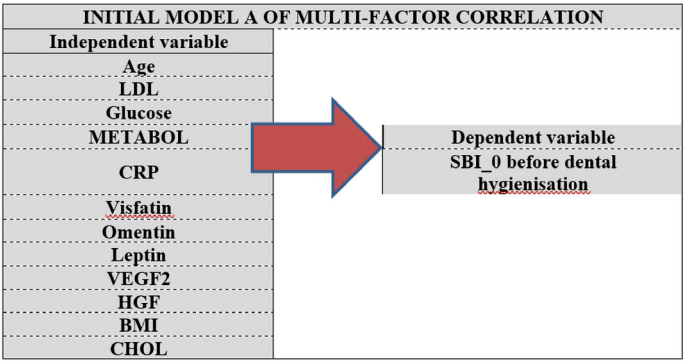


Table 6. The final assessment of the influence of the independent variables adopted in MODEL B on the dependent variable: SBI before dental hygienisation.

MODEL B: Dependent variable: SBI before dental hygienisation (SBI_0)						
R = 0.87308; R^2= 0.76227; **p <0.0001**; Std. Error of Estimation: 0.3548						
Independent variable	**BETA**	**BETA st. error**	**B**	**B st. error**	**t(31)**	**p-value**
Intercept			-6.7352	0.6599	-10.2062	**0.0000**
RRs	0.2543	0.0586	0.0115	0.0026	4.3359	**0.0000**
HOMA_IR	0.1894	0.0569	0.0556	0.0167	3.3305	**0.0013**
BMI	0.4394	0.0728	0.1262	0.0209	6.0328	**0.0000**
CHOL	0.2761	0.0703	0.2272	0.0579	3.9259	**0.0002**

Model B. Scheme

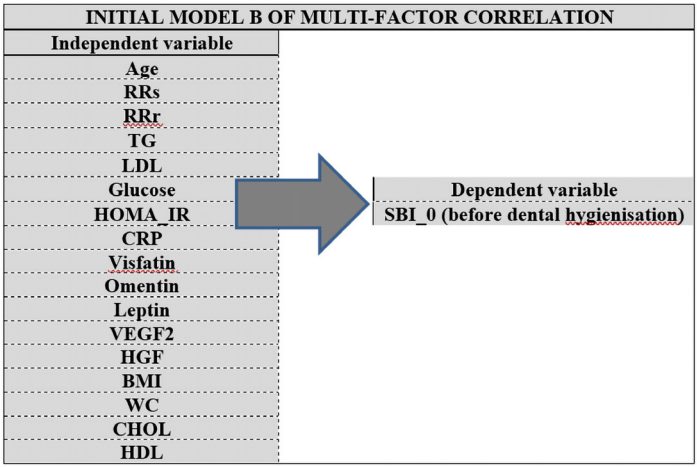
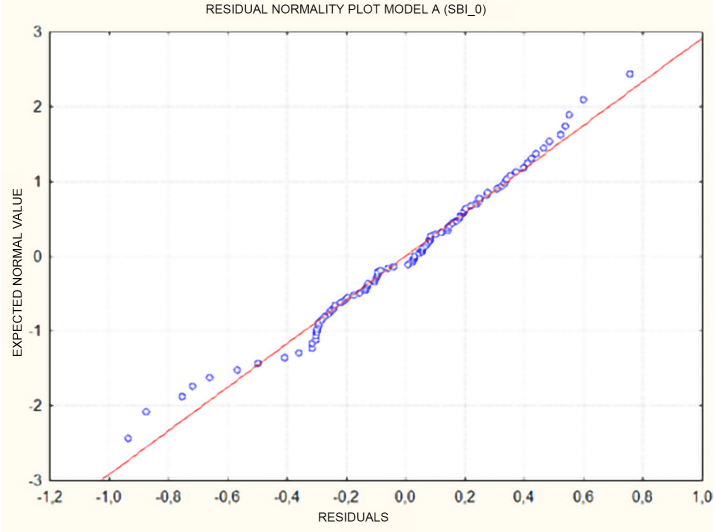
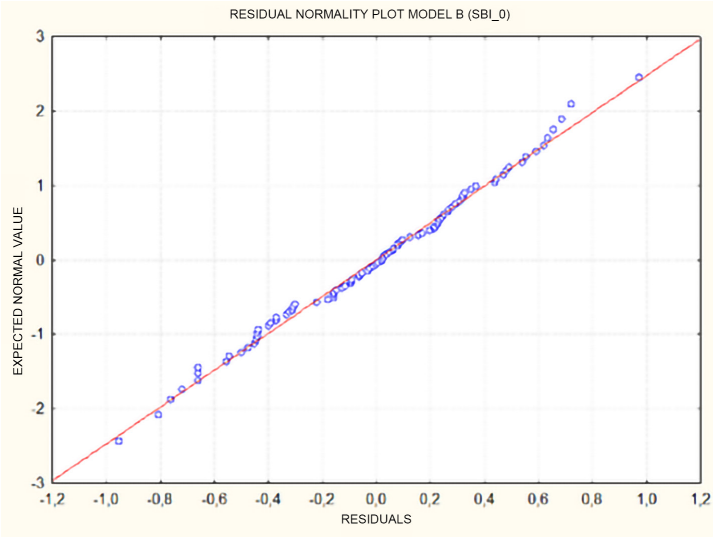


Figure 4. (A, B). Correlations between the SBI gingival bleeding index before hygienization and: vascular endothelial growth factor VEGF2 (A) and hepatocyte growth factor HGF (B)

A.



B.



Summary

Obesity constitutes one of the main health-related problems in 21st century. Harmful consequences obesity has on overall health condition indicate the need of further studies concerning correlations between excessive fat tissue in human body and the effect it exerts on the development of general diseases, including oral cavity diseases. Results of clinical studies referring to the effect of obesity on oral cavity condition seem to suggest that obese persons have intensified inflammatory reactions, and maybe even different periodontal micro-flora [76]. Taking into account the fact that response of the host on local bacterial threat constitutes the key determining susceptibility to periodontal disease, intensified inflammatory process observed in obese people may predispose them for more intense deterioration of periodontal tissues [151]. Numerous studies show that obesity and periodontitis may, individually or combined, affect local and systemic levels of adipokines, mainly pro-inflammatory ones.

In the light of the literature review and our research, further research on obesity as a risk factor for inflammatory periodontitis appears to be highly recommended. An explanation and understanding of possible causal links between obesity and periodontitis development is highly desirable to confirm or reject thesis that aforementioned afflictions are interlinked.

Conclusions

1. The number of metabolic syndrome features in the study group of obese women is closely related to the observed intensity of gingivitis.

2. The presence of arterial hypertension, considerable body weight and carbohydrate metabolism disorder had the biggest impact on gingivitis in obese women.

3. The levels of adipocytokines in the blood are well reflected in gingivitis.

4. The prognostic markers in the peripheral blood test for early periodontitis are: insulinemia, glycaemia and cytokines.

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