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COVID-19 AND MASSIVE EMBOLISM

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ABSTRACT

Objective : Hospitalized patients with COVID-19 were characterized by a high rate of thromboembolic complications and in hospital mortality.
The exact mechanisms of COVID-19 induced thrombosis have not been elucidated.
The early pathogenesis in COVID-19 (Huertas *et al*.) pneumonia defined by a widespread endotheliilitis affecting multiple organ systems, viral inclusion are observed within endothelial cells accompanied by apoptosis, inflammatory cell infiltration and microvascular thrombosis.
The primary infection initiates alveolar injury and the resulting inflammatory response, including production of inflammatory cytokines, including IL-6, as well as activation and recruitment of mononuclear cells and neutrophils causing more tissue damage, including damage to the capillary endothelium. In addition to the procoagulant effectors derived as the result of inflammation the usual thrombo-protective state of the vascular endothelial cells is disrupted;
Both pathophysiologic changes lead to the development of microvascular thrombosis. Over time the pathology of ARDS progresses to a proliferative and then a fibrotic state, which is fatal.
We presented one case when the patient developed severe respiratory failure after massive pulmonary embolism and coma after ischemic stroke. Patient had many comorbidities with COPD, heart failure (HFrEF) and diabetes mellitus.
Conclusion: High values of d-dimer could be related to a higher activation of blood coagulation in COVID-19 patients secondary to a systemic inflammatory response syndrome – or as a direct consequence of the SARS-CoV-2 itself. Pulmonary thrombosis was the confluence of processes, endothelial inflammation with no evidence of DVT. Tissue factor, up-regulated on platelets, leucocytes during inflammation, leading to activation coagulation pathways and promote the formation of fibrin. The profound hypoxaemia is a likely driver of vasoconstriction, inflammation and thrombosis. The origin of Covid-19-associated pulmonary emboli and lung microcirculatory thrombotic disease: Interaction of inflammation and coagulation
Keywords: Thrombosis, Pulmonary embolism, inflammation.

Introduction: Hospitalized patients with COVID-19 were characterized by a high rate of thromboembolic complications and in hospital mortality.
The exact mechanisms of COVID-19 induced thrombosis have not been elucidated.
The early pathogenesis in COVID-19 (Huertas *et al*.) pneumonia defined by a widespread endotheliilitis affecting multiple organ systems ,viral inclusion are observed within endothelial cells accompanied by apoptosis, inflammatory cell infiltration and microvascular thrombosis.
The primary infection initiates alveolar injury and the resulting inflammatory response, including production of inflammatory cytokines, including IL-6, as well as activation and recruitment of mononuclear cells and neutrophils causing more tissue damage, including damage to the capillary endothelium. In addition to the procoagulant effectors derived as the result of inflammation the usual thrombo- protective state of the vascular endothelial cells is disrupted;
Both pathophysiologic changes lead to the development of microvascular thrombosis. Over time the pathology of ARDS progresses to a proliferative and then ultimately a fibrotic state, which is fatal. We presented one case when the patient developed severe respiratory failure after massive pulmonary embolism and coma after ischemic stroke. Patient had many comorbidities with COPD, heart failure (HFrEF), chronic renal failure and diabetes mellitus.
Patient, male, 70 years old, was admitted in our hospital with respiratory failure and coma. Patient was started mechanical ventilation. CTPA revealed massive pulmonary embolism and bilateral infiltrates. Thrombotic masses are reflected at different levels in the bilateral pulmonary arteries. Areas of infarction-pneumonia are detected against the background of the right basal infiltration.

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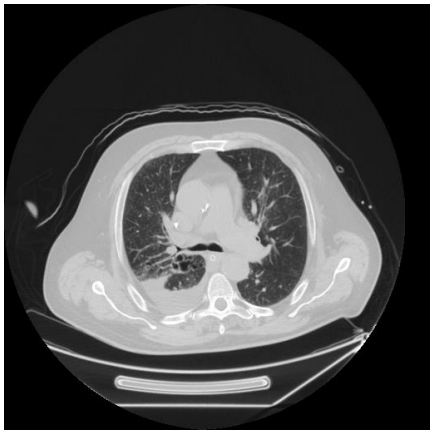
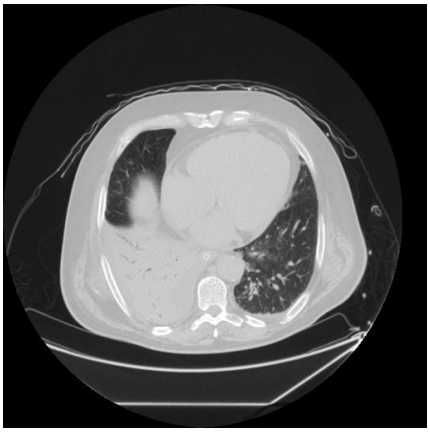
a  b 

Figure 1

Figure 1. 05/10/2020. Computed tomography, axial section. Lung window. Incision at the level of the tracheal bifurcation
a. Incision at the level of the basal segments of the lung
b. In the right parenchyma of the lung, there are foci of bronchiectasis and extensive basal compaction-infiltrative changes

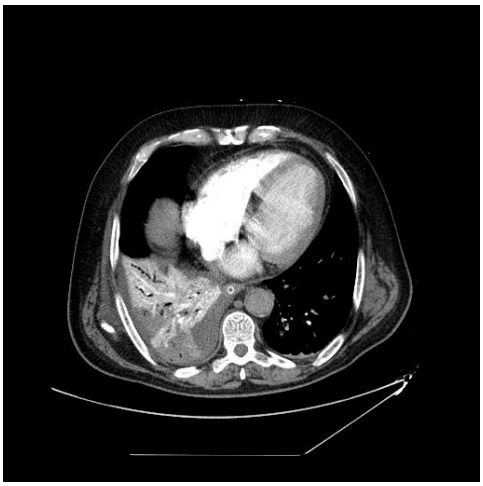
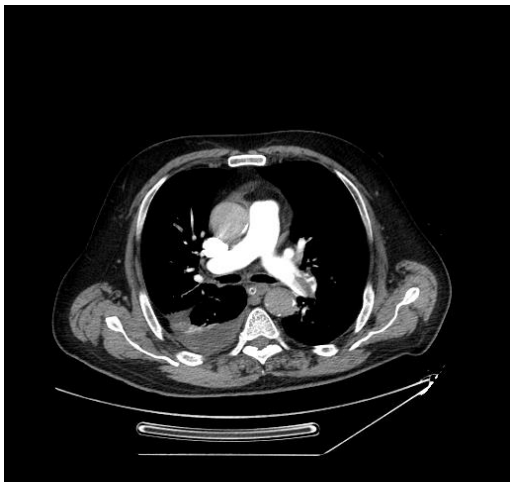
a  b 

Figure 2

Figure 2. 10.05.2020. Computed tomography, axial section. Vascular window. Incision at the level of basal segments
a. Incision at the level of the main arteries of the lung
b. Thrombotic masses are reflected at different levels in the bilateral pulmonary arteries. Areas of infarction-pneumonia are detected against the background of the right basal infiltration.

Echocardiographic findings of RV overload and/or dysfunction not detected, but was revealed left ventricle disfunction, EF -20 %,. RV dilation was not found on transthoracic echocardiography (TTE). The combination of a pulmonary ejection acceleration time (measured in the RV outflow tract) with a peak systolic tricuspid valve gradient was not present. PASP - 40 mm.Hg. “Buble” test was negative.
Pulmonary Embolism Severity Index (PESI) to assess a patient’s overall mortality risk and early outcome, was >125 points (Class V), was identify of very high mortality risk(10-24.5%)
.Haemodynamic instability(pressure ,supporting by norepinephrine), combined with PE confirmation on CTPA was sufficient to classify a patient into the high-risk PE category, but calculation of the PESI and measured of troponins (cardiac biomarker was high) essed the patient like in high mortality risk.

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Very elevated levels of D dimer have been observed, that was correlated with illness severity , like a marker of PE ,infectious and inflammatory diseases .
Venous thromboembolism (VTE) , including deep vein thrombosis was not detected .
Treatment was followed the ESC guidelines focusing on the clinical management of pulmonary embolism (PE) published in 2019
CT scan of brain was detected acute haemorrhagic infarction (Hemorrhagic transformation after cerebral infarction) in the right parietal lobe. There was a hypodenseous zone 5-6 cm, with blood-density inserts in the cortex and the phenomenon of periventricular luminescence, without displacement of the middle structures. Picture of cortical venous thrombosis and venous infarction in the right parietal lobe of the brain. Leukomalacia, leukoencephalopathy, cortical atrophy. Figure 3.

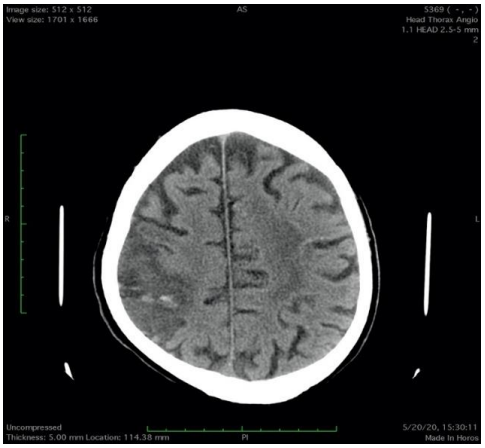
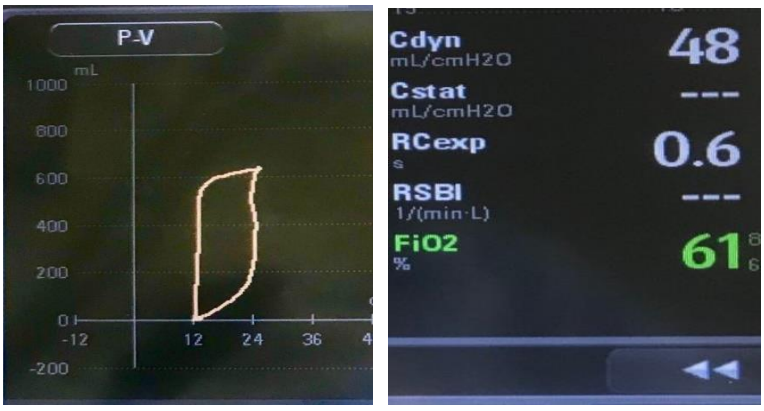


Figure 3
CT scan of brain was detected acute haemorrhagic infarction (Hemorrhagic transformation after vein cortical thrombosis and cerebral infarction) in the right parietal lobe.

Initial level of D dimer was high -20 mkg/ml ,Hs Troponin --24 ng/ml, Ferritin—430 ng/ml, IL-6—28.24 mkg/l, CRP-70mg/L PaO_2/FiO_2 <150 , patient was ventilated with DUOLEVEL mode and High PEEP-- 12 cm.H_2O , compliance C dyn -48ml/cm H_2O ,P plat -22 cm.H_2O



Laboratory finding:

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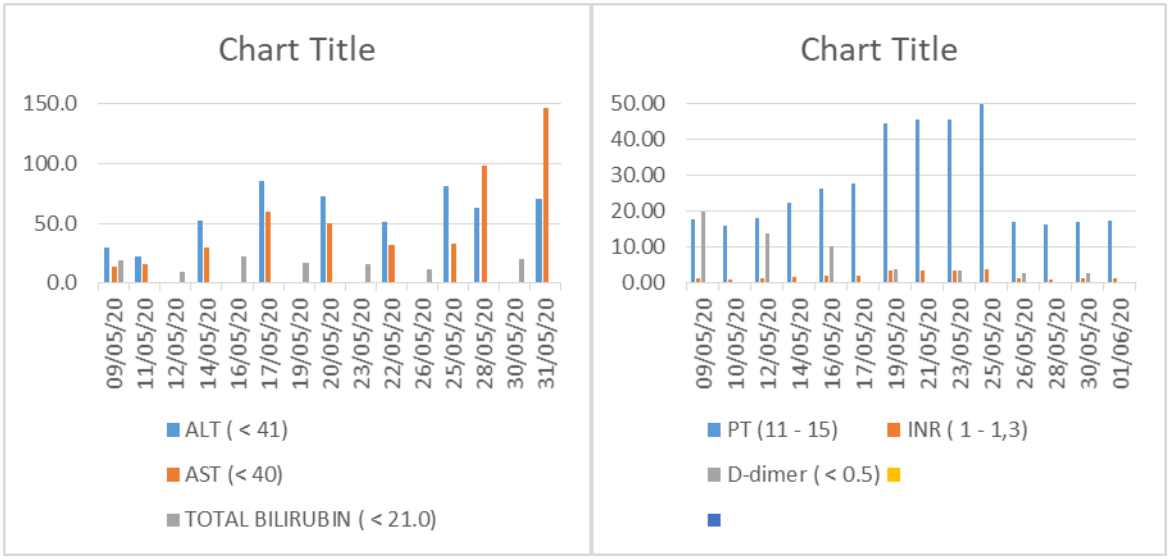

Table 1

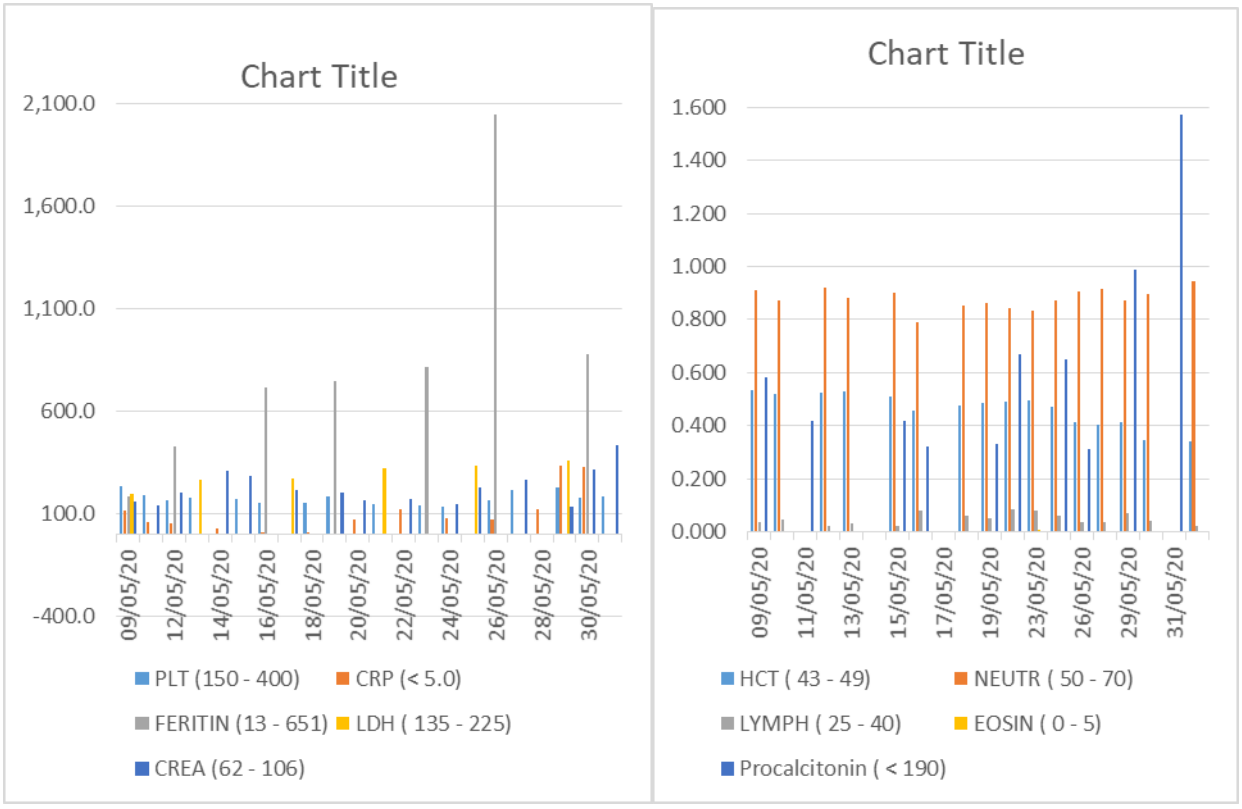

Table 2

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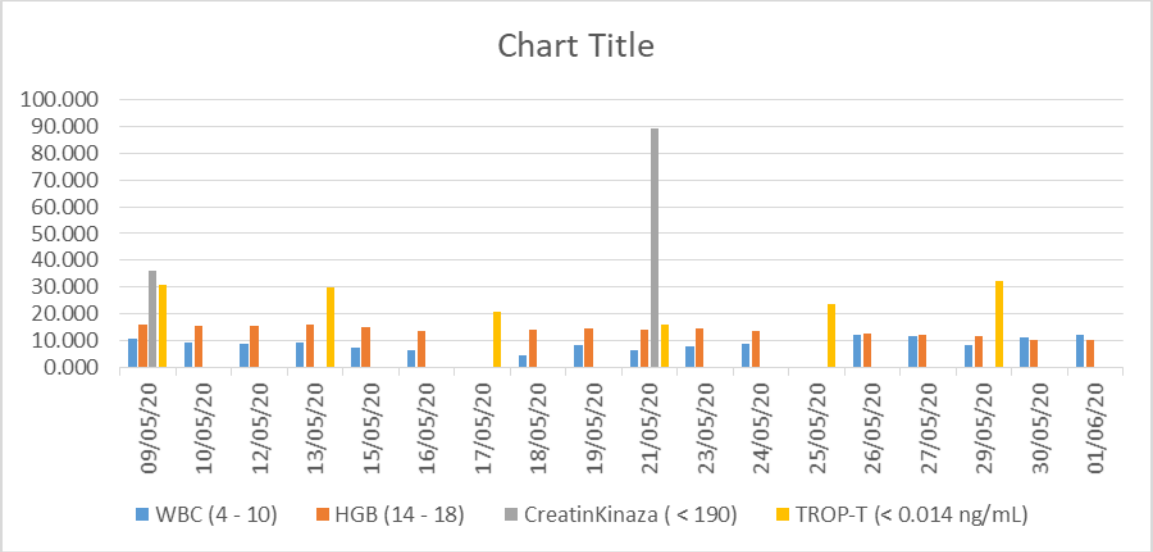

Table 3

Patient state was improuved. On the CT scan of brain was observed Blood density areas reduction In right parietal lobe .The density of haemorrhagic area is reduced(- positive X-ray dynamic). Fig.4

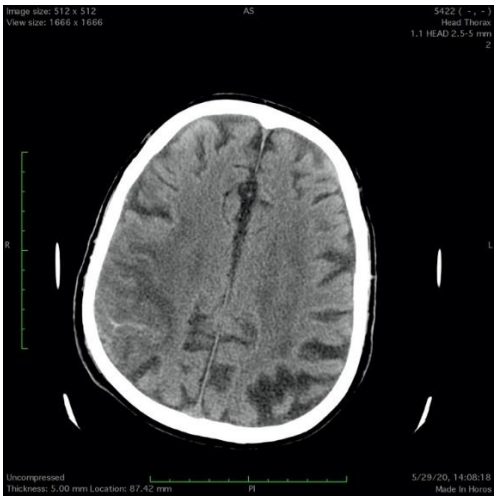

Figure 4

In the trunk of the pulmonary artery and in the main arteries a thrombus doas not revealed (Fig 5), but The volume of extensive inflammatory changes was reduced with thickening of interlobal pleuras.

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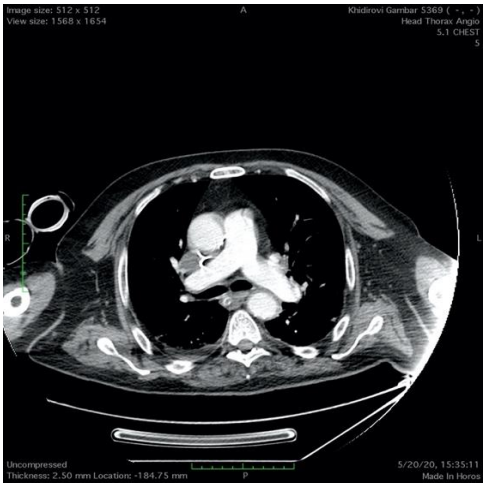
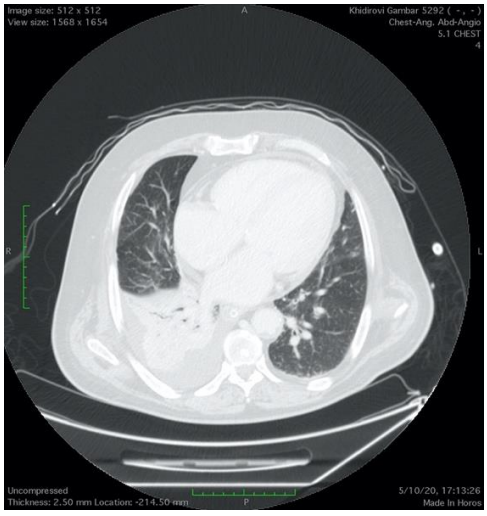


Figure 5

Thrombotic masses are no longer reflected in the lumen of the bilateral main artery in the pulmonary trunk. Against the background of the existing consolidation, a small triangular avascular zone is revealed.
Extensive consolidating infiltrative changes in the lower right part are reduced, it is observed the interlobar pleura is thickened on the same side, bronchiectasis in the upper part and bullous changes in the apex, mixed infiltrative changes in the middle lobe. The infiltration volume of the upper lobe was slightly increased, bilateral hydrothorax.(Fig.6)

a 

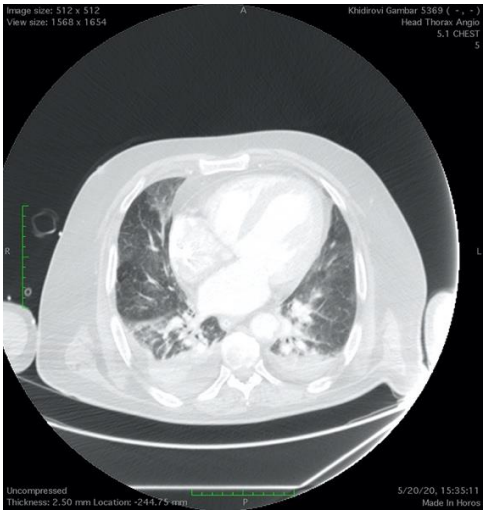
b 

Figure 6

a. In the lower part of right lung extensive inflammatory and consolidation lesions ,with airal bronchogramm.
b. The volume of extensive inflammatory changes is reduced with thickening of interlobal pleuras.

We presented case of vein embolism in the brain and in the bilateral pulmonary arteries in patient where comorbidities was different .Laboratory finding has shown changes of base parameters on different stage of illness and with correlation of disease severity(Table 1.2.3.) .
Bilateral pneumonia, systemic inflammation, endothelial dysfunction, coagulation activation, massive embolism, acute respiratory distress syndrome,coma and multiorgan failure we have described as key features of severe COVID-19 ilnes patient .
Hypothesis of the origin of Covid-19-associated pulmonary emboli and lung microcirculatory thrombotic disease: Interaction of inflammation and coagulation. active replication and release of the virus may cause the host cell to undergo pyroptosis (pro-inflammatory apoptosis) and release damage-associated molecular patterns, activating oxidant stress, and

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generating pro-inflammatory cytokine and chemokine release from nearby epithelial cells, endothelial cells and alveolar macrophages. Tissue factor, from the subendothelium, is upregulated on platelets, leucocytes and EC during inflammation, leading to activation of both the extrinsic and intrinsic coagulation pathways. Occluded small pulmonary blood vessels are likely to contain fibrin, platelets and coagulation factors, as well as neutrophils that pass through the lung.The infection initiates alveolar injury and the resulting inflammatory response, production of inflammatory cytokines, IL-6, which has been demonstrated significantly elevated in our patients, as well as activation and neutrophils causing more tissue damage, including damage to the capillary endothelium, resulting in microvascular thrombosis and VTE.

Conclusion: High values of d-dimer could be related to a higher activation of blood coagulation in COVID-19 patients secondary to a systemic inflammatory response syndrome – or as a direct consequence of the SARS-CoV-2 itself. Pulmonary thrombosis was the confluence of processes, endothelial inflammation with no evidence of DVT . Tissue factor, upregulated on platelets, leucocytes during inflammation, leading to activation coagulation pathways and promote the formation of fibrin. The profound hypoxaemia is a likely driver of vasoconstriction, inflammation and thrombosis. The origin of Covid-19-associated pulmonary emboli and lung microcirculatory thrombotic disease: Interaction of inflammation and coagulation.

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REPARATIVE OSTEOGENESIS IN DIABETES MELLITUS

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ABSTRACT

This study is intended for systematic analysis aimed at assessing the correlation between markers of bone metabolism and bone mineral density in patients with diabetes mellitus, for early prediction of destructive changes in bone tissue. Clinically, remodeling markers and bone mineral density are independent predictors of bone changes. However, the results of the analysis showed that the measurement of bone remodeling markers is more informative in type 2 diabetes compared with x-ray absorptiometry.

Key words: diabetes mellitus; bone remodeling markers; osteopathy

INTRODUCTION

Recent studies have identified osteopathy as a serious complication of diabetes mellitus (DM), refers to secondary osteoporosis, the prevalence of which is about 30-50%, is one of the promising areas of research. Diabetic osteopathy increases the risk of fractures due to a decrease in bone strength and quality, leading to a high level of disability and mortality [1]. According to statistics, over 9 million osteoporotic fractures occur worldwide every year. The incidence of hip fractures in people with type 1 diabetes mellitus (T1DM) was 383 per 100,000, which is six times higher than the incidence of hip fractures in the general non-diabetic population. The ratio of the risk of vertebral fracture in patients with type 2 diabetes mellitus (T2DM), according to statistics, is 1.86 higher in women and 4.73 in men, compared with the general population [8].

In T1DM, as a result of insulin deficiency, bone formation slows down, while bone resorption is relatively accelerated, leading to a decrease in bone density, impaired mineralization and bone microarchitectonics [5]. Bone metabolism disorders in patients with T2DM occur somewhat differently [9]. Individuals with T2DM have a 10–30% higher risk of vertebral, hip and other bone fractures than patients without diabetes who are comparable in age [4]. Bone loss is, in part, related to age, which makes the risk higher in the geriatric population (≥65 years). The risk remains high even after adjusting for factors contributing to fall, such as sensorimotor deficits and neuropathy [2, 6]. However, the paradox of low-traumatic fractures arising in type 2 diabetes is that data on bone mineral density (BMD) in the overwhelming number of patients with type 2 diabetes, in most published studies, indicate its increase, similar to what is observed in obese subjects, but at the same time, despite the relatively increased BMD, there is a decrease in the quality of the bone, its micro- and macroarchitectonics [3, 5]. This makes it difficult to properly screen this category of patients with a high risk of developing fractures.

Recent studies show that in patients with diabetes mellitus, bone metabolism is affected by the coincidence of many factors, such as hyperinsulinemia, obesity, as well as factors that lead to increased bone resorption [7]. Effective control of the glycemic profile have great importance for maintaining bone mass in patients with diabetes mellitus [8].

The study of the pathogenetic mechanisms of bone disorders in diabetes-related risk factors for osteoporosis are important in terms of the formation of risk groups and the timely implementation of preventive measures in patients with type 1 and type 2 diabetes.

AIM

To assess the effect of changes in the body of men and women with type 1 and type 2 diabetes on the state of bone mineral density and metabolic rate. Determine the direction of changes in serum markers of bone remodeling and bone mineral density of both gender patients with this disease.

MATERIALS AND METHODS

The research was provided according to the principles of the Helsinki Declaration and was approved by the Health Research Ethics Committee of Azerbaijan Medical University. After an explanation of the aim of the study, written informed consent from each participant was received.

98 patients with T1DM (57 female and 41 male) and 137 (52 men, 85 women) with T2DM were included into the study. The average of patients with T1DM was 55.8 ± 0.7 years, with T2DM was 58.9 ± 1.5 years. Duration of diabetes was 16.6 ± 0.6 and 8.1±0.7 years, BMI was 26.07 ± 0.2 and 30±0.4 kg / m2, HBA1c was 7.4 ± 0.2% and 7.9 ± 0.6%. The nondiabetic control group consisted of 82 patients (F: 48 and M: 34, mean±SD age 55.97 ± 0.9). Investigated the parameters of phosphorus-calcium metabolism (Ca 2+, P), calcitrop hormones level: 25 (OH)D3, PTH, Calcitonin, level of bone formation markers: alkaline phosphatase (ALP), aminoterminal propeptide of procollagen type I (PINP) and bone

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resorption marker - C-terminal telopeptide (b-CTx) by the immune-enzyme analysis method. The bone mineral density (BMD) measured by DXA absorptiometry at the lumbar spine (L1-L4), proximal femur and femoral neck area.
Statistical analyses were performed with standard software package "BioStat Pro 6.2.2.0". Statistical analysis was done using unpaired parametric data analyzed by Mann—Whitney U test. Spearman's rank correlation was calculated to assess the power of connection between the parameters. For all analyses, a value of $p < 0.05$ was considered statistically significant.

RESULTS

The results of the study demonstrated that the content of serum bone remodeling markers in patients with T1DM and T2DM, in comparison to the control group, indicate pathological processes in bone remodeling with decrease bone formation marker PINP in patients with T1DM by 16%, with T2DM by 12% in comparison with the control and an increase bone resorption marker b-CTx by 32% with T1DM and in 25% patients with T2DM, of whom of women were 1,5 times more than men. Patients with T2DM had lower b-CTx values and a relatively higher level of P1NP, which reflects a less pronounced change in bone turnover compared to patients with T1DM, regardless of age and duration of disease. T-score BMD of L1–L4 area was reduced in 64 and 44% of patients with T1DM and T2DM; T-score BMD of femoral neck area— in 41 and 36% of patients (Fig.1).

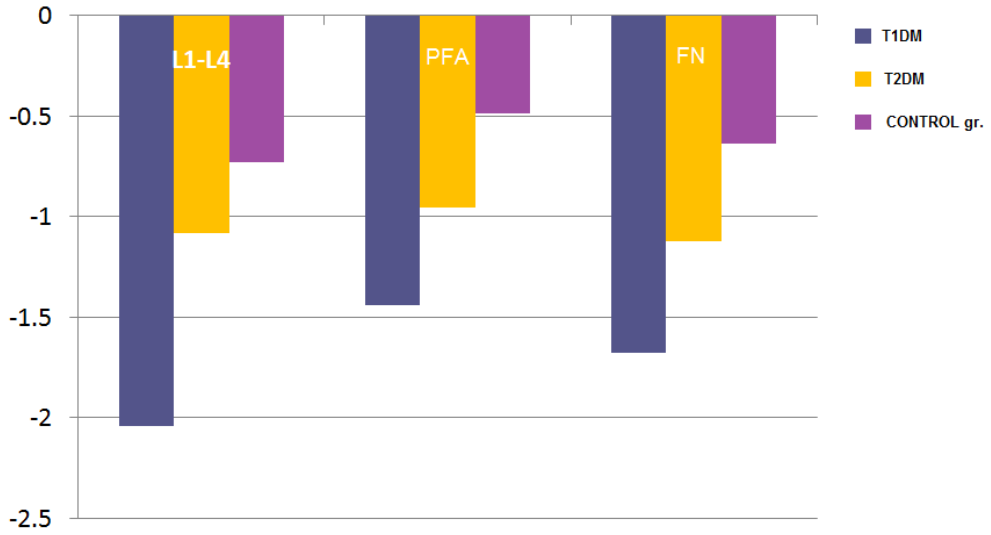

Figure 1. BMD assessment at the T-SD L1-L4, PFA and FN area in patients with T1DM, T2DM and a control group

DISCUSSION

The data has shown that females have the lowest T-score for lumbar spine and left hip, accounting for a total of 42% and 13% of the total population of patients with diabetes.It got noted that, low bone mineral density in patients with diabetes is associated with an increased bone resorption. The level of bone resorption marker b-CTx in patients with diabetes was higher in comparison with control group. Moreover, in male with T1DM, a statistically significant increase in the level of b-CTx ($p<0.05$) was observed in comparison with the control group. In T2DM, disorders of bone remodeling processes was accompanied by less significant changes in BMD.The study showed a relative increase in the concentration of b-CTx in the blood serum in patients with type 2 diabetes mellitus, which indicates bone resorptive activity. This observation indicates a slight increase in osteolysis in the considered group of patients, which may be accompanied by normal or slightly reduced bone mineral density and reflects on an increased risk of bone fractures, which is consistent with the data of a number of studies [5,8].
Authors who conduct similar studies also have showed that the bone resorption processes in patients with T2DM in most cases are within the reference values [1] or slightly increased compared to a decrease of bone formation processes [8,10], and only in a small the number of cases it can be reduced [2,7]. A slight decrease in serum P1NP levels in type 2 diabetes may be associated with inhibition of osteoblast function due to impaired insulin secretion and increased insulin resistance [10]. As the duration of diabetes increased, there was a decrease in the level of formation markers due to hyperglycemia-induced inhibition of osteoblastic function. Apparently, an increase in blood glucose levels suppresses bone formation and

increases markers of bone resorption in T2DM, which is consistent with the findings of Achemlal et al. [1]. A decrease in bone turnover in patients with type 2 diabetes mellitus with a decrease in bone formation and an increase in bone resorption, which is manifested by a low concentration of P1NP and a relatively increased concentration of b-CTx, was shown by Gilbert et al. [4]. Other researchers have also noticed a significant decrease in the activity of alkaline phosphatase as a marker of bone formation in patients with type 2 diabetes mellitus [10]. Our study found no significant differences in ALP values. Also, the role of glycemic control in maintaining bone mass in diabetes should be emphasized. The data support that bone formation abnormalities are mainly observed in patients with poorly controlled diabetes. Studies indicate that the end products of glycolysis inhibit osteoblast function [5,7]. Puspitasari et al. [8] showed that restoration of metabolic control of diabetes mellitus within a short time leads to inhibition of bone resorption and stabilization of bone mineral density. Other authors observed a negative correlation between the concentration of b-CTx and HbA1c, which may indicate the activation of resorptive processes in the bone tissue in patients with type 2 diabetes mellitus and the restoration of metabolic processes in the bone while improving the metabolic control of diabetes [1]. In our study, we did not confirm this connection. The concentration of b-CTx in the study group of patients was significantly associated with PTH ($r = 0.434$, $p = 0.001$), which may indirectly indicate a relationship between calcium-phosphorus metabolism and an increase in bone resorption. This association was seen in Yendt et al. [10], who showed a positive correlation between PTH and calcium clearance, BMD, and bone mass.According to the results of the study of the T-score for lumbar spine area, BMD was reduced in 44% of patients with DM2; in the area of the femoral neck in 36% of patients. Given from these studies, it is important to remember that fractures in patients with T2DM can occur even at high BMD values [1]. These results suggest that bone disorders and associated fracture risks are a clinically significant and often underestimated problem in type 2 diabetes.

The results of the study demonstrated that the content of markers of bone metabolism in the blood serum of patients with T2DM in comparison with the control group indicates a decrease in the bone formation marker PINP in patients with T2DM by 12%, in comparison with the control group and an increase in the marker of bone resorption b-CTx in 25 % of patients with type 2 diabetes, of which women were 1.5 times more than men. Patients with T2DM had lower b-CTx values and relatively higher P1NP levels, which reflects less pronounced changes in bone metabolism, regardless of age and duration of the disease. According to the results of the study of the T-score of the L1-L4 region, BMD was reduced in 44% of patients with DM2; in the area of the femoral neck in 36% of patients. These results suggest that bone disorders and associated fracture risks are a clinically significant and often underestimated problem in diabetes.

CONCLUSION

The results of T-score studying, confirmed that in both men and women with diabetes, in comparison with the control, the bone density in the vertebrae was reduced. The level of b-CTx showed a statistically significant negative correlation with the BMD of the lumbar spine, consisting mainly of a spongy bone with high metabolic activity. This indicates that both bones metabolism markers and DXA can be considered as independent indicators of changes in bone tissue, which can be of great importance for early diagnosis and evaluation of the effectiveness of the therapy.

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ANTI-STAPHYLOCOCCAL AND ANTI-PSEUDOMONAS ACTIVITY OF LACTOBACILLUS PLANTARUM MAL

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ABSTRACT

Lactobacillus plantarum Mal strain was screened against clinical isolates of 10 Staphylococcus aureus and 5 Pseudomonas aeruginosa that had isolated from patients diagnosed with Atopic dermatitis and Phlegmon. Antibiotic resistance of the isolates was checked against dozen widely used antibiotics in dermatology representing different classes and subsequently, Lactobacillus plantarum Mal was subjected for the antagonistic activity against the clinical isolates. Lactobacillus plantarum Mal strain showed antagonistic activity against all the isolates of Staphylococcus aureus and Pseudomonas aeruginosa with average inhibition zone of 27.95 mm and 28.22 mm, respectively.
The research results suggest that the strain could be very promising for targeting antibiotic resistant bacteria strains.
Keywords: Pseudomonas aeruginosa, Staphylococcus aureus, Lactic acid bacteria, Lactobacillus, antibiotics

АННОТАЦИЯ

Штамм Lactobacillus plantarum Mal подвергали скринингу в отношении клинических изолятов 10 штаммов Staphylococcus aureus и 5 штаммов Pseudomonas aeruginosa, выделенных у пациентов с диагнозом Атопический дерматит и Флегмона. Устойчивость к антибиотикам данных изолятов была проверена на широкоприменяемых в дерматологии антибиотиках, представляющих различные классы. В дальнейшем, антогонистическое действие штамма Lactobacillus plantarum Mal проверили против выделенных у дерматологических больных клинических изолятов. Штамм Lactobacillus plantarum Mal продемонстрировал антагонистическую активность в отношении всех изолятов Staphylococcus aureus и Pseudomonas aeruginosa. При этом, зона ингибирования составила в среднем 27,95 и 28,22 мм соответственно. Результаты исследований показывают, что этот штамм может быть очень перспективным в борьбе с бактериальными штаммами, устойчивыми к антибиотикам
Ключевые слова: Pseudomonas aeruginosa, Staphylococcus aureus, антибиотики, лактобактерии,

BACKGROUND

One of the most promising ways targeting any microorganism might be addressed by using antagonistic microorganisms. It is now a common knowledge that Lactic acid bacteria (LAB) strains play a key role in microbiological balance in the human body and they are considered to have a huge potential in targeting both sensitive and resistant bacteria strains including, *Staphylococcus aureus* and *Pseudomonas aeruginosa* strains.
LAB strains are the majority part of the human gut microbiome and antagonism against other microorganisms is one of the main characteristics for them. They could inhibit any pathogens or conditional pathogens by producing different substances, such as lactic acid, acetic acid, hydrogen peroxide and antimicrobial peptides – bacteriocins to the surroundings. In patients suffered from Atopic dermatitis and Phlegmon the balance of skin microbiome is disrupted mainly by *S.aureus* and *P. aeruginosa* strains and *Pseudomonas aeruginosa* is one of the most important strains that causes opportunistic infections.
According to WHO, the number of patients diagnosed with diabetes doubling in 15 years and increasing cases of necrotic bacterial infections in soft tissues among the patients have been reported and death cases are evaluated to be around 20% [1,21]. Usually, *Pseudomonas aeruginosa* va *Staphylococcus aureus* are responsible for the rotting infections of skin [2].
Pseudomonas aeruginosa has resistance against many antibiotics naturally and has the ability of acquire resistance against antibiotics, microorganisms and disinfection reagents within short periods and also the risks of spreading the bacteria from one patient to another is very high that make them really difficult to control [3].
Thus, targeting the infections caused by the *P. aeruginosa* strains using other alternatives than antibiotics is very important and over the past few decades special interest is paid to LAB strains and the antimicrobial substances since they showed almost no toxicity against eukaryotic cells when given in adequate amount.

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Aim of the study was determining the sensitivity of the *P.aeruginosa* and *S.aureus* clinical isolates against dozen of relatively widely used antibiotics and evaluate antagonistic potency of *L.plantarum* Mal *against that* which was isolated from a local plant *Malva neglecta* .

MATERIAL AND METHODS

Isolating the S.aureus and P.aeruginosa strains

The clinical samples were taken from skin of patients who were diagnosed with Atopic dermatitis and Phlegmon at Republican specialized scientific and practical medical center for dermenoverology and cosmetology of the ministry of health of the republic of Uzbekistan, Uzbekistan using conventional methods described elsewhere. The isolates were grown on selective agar medium according to protocol described by [4].
All indicator strains, were cultured in Mueller Hinton broth at 37oC and stored at - 80 C in Mueller Hinton (HiMedia, India) medium with 25% (v/v) glycerol.

Sensitivity to Antibiotics

Sensitivity tests against antibiotics were provided according to protocols MUK 4.2.1890-04 and other International common protocols using standard disks [5]. The results were evaluated by measuring the diameters of inhibition zones in mm.

Antagonistic tests of L.plantarum Mal

5 µl of fresh *L.plantarum* Mal culture that was grown in 5 ml MRS broth (HiMedia, India) media for 18-24 hours were spotted onto MRS agar and incubated at 37oC for 48 hours. Then, formed colonies were killed by applying chloroform vapor for 30 minutes and let the vapor escape from the Petri dishes by leaving them open in sterile lateral box for 10 minutes. Indicator isolates (~106-8 CFU/mL) in 5 mL melted soft Mueller Hinton agar (HiMedia, India) were poured and incubated 37oC for 18-24 hours and results were present in the mm of corresponding inhibition zone.
Statistical procedure
All the experiments were carried out three times independently and results were demonstrated as mean ± standard deviation of the experiments.

RESULTS

Isolating the S.aureus and P.aeruginosa strains

10 and 5 isolates Staphylococcus and Pseudomonas were isolated from the samples and were identified as *S.aureus* and *P. aeruginosa* strains based on selective media, cell morphology, physiological characteristics, and Gram staining properties. *P.aeruginosa* D-1 was isolated together with *S.aureus* D-1 from a patient suffering from Atopic dermatitis, however, the existence of *P.aeruginosa* strains in the rest samples taken from patients diagnosed with AD was not determined in our study, and only *S.aureus* strains were isolated. The rest 4 *P.aeruginosa* strains were isolated from patients diagnosed with Phlegmon.
Sensitivity to Antibiotics
Half of the *S.aureus* isolates namely, *S.aureus* D-1, D-6, D-8, D-9 and D-10 did not show any resistance against the screened antibiotics, meanwhile the rest 5 strains had a resistance at least one of the antibiotics (Table 1).
Table 1. Antibiotic sensitivity of *Staphylococcus aureus* isolates

№	Isolates/ Antibiotics	Class	*D-1*	*D-2*	*D-3*	*D-4*	*D-5*	*D-6*	*D-7*	*D-8*	*D-9*	*D-10*
1.	Doxylan	I	27	30	11	25	0	20	10	25	21	27
2.	Levomycetin	II	13	0	15	15*	0	40	0	20	18	11
3.	Ceftovan	III	15*	35	20	16	18	24	18	35	18	28
4.	Bactamed	IV	30	30	16	20	20	15	18	27	21	20
5.	Lemox		28	14	15	30	0	28	11	22	23	25
6.	Fosfomed		24	0	11	26	22	11*	23	25	21	15

7.	Moxifloxacin		35	29	19	40	16	30	25	30	27	30
8.	Polymic	V	23	0	0	0	0	18	9*	20*	23	20
9.	Ofor		30	20	19	30	0	22	11	22	17	18
10.	Orcipol	VI	30	0	17	32	0	22	10*	25*	25	30

Classes: I. Tetracyclines II. Levomycetin III. Cephalosporins IV. Penicillins V. Fluoroquinolones VI. Others
"*" – Bacteriostatic activity

The most resistant strains were *S.aureus* D-5 and D-2 which were not susceptible to the 6 and 4 antibitotics, respectively, out of 10 different antibiotics. Another interesting result was that Ceftovan, Bactamed and Moxifloxacin the representatives of Class II, III and V could inhibit the growth of all 10 strains while the representatives of other classes did not have inhibitory activity against all the strains.

In Figure 1, results of antibiotic tests for the *S.aureus* D-5 is illustrated where only 4 antibitoics could inhibit the growth of bacteria strain.

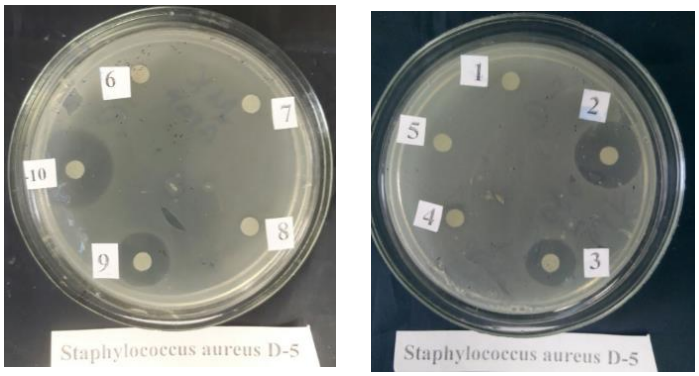

Figure1. Antibiotic resistance of *S.aureus* D-5

1-Orcipol, 2- Fosfomed, 3- Moxifloxacin, 4- Levomycetin , 5- Polymic,6- Doxylan, 7- Lemox, 8- Ofor , 9-Ceftovan,10-Bactamed)

Pseudomonas aeruginosa strains, in our study, even had greater resistance against antibiotics comparing to *S.aureus* strains, for example, *P. aeruginosa* D-5, D-3 and D-6 strains were not vulnerable to the effects of 10, 9 and 7 different antibiotics out of just 11. This might be because *Pseudomonas aeruginosa* strains [6]. None of the antibiotics could inhibit all of the strains, only Tetracycline and Rifampicin could somehow inhibit the growth of the 4 *P. aeruginosa* strains but activity still was very low.

Table 2. Antibiotic sensitivity of *Pseudomonas aeruginosa* strains

№	Strains/ Antibiotics	Class	P.aer. D-1	P.aer. D-2	P.aer. D-3	P.aer. D-5	P.aer. D-6
1.	Tetracycline	I	12*	12	0	9	21
2.	Chloramphenicol	II	0	20	0	0	0
3.	Rifampicin	III	9	22	12	0	9*
4.	Clarithromycin	IV	0	35 *	0	0	0
5.	Polymyxin B		20	0	0	0	0
6.	Ofloxacin		23	0	0	0	0

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7.	Sparfloxacin	V	28	0	0	0	0
8.	Co-trimoxazole	VI	0	35*	0	0	0
9.	Kanamycin		8	0	20*	0	10
10.	Streptomycin	VII	22	0	0	0	0
11.	Amikacin		26	0	0	0	15*
12	Cefotaxime	VIII	15	13	0	0	0

I.Tetracyclines II. Levomycetin III. Ansamycins IV. Macrolides V. Fluoroquinolones VI. Sulfonamides VII – Aminoglycosides VIII-Cephalosporins
"*" – Bacteriostatic activity

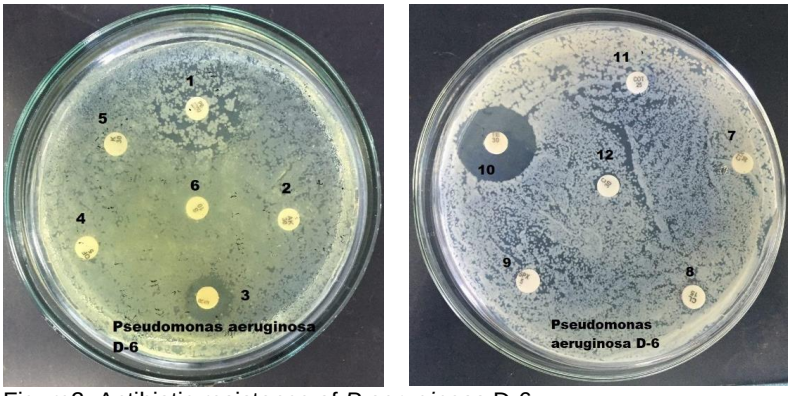

Figure2. Antibiotic resistance of *P.aeruginosa* D-6

1.Amikacin 2. Rifampicin 3. Ofloxacin 4. Polymyxin B 5. Kanamycin 6. Streptomycin 7.Cafotaxime 8. Clarithromycin 9. Sparfloxacin 10. Tetracycline 11. Co-trimoxazole 12. Chloramphenicol

Antagonistic tests of L.plantarum Mal
Antagonistic tests revealed that L.plantarum Mal could inhibit growth of all *S.aureus* and *P. aeruginosa* strains studied (Graph 1). The average inhibition zone was about 27.95 mm for *S.aureus* strains and 28.2 mm for *P. aeruginosa* strains which were relatively higher comparing to antibiotics (Table 1 and 2).

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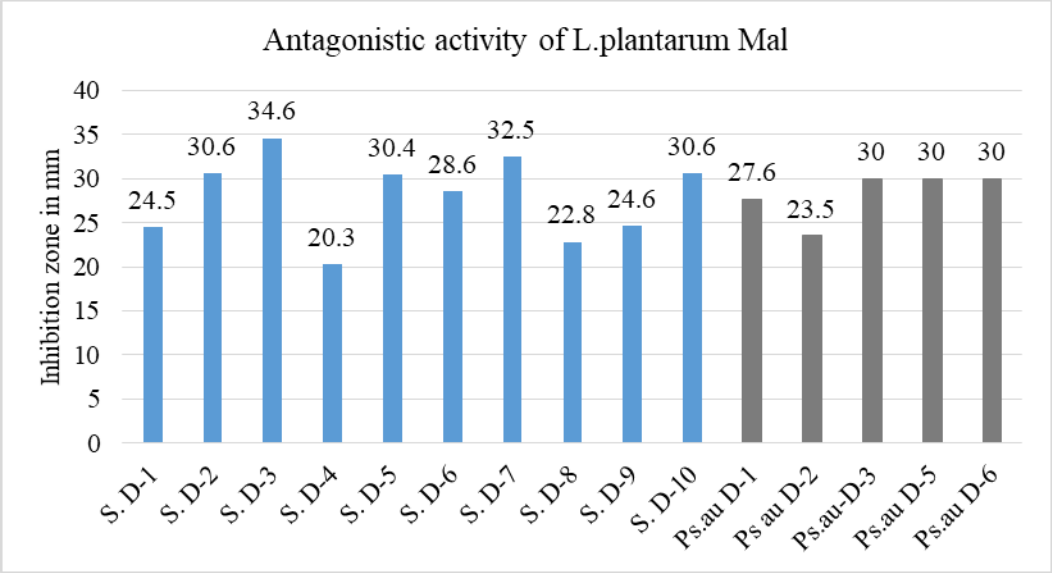
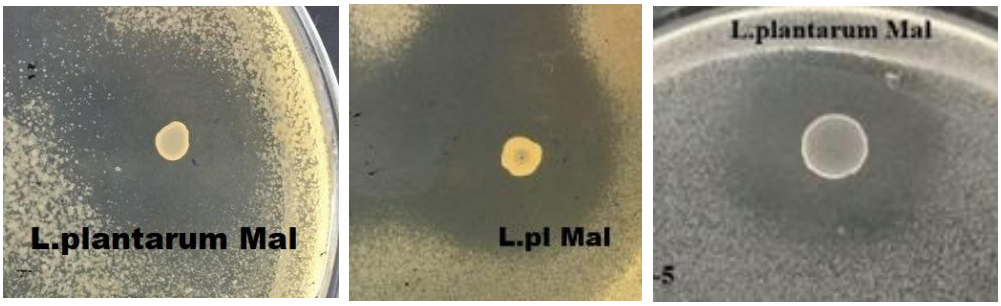


Interestingly, the inhibition zone for *P. aeruginosa* D-5 was 30 mm when subjected for antagonistic activity against *L.plantarum* Mal, meanwhile, the only antibiotic Tetracyclines that possessed inhibitory activity against the given strain showed an inhibition zone only 9 mm which was roughly 3 times lower (Figure 3B).



A. P.aer D-6 B. P.aer. D-5 C. *S.aureus* D-5

Figure 3. A. Antogonistic activity against *P. aeruginosa* D-6, B. against *P. aeruginosa* D-5 and C. against *S.aureus* D-5.

DISCUSSIONS

P. aeruginosa is one of the important bacteria that can cause huge burdens for public health today due to its ability to adapt its genome and physiology during chronic opportunistic infections. *P. aeruginosa* has inherent resistance to most available antibiotics, including aminoglycosides, anti-pseudomonal penicillins, newer cephalosporins, imipenem and flouroquinolones as treatment options for systemic infections. P. aeruginosa bacterium is one of the most critical bacteria according to the World Health Organization report in 2017, while S.aureus bacterium included in the list of high-risk bacteria with its antibiotic-resistant properties.[7]
Probiotics could be used to neutralize bacterial pathogens and has a potential to be alternative treatment to antibiotics[8]. Lactobacilli are able to inhibit the growth of *P. aeruginosa* by different mechanisms. These friendly bacteria could act as bio-therapeutic microorganisms and might be good candidates to overcome the growing challenge of nosocomial infections that caused by multi-drug resistant strains of *P. aeruginosa*.
Antimicrobial activity of *Lactobacillus* strains against bacterial pathogens emerges to be multifactorial and to include the production of hydrogen peroxide, lactic acid, exopolysaccharides[9], bacteriocin-like[11] molecules and unknown heat-stable, non-lactic acid molecules [4,10]. Other studies also show that lactobacilli strains could effectively inhibit the growth of *P. aeruginosa* and *S.aureus* strains [4,11].

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CONCLUSIONS

The study revealed that the L.plantarum Mal strain could effectively inhibit the growth of all 10 *Staphylococcus aureus* and 5 Pseudomonas aeruginosa strains isolated from patients who were diagnosed with Atopic dermatitis or Phlegmon. It is also worthy to note that the inhibitory activity of the given LAB strain was promisingly higher than the antibiotics used in this study, thus, the strain could be a promising candidate for targeting antibiotic-resistant strains in such diseases. Further research will be devoted to identifying the antimicrobial substances produced from *L.plantarum* Mal and evaluating their potential used in pharm industry to treat bacteria caused Atopic dermatitis and Phlegmon.

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PRE-IMPLANTATION GENETIC DIAGNOSIS IN THE PROGRAM OF ASSISTED REPRODUCTIVE TECHNOLOGY

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Pre-implantation Genetic Diagnosis (PGD) is the diagnosis of genetic disorders in human embryos prior to implantation into the endometrium, i.e. before the phase of transfer on the program of in vitro fertilization (IVF). A biopsy of one blastomer in an embryo that is at the cleavage stage (6-10 blastomeres) or a biopsy of the trophectoderm (the outer layer of cells) at the blastocyst stage (day 5 of embryo development) is typically performed for analysis. The main advantage of PGD is that there is no selective termination of pregnancy when it is used and the chance of giving birth to a child without any diagnosed genetic diseases is quite high [1,3,15].
There are discrepant data in literature on the effectiveness of PGD as part of the program of assisted reproductive technologies (ART) [2,6,8].
According to some studies including ASRM (American Society for Reproductive Medicine) data, application of PGD doesn't increase the frequency of pregnancies with in vitro fertilization (IVF). This may be due to imperfection of the technique of the blastomer sampling procedure or the choice of a laboratory screening method to diagnose aneuploidy and microstructural chromosomal abnormalities simultaneously in all chromosomes. The method of array comparative genomichybridization (CGH) showed high performance for clinical studies on embryo transfer within ART (69-70%). While there is the high genetic abnormalities detection rate in PGD based on many studies, the frequency of pregnancies with this method doesn't exceed 30-40% [4,7,11].
Study of the structure of embryo chromosomal disorders based on pre-implantation genetic diagnosis in the program of assisted reproductive technology as well as the impact of this procedure on the results of pregnancies is, therefore, of particular interest.

Study Materials and Methods

We studied chromosomal abnormalities of embryos in 86 females with different IVF outcomes. Pre-implantation study of the embryos was conducted by the FISH method in 42 females with positive IVF outcomes and in 44 females with negative IVF outcomes. The quality of the embryos was assessed on the third day of culture.
All female patients underwent a special examination before IVF: the hormonal panel was studied (FSH, LH, estradiol, TSH, free T3, free T4, TSH, thyroperoxidase antibodies, prolactin, progesterone, Anti-Mullerian Hormone, testosterone) and infectious status (TORCH-complex infection, STDs), papanicolau test, peripheral karyotype, determination of the vitamin D level in the blood, hysterosalpingography, hysteroscopy with pathohistological examination of endometrial biopsy material. Males underwent mandatory sperm examination with morphological indicators of spermatozoa, genetic analysis of sperm (FISN) and DNA fragmentation. The immune system of spouses and their compatibility by the 2nd class of HLA genes were also examined.
The exclusion criteria were the females with monogenic diseases and males with significant pathozoospermia. Controlled ovarian hyperstimulation was performed according to the standard antagonist protocol from day 2-3 of the menstrual cycle with preparations of recombinant follicle-stimulating hormone combined with preparations of human menopausal hormone. Ultrasound monitoring of follicle growth was performed by transvaginal ultrasonography 4-5 times during the multifollicular ovarian stimulation. When the maximum follicle of 14-15 mm was reached, a gonadotropin-releasing hormone antagonist was administered at a dose of 0.25 mg.
Oocyte retrieval was performed in 35-36 hours after the administration of ovulation trigger. Immediately after receiving oocytes and spermatozoa, their morphological assessment was performed. Morphological analysis of oocytes and spermatozoa was carried out immediately after retrieval. Mature, immature and degenerative oocytes can be retrieved by puncturing follicles. More thorough assessment of the state of oocytes can be carried out only after purification before ICSI. The first polar cell is determined in mature oocytes ready for fertilization and designated as M II in the embryological protocol [1,13].
Intracytoplasmic sperm injection was performed for all patients (ISCI method). Two pronuclei form in the normal course of fertilization in 18-20 hours after ICSI (on the 1st day). In this case, 2pn rating is assigned to them. Further development of embryo cleavage occurs within 5-6 days. The embryo quality was assessed 40-42 hours (on Day 2), 72-74 hours (on Day 3), and 20 hours (on Day 5) after fertilization. Embryo cleavage should be symmetrical and equal. Embryos of poor quality were not transferred to the uterine cavity. They were left till Day 5 and then frozen or transferred upon normal blastocyst formation [5,10,14].
It is known that embryos form a blastocyst on Day 5. The quality of blastocysts was assessed by their size from 1 to 5; by the state of the inner cell mass - from " A " to " C "and surrounding cells – trophoblast (from" A "to"C"). The best blastocysts for transfer were those of size 3-5 with the multicellular ICM and trophoblast. Further development of the embryo occurs in the uterus after the implantation. For successful implantation, the blastocyst must exit the surrounding

pellucid zone. This process is called hatching. In case of change in the pellucid zone and difficulties in the process of self hatching, auxiliary laser hatching is used [10,12,15].
Biopsy of the embryo was performed on Day 3 after the fertilization at phase 6-10 of blastomeres and blastocytes.
The FISH (fluorescence in situ hybridization) method was used to detect numerical and structural chromosomal abnormalities. This method involves DNA-probes which are a limited-size nucleotide sequence complementary to a specific region of nuclear DNA. The probe has a “tag”, i.e. it contains a nucleotide linked to fluorophore (a molecule capable of fluorescence).
After the procedure of hybridization with the formation of a hybrid DNA-probe and DNA-target molecule, fluorescence of specific DNA sequences on chromosomes or in nuclei can be observed on the study cytogenetic preparation by means of a fluorescent microscope [9,13].
Statistical data processing was performed using an application software package SPSS statistics 17.0. The Kruskal-Wallis test was used to evaluate the significance of intergroup differences in several independent samples.
In case of two samples the Mann-Whitney U-test was used for unlinked sequences. The inserted parts of genotypes were assessed for compliance with the Hardy–Weinberg principle by the X^2 criterion in comparison with expected genotype frequencies of equilibrium distribution. The significance of differences in the incidence of qualitative characters was determined by the criterion X^2.
Findings of Study
Mean age of females was 35.5 $\pm$1.0. Infertility duration was 7.5 $\pm$5 years. The patients were comparable ($p>0.005$) in their etiology of infertility, anamnestic data, mass-height index, structure of previous somatic and gynecological diseases, and surgical interventions. All patients had a normal karyotype.
The results of the study on the characteristics of embryos subjected to pre-implantation diagnosis are shown in Table 1. A total of 220 embryos were subjected to pre-implantation diagnosis: 111 embryos in Group A and 109 embryos in Group B. Patients of each study group were divided into subgroups by age: under the age of 35 and over 35. In Group A, among females aged <35, the number of embryos subjected to pre-implantation diagnosis was 52 and in females aged >35 the number of embryos subjected to pre-implantation diagnosis was 59. In Group B, 48 embryos were subjected to pre-implantation diagnosis in females aged <35 and 61 embryos in females aged >35.
The study findings showed that no pathology of embryos was observed both in females aged <35 and in females aged >35 in the group with successful IVF in 69.2% and 59.3% of cases respectively. These values are statistically significantly higher than similar values in the group of females with non-effective IVF results, respectively, 41.7% ($p< 0.01$) and 24.6 % ($p < 0.01$). Embryos with abnormalities were detected statistically more often in the group with negative IVF results (67.9%) than in the group of successful IVF (36.0%, $p < 0.01$).
Distribution of embryos with abnormalities showed that in the group of non-effective IVF results statistically significant increase in the relative incidence of embryo pathology was observed both in females aged <35 and in females aged >35 (58.3% and 75.4% respectively), as compared with the group of females with positive IVF outcomes in the relevant age group, 30.8% ($p<0.001$) and 40.7% ($p<0.001$) respectively (Table 1).

Table 1

Characteristics of embryos subjected to pre-implantation diagnosis

Value	Group A n=42		Group Б n=44		Total n=86
	Age < 35	Age > 35	Age < 35	Age > 35	
	abc %	abc %	abc %	abc %	abc %
Total embryos subjected to PD	52	59	48	61	220
Embryo pathologies by chromosomes, No	36 69.2	35 59.3	20 41.7**	15 24.6***	106
Embryo pathologies by chromosomes, Yes	16 30.8	24 40.7	28 58.3**	46 75.4***	114
Embryo pathologies by chromosomes within groups	40	36.0	74	67.9**	114

Note: *- ** $p< 0.05$-0.01 as compared to Group A of the same age

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In view of the fact that the frequency of viable embryos formation varies in both groups, studying the frequency and nature of pathologies of viable embryos in these groups is of great interest. Viable embryos reached 35% in the group of females with positive IVF outcomes that was statistically more than in the group of negative IVF result – 20.3% ($p<0.01$) (Table 2). A detailed study of the frequency of viable embryos in patients of different age subgroups showed statistically significant high values among females aged > 35 with positive IVF outcomes (37.5%) in comparison with females of the same age with negative IVF outcomes (15.2%, $p<0.05$).
The study of unviable embryos frequency showed a contrary picture. Unviable embryos were observed statistically more often in females aged >35 in the group with the negative IVF outcome (84.8%) as compared to females of the same age with the positive IVF outcome (62.5%, $p<0.05$). Among females aged <35, there was no relevant difference in the frequency of viable and unviable embryos between the study groups.

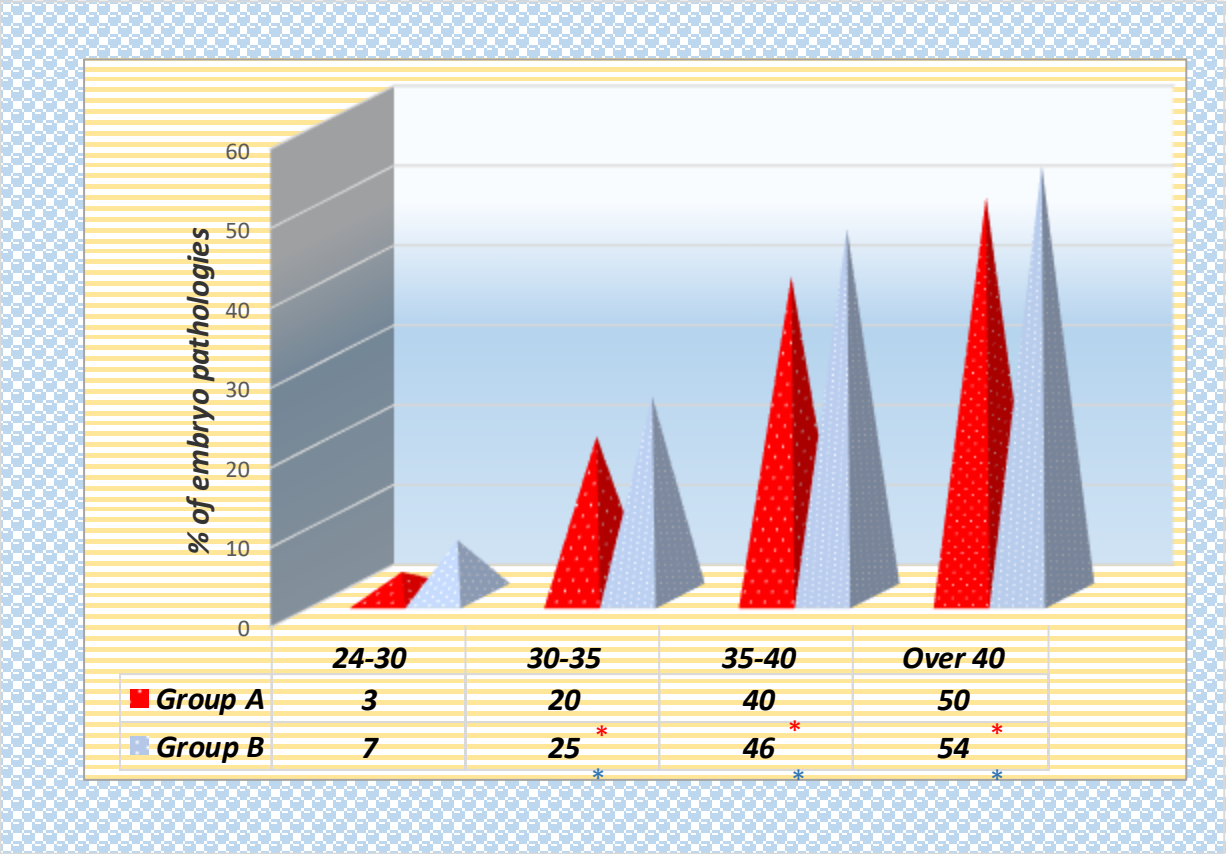
Table 2
Features of embryos with pathologies detected by pre-implantation diagnosis

Value	Group A n=40		Group B n=74	
	Age < 35	Age > 35	Age < 35	Age > 35
	abc %	abc %	abc %	abc %
Total embryos with pathologies	16	24	28	46
Unviable embryos	11 68.75	15 62.5	20 71.4	39 84.8*
Viable embryos	5 31.25	9 37.5	8 28.6	7 15.2*
Total viable embryos within groups	14 35.0		15 20.3**	

Note: *- ** p< 0.05-0.01 as compared to Group A of the same age

The study of the paternal age effect on the embryo pathology incidence revealed a direct dependence between a chromosomal abnormality and the paternal age (Figure 1). In group A, males aged 30-35 had embryo pathology in 20.0% of cases that is statistically higher than in males aged 24-30 years with embryo pathology observed in 3.0% of cases ($p<0.01$). Abnormalities were observed in 40.0% of males aged 35-40 and in 50.0% of males aged >40. The detected difference in the frequency of embryos with pathologies in different age subgroups for the Group A was statistically significant ($p< 0.01$).

Figure 1. Dependence of the embryo pathology incidence on the paternal age in the comparison groups



P < 0.01 as compared to the previous age within each group

A similar trend was observed in group B. The incidence of chromosomal abnormalities in embryos increased with increasing paternal age. The highest relative incidence of chromosomal abnormalities in embryos was observed in males of the older age subgroups. In persons aged >40, 54.0% abnormal embryos were observed, that is statistically more than in males aged 35-40 with the incidence of embryo abnormalities was fixed at the level of 46.0% ($p<0.05$). In males aged 30-35 this pathology was reported in 25.0% that is statistically less than in males of the older age groups ($p< 0.01$) and in males aged 24-30 ($p< 0.01$) (Figure 1).

Comparative analysis of the embryo pathology incidence among the study groups of similar age didn't show a relevant difference.

The study of the structure of chromosomal pathology of viable embryos in the comparison groups showed the following (Table 3). In Group A, trisomy 21 (Down syndrome) was diagnosed in 41.7% of embryos. In Group B, this syndrome was reported in 40.0% of embryos ($p>0.05$). Patau syndrome (trisomy 13) and Edwards syndrome (trisomy 18) were diagnosed in 25.0% and 16.7% of viable embryos of Group A that is comparable to the similar data in Group B where the incidence of the above mentioned syndromes diagnosed in embryos was 20.0% and 13.3% respectively ($p>0.05$). There was no relevant difference between the groups in the incidence of Klinefelter syndrome (XXY) and polysomy Y (XYY) in viable embryos ($p>0.05$).

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Table 3
Nature of chromosomal pathology in the studied pathological viable embryos

Viable embryos	Group A n=42		Group B n=44		Total	
	12		15		27	
	abc	%	abc	%	abc	%
Klinefelter syndrome (XXY)	0	0	1	6.7	1	3.7
Turner syndrome (X0)	1	8.3	1	6.7	2	7.4
Down syndrome (trisomy 21)	5	41.7	6	40.0	11	40.7
Patau syndrome (трисомия 13)	3	25.0	3	20.0	6	22.2
Edwards syndrome (trisomy 18)	2	16.7	2	13.3	4	14.8
Polysomy Y (XYY)	1	8.3	2	13.3	3	11.1

The study of the structure of chromosomal pathology in females of different age groups (>35 and <35) didn't reveal a relevant difference in the relative incidence of the above mentioned abnormalities (Table 4). Down syndrome was diagnosed in most cases in viable embryos both in females aged <35 and in females aged >35 (38.5% and 42.8% respectively, p>0.05). A relevant difference also was not revealed in the incidence of other syndromes in viable embryos with abnormalities in females of the experimental age groups.

Table 4
Nature of chromosomal pathology in pathological viable embryos in females of different age groups

Viable embryos	Group A + Group B				Total	
	Age <35		Age >35			
	abc	%	abc	%		
	13		14		27	100
Klinefelter syndrome (XXY)	1	7.7	0	0	1	3.7
Turner syndrome (X0)	1	7.7	1	7.1	2	7.4
Down syndrome (trisomy 21)	5	38.5	6	42.8	11	40.7
Patau syndrome (трисомия 13)	3	23.1	3	21.4	6	22.2
Edwards syndrome (trisomy 18)	2	15.4	2	14.3	4	14.8
Polysomy Y (XYY)	1	7.7	2	14.3	3	11.1

In summary, the study of pre-implantation embryo characteristics in the IVF program revealed higher indices for embryos without chromosomal abnormalities in the group with positive IVF outcomes and lower indices for the relative frequency of embryos with chromosomal abnormalities as against the group with negative IVF outcomes.

In females aged >35 from the group with positive IVF outcomes viable embryos were found more frequently and unviable embryos were found less frequently. The nature of chromosomal pathology in study females didn't show a relevant difference among the comparison groups.
Large enough quantity of morphologically healthy but genetically abnormal embryos was also detected. With no PGD an embryologist would undoubtedly choose the embryos that reached the blastocyst phase. And this would lead to a negative IVF outcome.
Along with this, there were also the embryos that were genetically healthy but morphologically defective. All these data suggest that the protocols of controlled ovarian hyperstimulation, used medicinal drugs, embryological phase and procedure of PGD itself need to be improved to obtain a high-quality embryo and positive IVF outcome.
So, while there are contradictory data, the analysis of the world literature data and the results obtained by us in the course of the study revealed great advantages of pre-implantation diagnosis. With its wide diagnostic capabilities, PGD as part of the ART program makes it possible to select and transfer embryos with no chromosomal abnormalities into the uterine cavity, to reduce the risk of miscarriage and multiple pregnancies and to improve the chances of successful implantation and the birth of a healthy child.

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EFFECT OF METAL-CERAMIC PROSTHESIS ON GINGIVAL MUCOSA

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ABSTRACT

The fixed dental prosthesis is one of the most commonly used prosthesis in dental clinical practice for restoring function and health of oral tissues. This type of dental prosthesis is not without complications, as these restorations often extend into the gingival sulcus, and gingival epithelial cells come into contact with them. Unfortunately, they also alter and modify oral microbial flora. The aim of the present study is to identify the dynamics of changes of mucosa in the region of metallo-ceramic prosthesis. We have examined three groups of patients, according to the length of wearing time of metallo-ceramic prosthesis: I group - 1year, II group – 1-5 years and III group – 6-10 years. Each group includes two subgroup, where was studied influence of supportive and intermediate parts of Metal-Ceramic prosthesis on gingival mucosa. The gingival mucosa was examined by Papanicolaou staining and cytomorphometric indexes. A review of the literature and the results of our study demonstrated the effect of metallo-ceramic prosthesis on the dynamics of changes in the surrounding gingival mucosa. At the same time, the literature searches around the present study also showed possible reasons for the changes mentioned above. It was shown that the success of fixed dental prosthesis depends on many factors which should be considered during treatment planning. Therefore, a detailed analysis of the changes in the gingival mucosa surrounding the fixed ceramic-metal prosthesis and their possible causes are necessary prerequisites for successful prosthetics.
Key words: Fixed Metal-Ceramic prosthesis; Gingival Mucosa; Cytomorphometric Indexes;

The fixed dental prosthesis is one of the most commonly used prosthesis in dental clinical practice for restoring function and health of oral tissues. [1] Substantial proportion of dental patients worldwide use fixed metallic restorations. In Europe, for instance, Sweden reported the highest use of fixed restorations (45%) followed by Switzerland (34%). Another study reported that 12.4% of Finnish men and 12.1% of women have crowns, whereas 4.8% and 8.0%, respectively, have fixed dental prostheses.[2] This type of dental prosthesis is not without complications, as these restorations often extend into the gingival sulcus, and gingival epithelial cells come into contact with them. [3] unfortunately, they alter and modify oral microbial flora.[4]

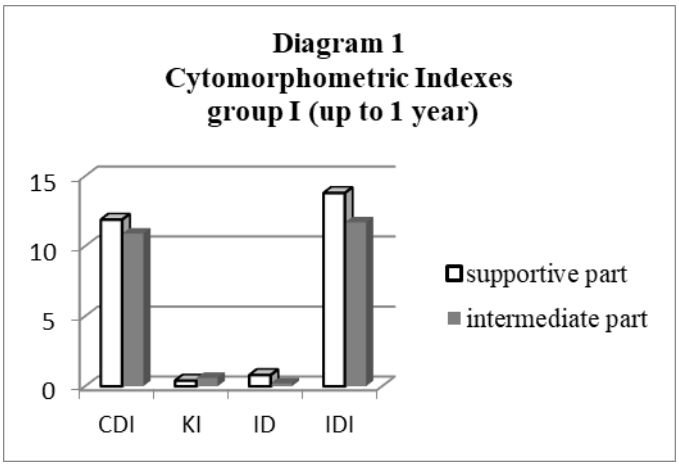
The aim of the present study is to identify the dynamics of changes of mucosa in the region of metallo-ceramic prosthesis.

MATERIALS AND METHODS

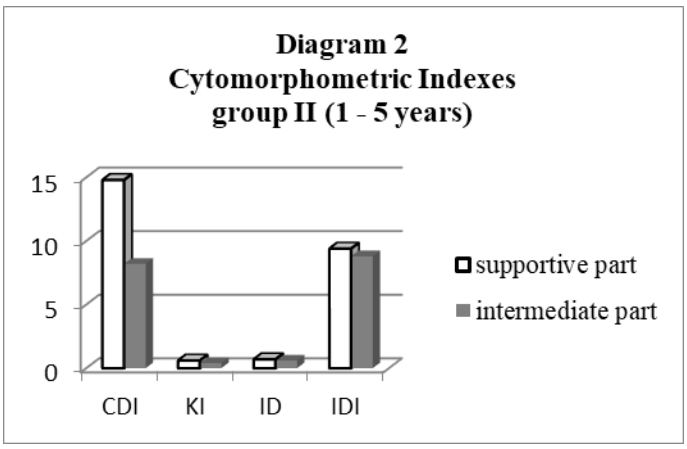
We have examined three groups of patients, according to the length of wearing time of metallo-ceramic prosthesis: I group - 1year (12 patients), II group – 1-5 years (28 patients) and III group – 6 -10 years (20 patients). Each group includes two subgroup, where was studied influence of fixed and intermediate parts of Metal-Ceramic prosthesis on gingival mucosa. The gingival mucosa was examined by Papanicolaou staining. The status of oral mucosa was evaluated using cytomorphometric indexes: index of cells differentiation (ICD), index of keratinization (KI), index of destruction (DI) and index of inflammation-destruction (IDI). The statistical significance of differences was measured by T-test. The data were considered reliable when $p < 0.05$.

RESULT

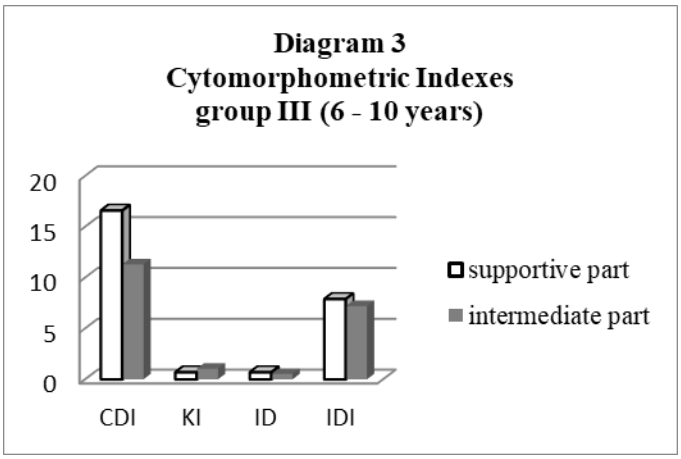
The comparative study of cytological data between supportive and intermediate parts of prostheses in group I (diagram 1) has showed that in gingival mucosa adjacent to intermediate part of prosthesis: the index of cell differentiation (CDI) is 1,1 times less ($p>0,05$), index of keratinization (KI) is 1,5 times more ($p<0,05$), index of destruction (DI) is 2,3 times less ($p<0,05$), index of inflammation - destruction (IDI) is 1,2 times less ($p<0,05$) in comparison to supportive part. No detectable amount of bacteria was found on the surface of epithelial cells. In this group was revealed particular changes in soft tissues, including gingival edema, bleeding and pain.



In group II (diagram 2) has showed that in gingival mucosa adjacent to intermediate part of prosthesis: the CDI is 1,8 times less (P<0,05), KI is 1,3 times less (p<0,05), DI is 1,3 times less (p<0,05) and IDI is 1,1 times less (p<0,05), in comparison to supportive part. The large number of epithelial cells was covered by bacteria. In this group was manifested following clinical symptoms: occasional bleeding, edema and pain.



In group III (diagram 3) has showed that in gingival mucosa adjacent to intermediate part of prostheses: the CDI is 1,5 times less (p<0,05), KI is 1,2 times more (p<0,05), DI is 1,3 times less (p<0,05) and IDI is 1,3 times less (p<0,05), in comparison to supportive part. The large number of epithelial cells was covered by bacteria. Clinically in this group was revealed: edema, and bad breath.



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DISCUSSION

A substantial proportion of dental patients use fixed prosthodontic prosthesis in dental clinical practice for restoring function and health of oral tissues. [1;3] As mentioned above this type of dental prosthesis is not without complications, as these restorations often extend into the gingival sulcus, and gingival epithelial cells come into contact with them. [3] Mechanical trauma due to pressure and friction between appliances and tissues can also lead to local tissue reactions. [5] An important aspect of stratified squamous epithelia is that the cells undergo a terminal differentiation program that results in the formation of a mechanically resistant and toughened surface composed of cornified cells that are filled with keratin filaments and lack nuclei and cytoplasmic organelles. In these squames, the cell membrane is replaced by a proteinaceous cornified envelope that is covalently cross linked to the keratin filaments, providing a highly insoluble yet flexible structure that protects the underlying epithelial cells. [6] Hyperkeratinization is the defect of epithelial cells. Normally, these epithelial cells shed or desquamate at regular intervals. In hyperkeratinization, this process is disturbed because of an excess of keratin formation and accumulation due to lack of adequate desquamation. It occurs as a secondary reaction to chronic irritation or some infection or malignancy. Hyperkeratinization which occurs because of chronic irritation is due to higher rate of proliferation of the epithelial cells. [7] Further, corrosion may adversely influence the mechanical integrity and biocompatibility, leading to compromised esthetics, physical weakness, and health hazards.[8] Biologic nature of the oral cavity qualifies it to be an active environment for the corrosion of metallic alloys that have low mechanical and biological properties.[9] Leakage of ions will cause a wide range of biological interactions. The subsequent soft tissue response can promote the adhesion of bacteria and lead to toxic or subtoxic effects or allergic responses.[10] The adaptation of dental crowns and bridges to the supporting prepared crowns is less than perfect, always creating a gap that promotes bacterial colonization.[7] It is a well-known fact that tooth decay, gingival inflammation and periodontal disease, quoted as the most common biological complications of fixed dental prosthesis, [1] are caused by bacteria settled in the dentogingival plaque accumulated due to insufficient oral hygiene, and consequently, for oral health the appropriate hygiene regime is crucial. The relationship between bacterial plaque accumulation and gingival inflammation has been well documented. Patient's susceptibility to gingival inflammation is not based solely on the quantity of dental plaque, [1] the presence of a unique immunological system tailored for both surveillance and repair programs. The delicate balance between microbiome/tissue injury and host responses at this interface is best reflected by the fact that this homeostasis is often lost, leading to destructive inflammation; specifically the development of the common inflammatory disease periodontitis. In periodontitis, a dysbiotic oral microbiome is considered the trigger of a chronic inflammatory response in the surrounding soft tissues [11], which causes destruction of supporting tissues and structures [12;13] Also including diseases of the digestive tract, liver, and disorders of the nervous system. Thus, it is possible to assume the presence of significant metabolic shifts in the body under the influence of the studied factors. [14] This review of literature explains the results of our study. According to the our results, a high rate of index of inflammation-destruction was observed in group 1 patients. The clinical studies have showed that supportive and intermediate parts of prosthesis have caused particular changes in soft tissues, including gingival edema, bleeding and pain. Matching with no detectable amount of bacteria on the surface of epithelial cells this clinical manifestation indicates that changes is likely to be a reaction of the gingival mucosa to the prosthesis. In group 2 and 3 patients occasional bleeding, edema, pain and bad breath with the high rate of index of destruction and the large number of epithelial cells covered by bacteria indicate that the damage to the mucosa of the gingiva is not a direct consequence of prosthetis, but rather the result of adhesion of microorganisms to the epithelium in the region of prosthesis.

CONCLUSIONS

A review of the literature and the results of our study demonstrated the effect of metallo-ceramic prosthesis on the dynamics of changes in the surrounding gingival mucosa. At the same time, the literature searches around the present study also showed possible reasons for the change mentioned above. It was shown that the success of fixed dental prosthesis depends on many factors which should be considered during treatment planning. Therefore, a detailed analysis of the changes in the gingival mucosa surrounding the fixed ceramic-metal prosthesis and their possible causes are necessary prerequisites for successful prosthetics.

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ASSOCIATION OF BLOOD GROUP AB0 WITH CORONARY ARTERY DISEASE IN YOUNG ADULTS IN GEORGIAN POPULATION

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ABSTRACT

OBJECTIVE: Several reports have suggested that ABO blood group system is associated with the risk of CAD.

Aim: establish the association of blood group AB0 with CAD in young adults in Georgian population.

METHODS: Under our observation were 107 patients with ischemic heart disease, aged 18-45 years, From the St. John The Merciful Private Clinic contingent. Examination: anamnesis, cardiography, echocardiography, coronography, blood lipid metabolism.
We used the distribution of blood groups in the general population of Georgia as a control
The differences between the frequency of ABO blood groups in CAD patients and healthy blood donors were tested using χ^2-test.

RESULTS: We studied the role of genetic predisposition in the development of cardiovascular disease in the Georgian population under 45 years of age. In 19 (21.6%) patients, early detection of ischemic heart disease (under 45 years of age) CVD was observed in first degree relatives.
Blood group 0 shows significantly associations with the early development of cardiovascular disease, frequency 0 antigen in CAD group - 74.77%, in population - 50.86%($p<0.0001$).
In case of group 0, the incidence of dyslipidemia is significantly high, then in group with A antigen – Respectively 38(46.91%) and 5(20.83), p=0.0224. In the case of group 0, compared to group A, significantly increased: the mass index - 32.05±5.44 and 29.38±4.20 p=0.0140 respectively, Tchol - 5.24±1.30 and 4.62±1.00, p=0.0180 and TG - 2.84±1.57 and 1.83±0.70, p=0.0029, the mean LDL is significantly low - 1.27±0.48 and 1.20±0.28, p=0.3602.
The 10-year risk is significantly higher in patients with blood type 0 4.46±3.15, than in group A - 2.42±2.45, p=0.0044

CONCLUSIONS: blood group 0 increased risk fatal cardiovascular disease in young Georgian population;
Study of blood groups during coronary heart disease will help to clarify the prognostic factors of the disease and reduce the global burden of cardiovascular disease.
Keywords: AB0, risk factors CAD, dyslipidemia.

INTRODUCTION

Coronary artery disease (CAD) is a common clinical problem. The risk factors include familial and genetic factors, and the presence of other disease entities. There is a consistent association between certain risk factors and the subsequent development of CAD. Several reports have suggested that ABO blood group system is associated with the risk of CAD[1].
The *ABO* gene is located on chromosome 9q34 with 3 variant alleles (A, B, and 0), which encodes glycosyltransferases with different substrate specificities and determines blood type[2].
Blood groups vary according to populations, as well as different associations between diseases and blood groups.
Association between AB0 blood group and severity of coronary artery disease in unstable angina, Compared to the non-0 groups, the 0 group had more severe coronary artery involvement (p= 0.004)[3].
Analysis did not show any significant difference between the frequency of AB0 blood groups in coronary artery disease patients compared to the Iranian general population, moreover, the prevalence of major risk factors was equal in patients with different blood groups, and blood groups had no impact on development of premature coronary artery disease in individual subjects[4].

Blood group A is an independent risk factor for CAD and MI in young people in Taiwan.
Group non-0 is associated with increased mortality in patients with ischemic heart disease. Group non-0 increases the risk for cardiac death in non-elderly patients, particularly in younger females, and groups A and B prevail in myocardial infarction. AB0 group determination might aid in genetic screening for ischemic heart disease and become relevant in the management of risk factor control[5].
No association between AB0 blood groups and the extent of coronary atherosclerosis in Croatian CAD patients is observed. Observation that AB blood group might possibly identify Croatian males at risk to develop the premature CAD has to be tested in larger cohort of patients[6].
Premature coronary artery disease is characterized by an unfavourable lipid profile, low concentrations of HDL-C and high triglyceride levels, in association with high Lp(a) and a hypercoagulable state (high fibrinogen and D-dimer levels)[7].
The aim of our research is to establish the association of Blood Group AB0 with Coronary Artery Disease in Young Adults in Georgian population

METHODS

Under our observation were 107 patients with ischemic heart disease, aged 18-45 years, patients From the **St. John the Merciful Private Clinic.** Research methods: taste, anamnesis, cardiography, echocardiography, coronography. patients were alse diagnosed with blood lipid metabolism.
We used the distribution of blood groups in the general population of Georgia as a control[8].
Statistical analysis:
In estimating the quantitative indicators, we considered the mean, mean square deviation. In case of quantitative indicators, we determined the reliability of the difference between the groups by using the student t criterion. For qualitative indicators, we calculated the average frequency, the mean square deviation. We assessed the difference between the groups using the F (Fisher) criterion. The differences between the frequency of ABO blood groups in CAD patients and healthy blood donors were tested using χ^2-test.
The difference was considered significant when $p < 0.05$.
Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 23.0 (SPSS Inc., Chicago, Illinois, USA)
RESULTS
We studied the role of genetic predisposition in the development of cardiovascular disease in the Georgian population under 45 years of age. In 19 (21.6%) patients, early detection of ischemic heart disease (under 45 years of age) CVD was observed in first degree relatives.
The study of AB0 blood isoantigens showed that the frequency of group 0 is high in both the study group and the control group, however, group 0 shows significantly associations with the early development of cardiovascular disease (table 1).

Table 1. Distribution of blood groups in patients with CVD and control

		0	A	B	AB	□□(0/A)	□□(0/A+B+AB)
Group I	N	80	25	2	0	14.11,	24.88,
	%	74.77	23.36	1.87	0.00	p<0.001	p<0.001
Group II	N	713	529	143	17		
	%	50.86	37.73	10.20	1.21		

In the next stage of the study, we compared the cardiovascular risk characteristics by blood groups 0 and A (Table 2).
Table 2. Evaluation of cardiovascular risk characteristics according to blood groups 0 and A.

	Blood group 0 N=81	Blood group A N=24	t or F	P
	Mean± Std. Dev. or n(%)	Mean± Std. Dev. or n(%)		

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Hypertension	53(65.43%)	15(62.50%)	0.07	0.7941
Diabetes mellitus	11(13.58%)	0(0.00%)	3.70	0.0572
Dyslipidemia	38(46.91%)	5(20.83)	5.38	0.0224
Age of disease manifestation	34.31±6.93	34.88±5.67	-0.41	0.6858
Mass index	32.05±5.44	29.38±4.20	2.55	0.0140
Tchol mm / l	5.24±1.30	4.62±1.00	2.45	0.0180
TG	2.84±1.57	1.83±0.70	3.05	0.0029
LDL	3.30±1.34	2.71±0.97	2.37	0.0218
HDL	1.27±0.48	1.20±0.28	0.92	0.3602
INR	1.13±0.40	1.09±0.29	0.53	0.5984
Prothrombin index	97.91±10.69	97.20±11.83	0.26	0.7971
Fibrinogen concentration	368.33±114.75	397.48±139.45	-0.86	0.3983
Troponin ng / ml	91.93±123.49	35.78±86.73	1.80	0.0763
Serum creatinine mmol / l	101.73±69.88	98.70±54.06	0.15	0.8801
TSH	1.55±1.29	1.93±1.30	-1.21	0.2335
Glucose	5.05±2.62	4.91±1.16	0.25	0.8038
Assessment of 10-year risk of fatal cardiovascular disease/accident with SCORE	4.46±3.15	2.42±2.45	2.92	0.0044

In case of group 0, the incidence of dyslipidemia is significantly high, then in group with A antigen. diabetes is found only in case of group 0, no significant difference was found in hypertension.
In the case of group 0, compared to group A, significantly increased: the mass index, Tchol and TG, the mean LDL is significantly low.
No significant differences were found between the groups according to the mean values of INR, Prothrombin index, Fibrinogen concentration, Troponin, Serum creatinine, TSH and Glucose.
The 10-year risk of fatal cardiovascular disease / accident with SCORE is significantly higher in patients with blood type 0 than in group A.

DISCUSSION

Omidi N et al. showed that patients with blood group 0 had more severe form of coronary involvement[3]. In study Wu et al., based upon 19 studies, group A was associated with a similar increase in MI risk (OR = 1.29, 95% CI = 1.16– 1.45, p < 0.00001) to that observed with non-A[9]. Ba DM, et al. suggests an association between blood group A and ID in sub-Sahara Africans. [10]
Our study showed that 0 group significantly increased the risk CAD in young adults Georgian population.
Disruption of the triglyceride ratio is an indicator of an atherogenic lipid profile and poses a risk of developing coronary heart disease. [11]
Biswas et al. showed that blood group 0 was associated with low HDL-C level, which was the same as our result. Although HDL-C showed statistically significant difference between the 0 and non-0 groups [12]

According our study, In the case of group 0, the mean Tchol and TG are snnificantly increased, and the mean LDL is significantly decreased then at A group. The incidence of dyslipidemia in group 0 patients was significantly higher than in group A patients.
Data on mass index are also different. The blood group 0 showed the significant positive association with obesity[13]. However, according to Parveen N.'s research, Blood group “A” and Rhesus-D positive subjects were found to have significantly higher levels of body mass index compared to other blood types especially in males thus rendering them to higher risk of developing obesity. [14]
Our study suggests an association between blood group 0 and 10-year risk of fatal cardiovascular disease / accident with SCORE in young Georgian population.

CONCLUSIONS

- Blood group 0 increased risk fatal cardiovascular disease in young Georgian population
- Study of blood groups during coronary heart disease will help to clarify the prognostic factors of the disease and reduce the global burden of cardiovascular disease.

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PRE-IMPLANTATION GENETIC DIAGNOSIS

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Pre-implantation Genetic Diagnosis (PGD) is the diagnosis of genetic disorders in human embryos prior to implantation into the endometrium, i.e. before the phase of transfer on the program of in vitro fertilization (IVF). A biopsy of one blastomer in an embryo that is at the cleavage stage (6-10 blastomeres) or a biopsy of the trophectoderm (the outer layer of cells) at the blastocyst stage (day 5 of embryo development) is typically performed for analysis. The main advantage of PGD is that there is no selective termination of pregnancy when it is used and the chance of giving birth to a child without any diagnosed genetic diseases is quite high . There are discrepant data in literature on the effectiveness of PGD as part of the program of assisted reproductive technologies (ART) .

According to some studies including ASRM (American Society for Reproductive Medicine) data, application of PGD doesn't increase the frequency of pregnancies with in vitro fertilization (IVF). This may be due to imperfection of the technique of the blastomer sampling procedure or the choice of a laboratory screening method to diagnose aneuploidy and microstructural chromosomal abnormalities simultaneously in all chromosomes. The method of array comparative genomichybridization (CGH) showed high performance for clinical studies on embryo transfer within ART (69-70%). While there is the high genetic abnormalities detection rate in PGD based on many studies, the frequency of pregnancies with this method doesn't exceed 30-40% .

Study of the structure of embryo chromosomal disorders based on pre-implantation genetic diagnosis in the program of assisted reproductive technology as well as the impact of this procedure on the results of pregnancies is, therefore, of particular interest.

We studied chromosomal abnormalities of embryos in 86 females with different IVF outcomes. Pre-implantation study of the embryos was conducted by the FISH method in 42 females with positive IVF outcomes and in 44 females with negative IVF outcomes. The quality of the embryos was assessed on the third day of culture.

In summary, the study of pre-implantation embryo characteristics in the IVF program revealed higher indices for embryos without chromosomal abnormalities in the group with positive IVF outcomes and lower indices for the relative frequency of embryos with chromosomal abnormalities as against the group with negative IVF outcomes.

In females aged >35 from the group with positive IVF outcomes viable embryos were found more frequently and unviable embryos were found less frequently. The nature of chromosomal pathology in study females didn't show a relevant difference among the comparison groups.

Large enough quantity of morphologically healthy but genetically abnormal embryos was also detected. With no PGD an embryologist would undoubtedly choose the embryos that reached the blastocyst phase. And this would lead to a negative IVF outcome.

Along with this, there were also the embryos that were genetically healthy but morphologically defective. All these data suggest that the protocols of controlled ovarian hyperstimulation, used medicinal drugs, embryological phase and procedure of PGD itself need to be improved to obtain a high-quality embryo and positive IVF outcome.

So, while there are contradictory data, the analysis of the world literature data and the results obtained by us in the course of the study revealed great advantages of pre-implantation diagnosis. With its wide diagnostic capabilities, PGD as part of the ART program makes it possible to select and transfer embryos with no chromosomal abnormalities into the uterine cavity, to reduce the risk of miscarriage and multiple pregnancies and to improve the chances of successful implantation and the birth of a healthy child.

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ASSESSMENT OF MOVEMENT IN THE JOINT AFTER HIP REPLACEMENT WITH THE INCLUDING OF DEEP OSCILLATION IN POSTOPERATIVE REHABILITATION

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ABSTRACT

ABSTRACT

OBJECTIVE: Deep Oscillation® is an electromechanical procedure with deep therapy that allow to create a pulsed electrostatic field between the hand applicator and the processing better tissue nutrition, enhanced cellular metabolism, faster healing.
The purpose of this work is to evaluate the movement of the joint during the inclusion of deep oscillation method in standard therapy after endoprosthesis.
METHODS: We studied 52 patients from the Arena 2 rehabilitation center during the endoprosthetic rehabilitation period who underwent comprehensive treatment according to our scheme - the inclusion of deep vibrations in traditional treatment. 80 patients who were rehabilitated by traditional methods were used as control.
RESULTS: In the study group, the length of rehabilitation time was significantly reduced compared to the control group.
The frequency of patients with more than 90^0 flexions is significantly higher in the study group and the frequency of patients with 90^0 and less flexions is significantly lower.
The study group has a significantly higher incidence of patients with more than 30^0 abduction and a significantly lower incidence of those with 15^0 or fewer abduction; had a significantly higher incidence of patients with more than 15^0 adduction and a significantly lower incidence of patients with an adduction of 15^0 and less and had a significantly higher frequency of patients with more than 30^0 external rotations and a significantly lower frequency of patients with more than 30^0 external rotations.
CONCLUSION: Involvement of deep oscillation in the rehabilitation program after hip joint arthroplasty, reduces the timing of rehabilitation and increases the parameters of movement in the joint
Keywords: deep oscillation, hip arthroplasty, movement in the joint.

Background: DEEP Oscillation® (Deep Vibration) is an electromechanical procedure with deep therapy that allow to create a pulsed electrostatic field between the hand applicator and the processing better tissue nutrition, enhanced cellular metabolism, faster healing.
The purpose of this work is to evaluate the movement of the joint during the inclusion of deep oscillation method in standard therapy (complex rehabilitation) after endoprosthesis.

Methods: From January, 1st 2018 until December, 31st 2020 a total of n= 52 patients (21 men and 43 women) with a mean age of 65.4 years were enrolled in this study.
We studied patients from the Arena 2 rehabilitation center during the endoprosthetic rehabilitation period who underwent comprehensive treatment according to our scheme - the inclusion of deep vibrations in traditional treatment. Clinical data from 80 patients who were rehabilitated by traditional methods were used as control.
Both groups were treated orthopedic rehabilitation program (follow-up treatment). The Treatment spectrum included: u. a. Pain therapy procedures, strength training of the muscles that guide the hip joint, coordination exercises, including manual medical treatment techniques, Ergometer training, occupational therapy, medical training therapy and physical Therapy. In addition to the appropriate supply of aids orthopedic shoe adjustments were also made if necessary.
In experimental group the additional DEEP OSCILLATION® treatment was carried out with portable devices "DEEP OSCILLATION® PERSONAL" (Physiomed, Schnaittach /Laipersdorf, Germany) by Hand applicator. The Individual treatment lasted 18 minutes and was done once daily, in total in 15 to 20 Units performed. Here came a treatment program with the frequencies 160 Hz (8 min) and 60 Hz (10 min) for Application that had been preprogrammed on special treatment cards. The standardized treatment on operated leg was done in the direction of movement of a lymphatic drainage.
Kinesetherapy program including positional treatment of the operated leg, aiming anti-edema effect, passive and active musculoskeletal exercises and joint mobilization techniques to strengthen the muscles of the thigh and gluteal muscles, as

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well as to increase the volume of movement in the hip joint. Functional medical gymnastics, including sitting training and getting up from a sitting position.

Statistical analysis: The Statistical significance was defined as a p value of <0.05. Data were analyzed using the SPSS 23.

Results: There is no reliable difference between the sexes and age groups.
In the study group, the length of rehabilitation time was significantly reduced compared to the control group.
The frequency of patients with more than 90^0 flexions is significantly higher in the study group and the frequency of patients with 90^0 and less flexions is significantly lower.
The study group has a significantly higher incidence of patients with more than 30^0 abduction and a significantly lower incidence of those with 15^0 or fewer abduction; had a significantly higher incidence of patients with more than 15^0 adduction and a significantly lower incidence of patients with an adduction of 15^0 and less and had a significantly higher frequency of patients with more than 30^0 external rotations and a significantly lower frequency of patients with more than 30^0 external rotations.

Conclusion: Involvement of deep oscillation in the rehabilitation program after hip joint arthroplasty, reduces the timing of rehabilitation and increases the parameters of movement in the joint

РЕЗЮМЕ

Целью данной работы является оценка движения сустава при включении метода глубоких колебаний в стандартную терапию (комплексная реабилитация) после эндопротезиоования тазобедренного сустава.

Методы: Под нашим наблюдением находились 52 пациента из контингента реабилитационного центра в течение периода реабилитации после операции эндопротезирования тазобедренного сустава, которые прошли комплексное лечение по нашей схеме - с включением глубоких колебаний в традиционное лечение. В качестве контроля использовали клинический материал 80 пациентов, которые были реабилитированы традиционными методами.

Спектр лечения включал: Процедуры обезболивания, силовая тренировка мышц, управляющих тазобедренным суставом, координационные упражнения, в том числе мануальные методы лечения, тренировка на эргометре, медицинская физкультура и физиотерапия. В дополнение к соответствующей поставке вспомогательных приспособлений, при необходимости, также вносились коррективы в ортопедическую обувь. Программа Kinesetherapy включая позиционную обработку оперированной ноги, направленный против отеков, пассивные и активные упражнения опорно-двигательного аппарата и совместных методов мобилизации для укрепления мышц бедра и ягодичных мышц, а также для увеличения объема движения в тазобедренный сустав. Функциональная лечебная гимнастика, в том числе сидячая тренировка и вставание из сидячего положения.
В экспериментальной группе дополнительная обработка DEEP OSCILLATION® проводилась с помощью портативных устройств «DEEP OSCILLATION® PERSONAL» (Physiomed, Schnaittach / Laipersdorf, Германия) с помощью ручного аппликатора. Индивидуальное лечение длилось 18 минут и проводилось один раз ежедневно, всего от 15 до 20 исполняемых единиц. Использовали программу лечения с частотами 160 Гц (8 минут) и 60 Гц (10 минут) для приложения, которое было предварительно запрограммировано на специальных картах лечения. Стандартизированное лечение оперированной ноги проводилось в направлении движения лимфодренажа.

Результаты: В основной группе продолжительность реабилитации значимо сократилась по сравнению с контрольной группой – соответственно 5.4 и 7.9 недели($p<0.05$).
Частота пациентов с более чем 90^0 флексией значительно выше в основной группе, а частота пациентов с 90^0 и менее - значительно ниже.
В основной группе отмечается значимо высокая частота пациентов с более чем 30^0 абдукцией и значимо низкая частота пациентов с аддукцией менее 15^0, чем в контрольной группе. В основной группе выявили значимо высокую частоту пациентов с более чем 15^0 аддукцией и значимо более низкую частоту пациентов с аддукцией 15^0; и значимо высокую частоту пациентов с более чем 30^0 внешней ротации и значимо низкую частоту пациентов $>30^0$ внешней ротации.

Вывод: Включение глубоких колебаний в программу реабилитации после эндопротезирования тазобедренного сустава, сокращает срок реабилитации и увеличивает параметры движения в суставе.

INTRODUCTION

Joint arthroplasty constitutes a major advance in the treatment of chronic refractory joint pain [1]. And rehabilitation is key to optimize outcomes [2,3].
DEEP Oscillation® (Deep Vibration) is an electromechanical procedure with deep therapy tools OSCILLATION® EVIDENT and DEEP OSCILLATION® PERSONAL (Physiomed, Germany) that allow to create a pulsed electrostatic field between the hand applicator and the processing better tissue nutrition, enhanced cellular metabolism, faster healing. It has anti-edema, lymphatic drainage, anti-brachial and detoxifying properties, promotes rapid healing of open wounds, alleviates pain and swelling, stimulates collagen and tissue regeneration.[4,5,6].
The electrostatic field, at the level of connective tissue, generates intense resonant vibrations, and the repetition of this phenomenon rapidly results in a rhythmic deformation of the tissue (skin, connective tissue, and muscle). The resulting effects include improved microcirculation,
It is said to be effective in damaging the brain and helping to increase its flexibility.
There is scant literature on the use of this method for further rehabilitation of the endoprosthesis of the pelvic joint.
The purpose of this work is to evaluate the movement of the joint during the inclusion of deep oscillation method in standard therapy (complex rehabilitation) after endoprosthesis.

METHOD

From January, 1st 2018 until December, 31st 2020 a total of n= 52 patients (21 men and 43 women) with a mean age of 65.4 years were enrolled in this study.
We studied patients from the „Arena 2 rehabilitation center“ during the endoprosthetic rehabilitation period who underwent comprehensive treatment according to our scheme - the inclusion of deep vibrations in traditional treatment. Clinical data from 80 patients who were rehabilitated by traditional methods were used as control.
A non-randomized controlled trial was performed.
The research protocol has been approved by the University Ethics Committee
Both groups were treated orthopedic rehabilitation program (follow-up treatment). The Treatment spectrum included: u. a. Pain therapy procedures, strength training of the muscles that guide the hip joint, coordination exercises, including manual medical treatment techniques, Ergometer training, occupational therapy, medical training therapy and physical Therapy. In addition to the appropriate supply of aids orthopedic shoe adjustments were also made if necessary.
In experimental group the additional DEEP OSCILLATION® treatment was carried out with portable devices "DEEP OSCILLATION® PERSONAL" (Physiomed, Schnaittach /Laipersdorf, Germany) by Hand applicator. The Individual treatment lasted 18 minutes and was done once daily, in total in 15 to 20 Units performed. Here came a treatment program with the frequencies 160 Hz (8 min) and 60 Hz (10 min) for Application that had been preprogrammed on special treatment cards. The standardized treatment on operated leg was done in the direction of movement of a lymphatic drainage.
Kinesetherapy program including positional treatment of the operated leg, aiming anti-edema effect, passive and active musculoskeletal exercises and joint mobilization techniques to strengthen the muscles of the thigh and gluteal muscles, as well as to increase the volume of movement in the hip joint. Functional medical gymnastics, including sitting training and getting up from a sitting position.
Statistical analysis: In the assessment of quantitative indicators, we have counted an average, a standard deviation. The reliability of the differences between the groups, in case of the quantitative indicators were determined by the means of Student`s *t* test, the equilibrium of dispersions was assessed according to Levene's Test while making the comparison. We counted percent for qualitative indicators and evaluated the differences between groups by means of χ^2 (Pearson) criteria. The Statistical significance was defined as a p value of <0.05. Data were analyzed using the SPSS 23.

RESULTS

The demographic characteristics of the patients are given in Table 1

		DEEP Oscilation group N=52		Standard treatment group N=80		χ^2	P
		abs	%				
Sex	Women	36	69.23	33	41.25	1.16	0.282
	Men	16	30.77	47	58.75	1.16	0.282
Age	<35	10	19.23	15	18.75	0.01	0.946

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	36-55	15	28.85	22	27.5	0.03	0.867
	55-75	21	40.38	34	42.5	0.06	0.81
	>75	6	11.54	9	11.25	0.003	0.96

As can be seen from the table, there is no reliable difference between the sexes and age groups
In the study group, the length of rehabilitation time was significantly reduced compared to the control group (fig.1)

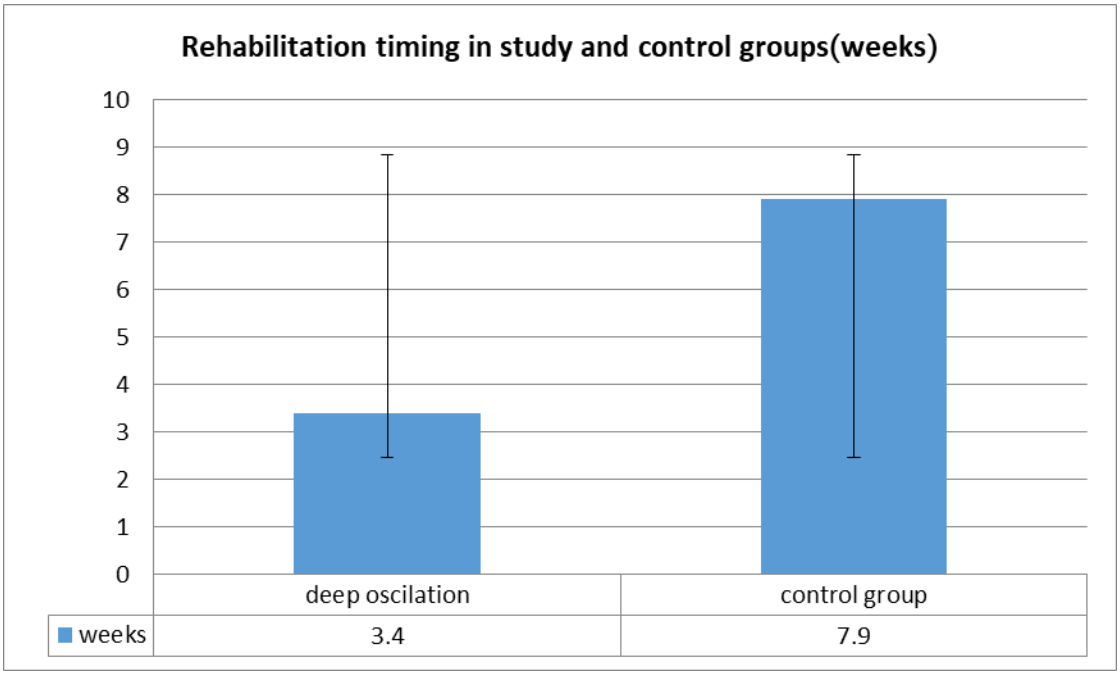

Figure 1
Enhancements movement of the joint is of particular importance during the rehabilitation process.
Our study showed that after standard DEEP Oscilation involvement in standard treatment, joint movement parameters increased (Table 1).

Table 1
Joint movement parameters after standard DEEP Oscilation involvement in standard treatment

		DEEP Oscilation group N=52		Standard treatment group N=80		□2	P
		abs	%	abs	%		
Flexion	$0\text{-}45^0$	2	3.84	16	20.00	9.18	0.003
	$45^0\text{-}90^0$	15	28.84	27	33.75	4.30	0.039
	$91^0\text{-}110^0$	22	42.30	30	37.50	4.26	0.040
	$111^0\text{-}140^0$	13	25.00	7	8.75	6.47	0.011
Abduction	$0^0\text{-}15^0$	11	21.15	39	48.75	10.20	0.002

	16^0-30^0	27	51.92	31	38.75	2.22	0.564
	31^0-60^0	14	26.92	8	10.00	6.50	0.011
Adduction	0^0-15^0	15	28.85	42	52.50	7.19	0.005
	16^0-60^0	37	71.15	38	47.50	7.19	0.008
External rotation	0^0-30^0	17	32.69	45	56.25	7.02	0.009
	31^0-60^0	35	67.31	35	43.75	7.02	0.009

As we can see, the frequency of patients with more than 90^0 flexions is significantly higher in the study group and the frequency of patients with 90^0 and less flexions is significantly lower.
The study group has a significantly higher incidence of patients with more than 30^0 abduction and a significantly lower incidence of those with 15^0 or fewer abduction; had a significantly higher incidence of patients with more than 15^0 adduction and a significantly lower incidence of patients with an adduction of 15^0 and less and had a significantly higher frequency of patients with more than 30^0 external rotations and a significantly lower frequency of patients with more than 30^0 external rotations.

DISCUSSION

Arthroplasty is the most frequent amongst the interventions in orthopaedics and traumatology. Rehabilitation is the final stage of hip joint arthroplasty with great importance concerning the rate and stage of functional recovery [7]. Small accessory oscillation movements stimulate joint mechanoreceptors that assist in pain modulation while helping to maintain capsular mobility [8]. Deep Oscillation promotion of motoricity[9]. Our research has shown that the use of deep oscillation compared to the control group reliably reduces rehabilitation time and increases Flexion, Abduction, Adduction and External rotation.

CONCLUSION

Involvement of deep oscillation in the rehabilitation program after hip joint arthroplasty, reduces the timing of rehabilitation and increases the parameters of movement in the joint

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RECIPROCAL TRANSLOCATION t (6; 8) (q25-27; q23): CASE REPORT

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ABSTRACT
Reciprocal translocations are the most common structural chromosomal abnormalities in humans. In this study, the results of cytogenetic analysis performed on a couple with a reproductive history of three abortions and one intrauterine death referred to our laboratory are presented. Normal karyotype (46, XY) in male and reciprocal translocation 46XX t (6; 8) (q25-27; q23) in female were determined. In about 4% of couples with recurrent miscarriages, one of the parents is either a balanced reciprocal translocation or a robertsonian translocation carrier. Therefore, cytogenetic analysis should be recommended to couples with recurrent miscarriages.
Keywords: Recurrent Abortions, Fetal Wastage, Reciprocal Translocation

INTRODUCTION

Studies report that 10-20% of all pregnancies result in miscarriage. Miscarriages can occur for many different reasons such as anatomical, endocrinological, infectious, immunological, environmental or chromosomal disorders. In about 4% of couples with recurrent miscarriages, one of the parents is either a balanced reciprocal translocation or a robertsonian translocation carrier.

Reciprocal translocations are the most common structural rearrangements in humans. Robertsonian translocations are seen at a frequency of 1 in 1000 in the general population, while reciprocal translocations are seen approximately 1 in 500 individuals. Balanced carriers of these rearrangements are phenotypically normal, but may result in recurrent miscarriages, infertility, and a child with abnormal phenotype due to abnormal segregation during meiosis. Although reciprocal translocations are relatively common rearrangements, little is known about the mechanisms that result in translocation formation.

Balanced reciprocal translocations do not cause changes in the amount of chromosomes and genetic materials. Although these carriers do not have any problems, they cause unbalanced chromosomal formation during parental gamete formation. In this study, as a result of the cytogenetic analysis performed in the couple referred to our laboratory due to recurrent miscarriages, 46, XX, t (6; 8) (6q 25-27; 8q 23) karyotype is evaluated according to the literature.

A Case Report with 6; 8 Translocations

Proban is a 30-year-old woman. He was married to a 33-year-old healthy man for 6 years and was sent to our center for cytogenetic research due to recurrent miscarriage. There is no kinship between parents. Our case has no surviving children with a reproductive history including 3 miscarriages (2 months old) and a 6-week intrauterine death. One of the miscarriages occurred as a result of pregnancy provided by IVF. The proband is a total of 6 siblings, 3 girls and 3 boys. The siblings are all married and no one has a miscarriage. There is no miscarriage story in the mother of the proband. Physical examination of the proband is normal, but ultrasound examination revealed that kidney localizations are different from each other.

Standard cytogenetic methods were used for karyotype analysis of the proband and her partner. A 72-hour culture was performed using phytohemagglutinin (PHA) -induced peripheral blood lymphocytes. The metaphase preparations obtained after the culture were stained with GTG banding method and chromosomes in 30-50 metaphase plates were evaluated in terms of numerical and structural irregularities. As a result of the chromosome analysis of the case, 46, XX, t (6; 8) (6q 25-27; 8q 23) karyotype was determined. His wife's karyotype was determined as normal (46, XY). Chromosome analysis could not be performed because the proband's parents and siblings were far away.

DISCUSSION

In individuals with balanced reciprocal translocation carriers, genetic information is completely present, although it has been rearranged differently. Therefore, individuals carrying balanced reciprocal translocation have a significantly increased risk of producing phenotypically normal but chromosomally unbalanced gametes1.

During meiosis, chromosomes with balanced reciprocal translocation form a quadrivalent shape and match with its homologous segment. Segregation can occur in 5 different ways: alternate (normal or balanced gametes are produced), adjacent 1, adjacent 2, 3: 1, and 4: 0 (all gametes are unbalanced). Half of the gametes formed in alternative separation are stable chromosome carriers, while the other half have normal chromosome content. The gametes formed in alongside of 1 and 2 separation form partial monosomic and partial trisomic products with unbalanced chromosome content.

All pregnancies of these couples have the likelihood of miscarriage, intrauterine fetal death, a baby with a congenital anomaly, a baby with a chromosomal damage (carrier), but also a normal phenotype or a completely healthy baby.

As a result of our study, we performed molecular cytogenetic analysis of fracture points in balanced reciprocal translocation carriers, and we found that balanced reciprocal translocations in phenotypically normal patients did not have an imbalance in the fracture points, whereas in phenotypically abnormal patients, translocation fracture points were mostly associated with cryptic imbalances. However, we have suggested that phenotypically normal and abnormal individuals may have impaired genes and thus be inactivated by one of the breakpoints.
Preimplantation genetic diagnosis (PGD) is recommended for reciprocal translocation carriers as an alternative to prenatal diagnosis and pregnancy termination of unstable fetuses. In this way, it is also aimed to reduce the number of spontaneous abortions.
Parents with balanced chromosomal disorders constitute an important group among prenatal cytogenetic diagnosis indications, since the risk of fetus with unbalanced chromosomal disorder is 10-15%. This reveals the necessity of prenatal cytogenetic diagnosis in all subsequent pregnancies of parents with reciprocal translocation1.
In this study, during the genetic counseling process, the family was informed about balanced reciprocal translocation carriage, the possibilities of their next pregnancy, PGD and prenatal diagnosis for their next pregnancy. The family is considering PGD application and is followed up during the genetic counseling process.

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