



ISSN: 1987-6521; E-ISSN:2346-7541

DOI: 10.36962/GBSSJAR55042020

JUNE-SEPTEMBER 2020 VOLUME 55 ISSUE 04

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SCIENTIFIC JOURNAL OF ACADEMIC RESEARCH

APPLIED SOCIAL RESEARCH & BEHAVIORAL SCIENCES
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APPLIED SOCIAL RESEARCH & BEHAVIORAL SCIENCES



"An investment in knowledge always pays the best interest." Benjamin Franklin

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JOURNAL INDEXING

Crossref

Catalogue of Russian Journals Impact Factor (2016) – 0.171

Impact factor ПИИЦ 2017-0.041

UNITED KINGDOM, LONDON 2020

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ISSN: 1987-6521; E-ISSN: 2346 – 7541; UDC: 551.46 (051.4) / B-64

©**Publisher:** LTD Aspendos International Academy of Medical and Social Sciences. (UK, London).

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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° flexions is significantly higher in the study group and the frequency of patients with 90° and less flexions is significantly lower.

The study group has a significantly higher incidence of patients with more than 30° abduction and a significantly lower incidence of those with 15° or fewer abduction; had a significantly higher incidence of patients with more than 15° adduction and a significantly lower incidence of patients with an adduction of 15° and less and had a significantly higher frequency of patients with more than 30° external rotations and a significantly lower frequency of patients with more than 30° 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.

Kinesotherapy 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: 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° flexions is significantly higher in the study group and the frequency of patients with 90° and less flexions is significantly lower.

The study group has a significantly higher incidence of patients with more than 30° abduction and a significantly lower incidence of those with 15° or fewer abduction; had a significantly higher incidence of patients with more than 15° adduction and a significantly lower incidence of patients with an adduction of 15° and less and had a significantly higher frequency of patients with more than 30° external rotations and a significantly lower frequency of patients with more than 30° 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

აბსტრაქტი

ნაშრომის მიზანია სახსარში მოძრაობის შეფასება ენდოპროთეზირების შემდგომ სტანდარტულ რეაბილიტაციაში ღრმა ოსცილაციის მეთოდის ჩართვის შემდეგ.

მეთოდები

შევისწავლეთ 52 პაციენტი „სარეაბილიტაციო ცენტრის არენა 2-ის“ კონტინგენტიდან ბარძაყის სახსრის ენდოპროთეზირების შემდეგ, რეაბილიტაციის პერიოდში, რომლებმაც გაიარეს კომპლექსური მკურნალობა ჩვენი სექციის მიხედვით - ტრადიციულ მკურნალობაში ღრმა ოსცილაციის ჩართვით. საკონტროლოდ გამოიყენებოდა 80 პაციენტის კლინიკური მასალისა, რომლებსაც რეაბილიტაცია ჩაუტარდა ტრადიციული მეთოდით.

მკურნალობის სპექტრი მოიცავდა: ანესთეზიის პროცედურებს, თემოს სახსრის კუნთების ძალის ვარჯიშს, საკოორდინაციო ვარჯიშებს, ერგომეტრზე ვარჯიშს, სამედიცინო ფიზკულტურას და ფიზიოთერაპიას.

ექსპერიმენტულ ჯგუფში ჩატარდა დამატებითი DEEP OSCILLATION®-ით მკურნალობა პორტატული DEEP OSCILLATION® PERSONAL მოწყობილობების გამოყენებით. ინდივიდუალური მკურნალობა გრძელდებოდა 18 წუთის მანძილზე და ტარდებოდა დღეში ერთხელ - ყოველდღიურად, 15-დან 20 ერთეულამდე. გამოიყენებოდა სამკურნალო პროგრამა, რომელიც წინასწარ იყო დაპროგრამებული სპეციალურ სამკურნალო ბარათებზე. სიხშირე შეადგენდა 160 ჰერცს (8 წუთი) და 60 ჰც (10 წუთი), ნაოპერაციები ფეხის სტანდარტიზებული მკურნალობა ჩატარდა ლიმფური დრენაჟის მოძრაობის მიმართულებით.

კინეზოთერაპიის პროგრამა მოიცავდა ნაოპერაციები ფეხის მკურნალობას შეშუპების საწინააღმდეგოდ, კუნთოვანი სისტემის პასიური და აქტიური ვარჯიშებისა და სახსრების მობილიზაციის მეთოდებით, კუნთების გასაძლიერებლად, აგრეთვე თემოს სახსარში მოძრაობის დიაპაზონის გასაზრდელად.

შედეგები

ძირითად ჯგუფში, საკონტროლო ჯგუფთან შედარებით სარწმუნოდ შემცირდა რეაბილიტაციის ხანგრძლივობა - 4.4 და 7.9 კვირა შესაბამისად ($p < 0.05$).

ოსცილაციის ჯგუფში საკონტროლოსთან შედარებით სარწმუნოდ ნაკლებია 45° -ზე ნაკლები ფლექსიის მქონე პაციენტების სიხშირე - შესაბამისად 3.84% და 20.00%, და მაღალია 110° -ზე მეტი ფლექსიის სიხშირე შესაბამისად 25% და 8.75%

ძირითად ჯგუფში საკონტროლოსთან შედარებით აღინიშნა იმ პაციენტების სარწმუნოდ მაღალი სიხშირე, რომელთაც აქვთ 30° -ზე მეტი აბდუქცია - 46.15 და 37.50 და იმ პაციენტთა სარწმუნოდ დაბალი სიხშირე, რომელთაც აღენიშნათ 15° -ზე ნაკლები აბდუქცია - 26.92% და 10.00%,. ძირითად ჯგუფში, გამოვლენილია პაციენტთა სარწმუნოდ მაღალი სიხშირე, რომელთაც აქვთ 15° -ზე მეტი ადდუქცია - 28.85% და 52.50% და იმ პაციენტთა სარწმუნოდ დაბალი სიხშირე, რომლებსაც აქვთ 15° -ზე ნაკლები ადდუქცია შესაბამისად 71.15 და 47.50. აგრეთვე 30° -ზე მეტი გარე როტაციის მქონე პაციენტების მნიშვნელოვნად მაღალი სიხშირე 32.69 და 56.25 და 30° -ზე ნაკლები გარე როტაციის მქონე პაციენტების მნიშვნელოვნად დაბალი სიხშირე, ვიდრე საკონტროლო ჯგუფში - შესაბამისად 67.31 და 43.75.

დასკვნა: მეჩქ-ბარძაყის სახსრის ენდოპროტეზირების შემდგომი რეაბილიტაციის პროგრამაში ღრმა ოსცილაციის ჩართვა, ხელს უწყობს რეაბილიტაციის პერიოდის შემცირებას და სახსარში მოძრაობის პარამეტრების გაუმჯობესებას.

РЕЗЮМЕ

Целью данной работы является оценка движения сустава при включении метода глубоких колебаний в стандартную терапию (комплексная реабилитация) после эндопротезирования 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 Kinesotherapy 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 значительно сократилась по сравнению с контрольной группой – соответственно 5.4 и 7.9 недели ($p < 0.05$).

Частота пациентов с более чем 90° флексией значительно выше в основной группе, а частота пациентов с 90° и менее - значительно ниже.

В основной группе отмечается значимо высокая частота пациентов с более чем 30° абдукцией и значимо низкая частота пациентов с аддукцией менее 15°, чем в контрольной группе. В основной группе выявили значимо высокую частоту пациентов с более чем 15° аддукцией и значимо более низкую частоту пациентов с аддукцией 15°; и значимо высокую частоту пациентов с более чем 30° внешней ротации и значимо низкую частоту пациентов >30° 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.

Kinesiotherapy 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 Oscillation 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
	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)

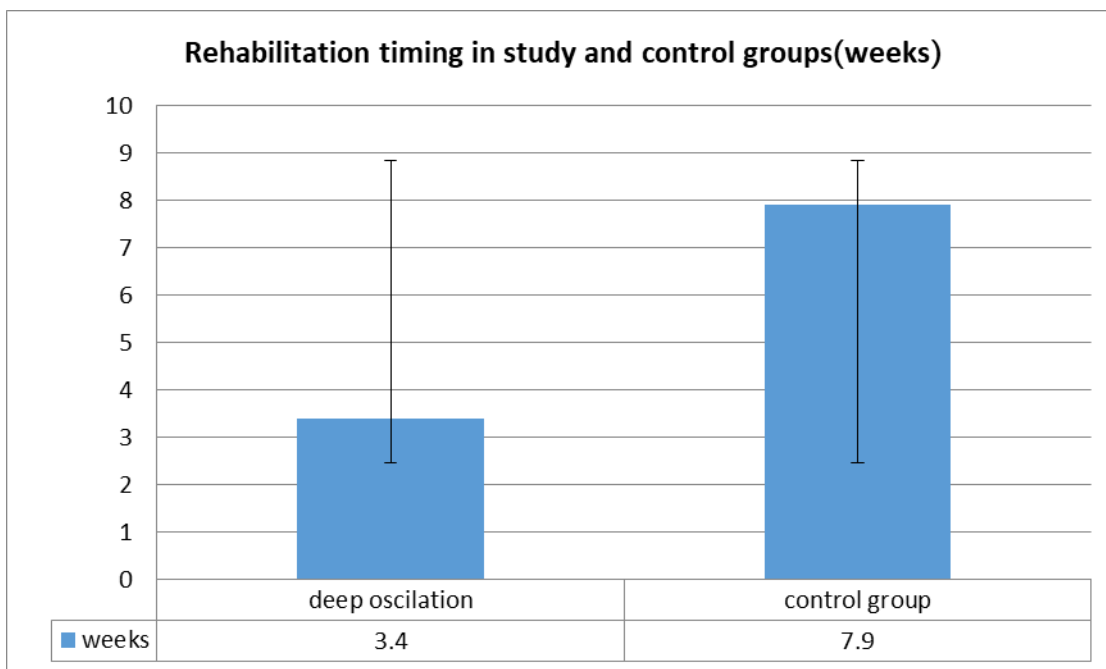


Figure 1

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

Table 1

Joint movement parameters after standard DEEP Oscillation involvement in standard treatment

		DEEP Oscillation group N=52		Standard treatment group N=80		t	P
		abs	%	abs	%		
Flexion	0-45°	2	3.84	16	20.00	9.18	0.003
	45°-90°	15	28.84	27	33.75	4.30	0.039
	91°-110°	22	42.30	30	37.50	4.26	0.040
	111°-140°	13	25.00	7	8.75	6.47	0.011
Abduction	0°-15°	11	21.15	39	48.75	10.20	0.002
	16°-30°	27	51.92	31	38.75	2.22	0.564
	31°-60°	14	26.92	8	10.00	6.50	0.011
Adduction	0°-15°	15	28.85	42	52.50	7.19	0.005
	16°-60°	37	71.15	38	47.50	7.19	0.008
External	0°-30°	17	32.69	45	56.25	7.02	0.009

rotation	31 ⁰ -60 ⁰	35	67.31	35	43.75	7.02	0.009
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As we can see, the frequency of patients with more than 90⁰ flexions is significantly higher in the study group and the frequency of patients with 90⁰ and less flexions is significantly lower.

The study group has a significantly higher incidence of patients with more than 30⁰ abduction and a significantly lower incidence of those with 15⁰ or fewer abduction; had a significantly higher incidence of patients with more than 15⁰ adduction and a significantly lower incidence of patients with an adduction of 15⁰ and less and had a significantly higher frequency of patients with more than 30⁰ external rotations and a significantly lower frequency of patients with more than 30⁰ 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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THE KEY DETERMINANTS OF THE INNOVATIVE ORIENTED ECONOMIES FORMING IN THE CONTEXT OF THE WORLD'S COUNTRIES PROSPERITY ENSURING

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SUMMARY

The paper is devoted to the evaluation the impact of key determinants of innovation development and ensuring the worlds' countries prosperity and working out the ways of increasing the innovative economic growth. By using the international statistic data of 40-ty countries, there were analyzed such indicators, as the level of GDP per capita and other indicators, such as expenditure on education, tertiary enrolment, graduates in science & engineering, number of researchers, gross expenditure on R&D, knowledge-intensive employment, intellectual property payments, high-tech imports, high-tech net exports and creative goods exports. As a result of calculating pairwise correlation coefficients between indicators, it was determined, that the most significant influence on the level of GDP per capita make such three variables: number of researchers, gross expenditure on R&D, knowledge-intensive employment. There were suggested the main directions of innovative development and prosperity raising for four groups of actors within the Quadruple Helix Model: state (government), universities and scientific institutions, business, civil society.

Keywords: innovation, prosperity, human resources, research activity, education, expenditure, knowledge, high-tech technology, creativity

INTRODUCTION

Under modern conditions, the development of innovative model of the economy and the worlds' countries prosperity depend on many factors. The most important among these factors are the development of human resources, research activity, quality of education, financial and organizational support for innovation and others. Nowadays a significant differentiation between the countries of the world in terms of GDP per capita, income, opportunities for intellectual development, quality of life exists. That's why it is necessary to analyze the key determinants of the impact on the level of countries economic development and prosperity, to justify the relevant areas for improvement in the current and long terms.

Literature review. The key determinants of innovative development in the international dimension are the subject of scientific research of many authors. So, some scientists focus on the "relevance of innovation oriented and human resource development policy that impacts small and medium enterprises' new markets and products" (Kuntonbutr C., Jaturat N., Tsutomu Konosu T., & Wilairatana P., 2017) [1].

The World Bank Experts emphasize on "three central determinants of innovation performance: the critical complements to innovation investment needed to realize the high potential returns; the range of firm capabilities required to undertake innovation and take it to market; and the required government capabilities for implementing effective innovation policies" (Cirera, Xavier, & William F. Maloney, 2017) [2].

It's very important to take into account, that the "innovation goes beyond science and technology, and involves investments in a wide range of knowledge-based assets that extend beyond research and development" (OECD, 2015) [3]. Under the modern conditions, "scientific development, technological development, innovations increasing competitiveness, economic growth and development lead to welfare of nations increasing" (Sefer Şener and Ercan Saridoğan, 2011) [4]. We agree with the affirmation, that the "growth or economic performance is relevant for evaluating competitiveness but a number of other factors such as environment, quality of life, technology, knowledge transfer, and scientific research could be more important" (Dima A.M., Begu L., Vasilescu M.D. & Maassen M.A., 2018) [5]. The main factors of innovation process activation also can be divided into "legislative, normative, research, personnel, financial, material and resource, technological, infrastructure, informational and communicative" (Levchenko O., Tkachuk O., Tsarenko I., 2019) [6]. So, the above mentioned actualizes the need of "increasing the flow and accessibility of investment

to new ideas, inventions, human capital, increasing the level of technological transfers of innovations, innovative counseling of all participants in the innovation process" (Yurynets Z., Bayda B., Petrukh O., 2015) [7].

Despite on the significant interest of scientists in the issues of innovative development and countries' prosperity increasing, it's necessary to conduct more detailed analysis, taking into account the conditions of the external and internal environment, which are constantly changing.

Purpose of the study. The aim of the paper is to assess the impact of key determinants of innovation development and ensuring the worlds' countries prosperity through the comparative analysis of statistic data and to develop the effective measures of accelerating the economic growth on the innovative basis.

Results. The working hypothesis of our study is to predict the relationship between the level of GDP per capita and other indicators, such as expenditure on education, tertiary enrolment, graduates in science & engineering, number of researchers, gross expenditure on R&D, knowledge-intensive employment, intellectual property payments, high-tech imports, high-tech net exports and creative goods exports. For the analysis, we selected 40 countries, including the most developed countries in Europe and the world, as well as post-Soviet countries (Table 1).

Table 1 – The data for analysis of innovation development and the worlds' countries prosperity

	GDP per capita, PPP\$	Expenditure on education, % GDP	Tertiary enrolment, % gross	Graduates in science & engineering, %	Researchers, FTE/mn pop	Gross expenditure on R&D, % GDP	Knowledge-intensive employment, %	Intellectual property payments, % total trade	High-tech imports, % total trade	High-tech net exports, % total trade	Creative goods exports, % total trade
Armenia	10176,1	2,8	52,2	14,7	x	0,2	29,4	0,0	4,8	0,6	0,6
Austria	52137,4	5,5	86,3	30,3	5439,8	3,2	41,6	0,8	8,2	7,5	0,9
Azerbaijan	18075,9	2,9	27,1	23,6	x	0,2	23,3	0,1	2,8	0,1	0,0
Belarus	20003,0	4,8	86,7	33,2	x	0,6	39,2	0,4	5,1	1,8	0,4
Belgium	48244,7	6,6	75,9	17,1	4905,5	2,6	47,6	0,8	7,4	8,1	1,6
Bulgaria	23155,6	4,1	71,2	19,7	2130,5	0,8	31,4	0,5	6,7	3,8	0,8
Canada	49651,2	5,3	67,0	21,3	4274,7	1,7	43,7	2,2	10,0	4,9	1,0
China	18109,8	x	51,0	x	1234,8	2,1	x	1,1	23,3	27,9	11,9
Croatia	26221,4	4,6	67,5	25,3	1865,4	0,9	36,3	1,1	6,1	3,1	0,8
the Czech Republic	37371,0	5,8	63,7	23,5	3689,9	1,8	38,0	0,8	17,4	17,1	10,1
Denmark	52120,5	7,6	81,1	21,0	7923,2	3,1	46,3	1,0	5,7	5,2	1,6
Estonia	34095,8	5,2	71,4	27,5	3568,9	1,3	45,5	0,3	9,6	8,6	1,4
Finland	46429,5	7,1	87,0	29,5	6707,5	2,8	47,4	1,0	7,7	4,4	0,5
France	45775,1	5,5	64,4	25,6	4441,1	2,2	45,1	1,9	10,8	12,8	1,7

Georgia	11485,4	3,8	57,5	21,9	1336,6	0,3	25,3	0,2	7,5	0,3	0,1
Germany	52558,7	4,8	68,3	36,0	5036,2	3,0	44,7	0,8	9,6	11,5	2,2
Greece	29123,0	x	x	28,2	3152,8	1,1	29,8	0,5	5,4	2,0	1,1
Hungary	31902,7	4,6	48,0	22,8	2924,0	1,4	34,3	1,5	13,2	12,5	6,1
Italy	39637,0	4,1	63,0	23,3	2294,5	1,4	36,1	0,9	6,7	5,3	2,2
Japan	44227,2	3,5	x	x	5304,9	3,2	25,2	2,4	13,8	12,1	2,0
Kazakhstan	27549,8	2,9	53,3	24,8	687,6	0,1	33,3	0,3	6,5	3,6	0,1
Latvia	29901,3	5,3	88,1	20,5	1785,9	0,5	42,1	0,2	11,9	7,4	3,1
Lithuania	34825,8	4,2	71,1	23,8	3013,2	0,9	41,8	0,2	6,5	5,9	2,0
the Netherlands	56383,2	5,4	80,4	14,1	5007,1	2,0	46,8	8,1	11,5	11,2	4,1
Norway	74356,1	7,6	82,0	20,5	6407,5	2,1	52,5	0,4	6,6	3,0	0,5
Poland	31938,7	4,8	66,6	22,9	3001,9	1,0	38,6	1,1	9,3	6,5	4,4
Portugal	32006,4	4,9	62,9	29,0	4350,5	1,3	36,1	0,9	6,9	2,7	1,5
the Republic of Moldova	7304,5	6,7	41,1	22,3	723,9	0,3	26,5	0,5	7,4	0,7	0,2
Romania	26446,7	3,1	48,0	28,8	890,2	0,5	23,3	1,0	9,8	4,2	0,7
Serbia	17555,2	3,9	66,5	26,6	2079,1	0,9	28,5	1,0	5,4	1,6	0,7
Slovakia	35129,8	4,6	47,8	21,1	2795,0	0,9	32,0	0,8	13,4	9,2	8,5
Slovenia	36745,9	4,9	77,6	25,0	4467,8	1,9	43,1	0,7	5,4	4,5	1,0
Spain	40138,8	4,3	91,2	23,9	2873,4	1,2	33,2	1,2	6,8	3,9	0,9
Sweden	52984,1	7,6	63,5	26,6	7268,2	3,4	52,3	1,7	7,8	7,3	1,8
Switzerland	64649,1	5,1	57,9	24,5	5257,4	3,4	52,9	3,1	6,1	7,2	3,8
Tajikistan	3415,8	5,2	30,9	22,0	x	0,1	16,1	0,0	x	x	x
Turkey	27956,1	4,3	x	20,2	1385,8	1,0	21,0	0,3	9,9	1,4	2,9
Ukraine	9283,4	5,0	83,4	24,2	1119,5	0,4	36,9	0,7	8,8	2,0	0,2
the United Kingdom	45704,6	5,5	59,4	26,3	4377,0	1,7	48,6	1,5	11,9	9,0	2,9
the United States of America	62605,6	5,0	88,8	17,9	4256,3	2,8	47,3	1,8	17,2	5,8	3,3

Source: formed by the authors at the base of The Global Innovation Index 2019 [8].

As we can see from the Fig. 1, the level of GDP per capita among the selected countries is very different. So, in Norway the meaning of this indicator is 74356,1 PPP\$, in Switzerland – 64649,1 PPP\$, in the United States of America – 62605,6 PPP\$, in the Netherlands – 56383,2 PPP\$. At the same time, the majority of post-Soviet countries have much lower level of GDP per capita. The most positive situation among them is observed in Lithuania (34825,8 PPP\$), Estonia (34095,8 PPP\$) and Latvia (29901,3 PPP\$). Lower meanings take place in Georgia (11485,4 PPP\$), Armenia (10176,1 PPP\$), Ukraine (9283,4 PPP\$), the Republic of Moldova (7304,5 PPP\$), Tajikistan (3415,8 PPP\$).

Another important indicator is the expenditure on education (% of GDP). From Fig. 2 we can predict, that the quality of education in different countries depends mostly on the value of absolute expenditure on education for one student, than on the percentage value

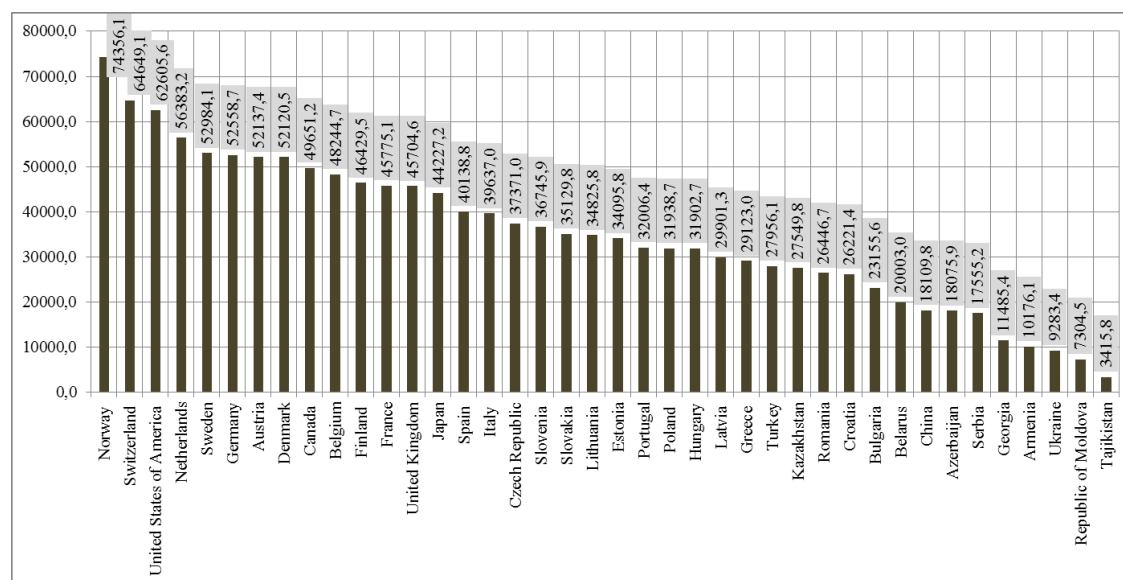


Figure 1. The rating of the countries by level of GDP per capita in 2019, PPP\$
Source: formed by the authors at the base of The Global Innovation Index 2019 [8].

For example, the percentage value of expenditure on education is the same in Ukraine (5,0% GDP) and in the United States of America (5,0% GDP). But, the countries with a low level of GDP spend on the education much smaller, even if the percentage value of expenditure is rather high.

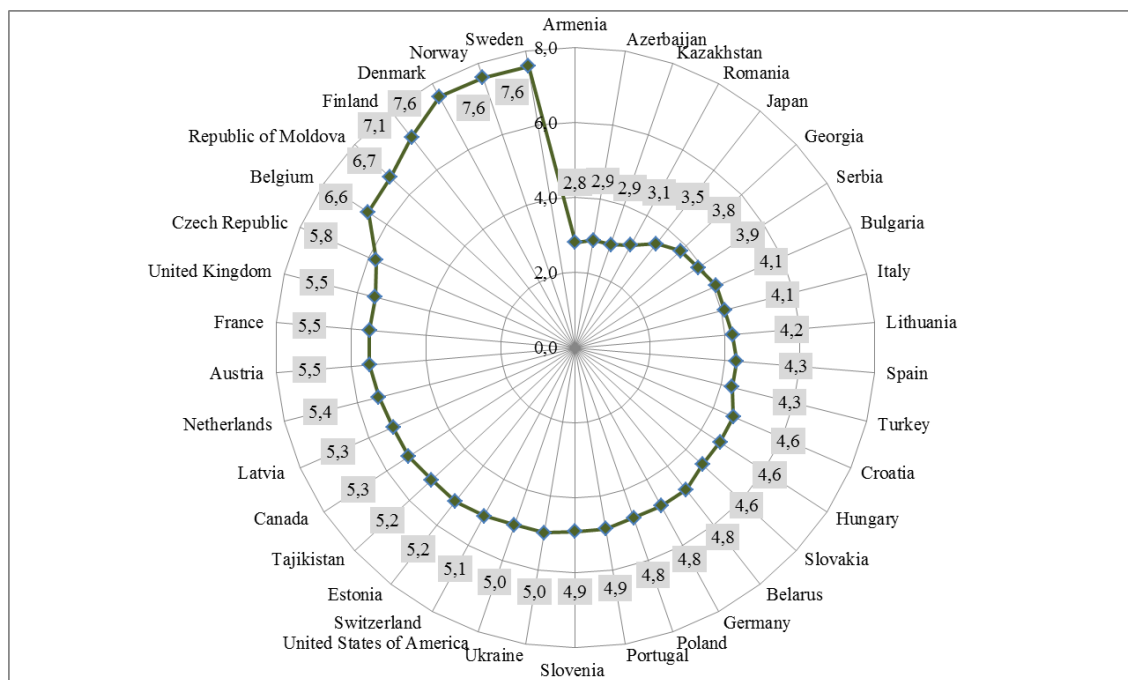


Figure 2. The rating of the countries by level of expenditure on education in 2019, % GDP

Source: formed by the authors at the base of The Global Innovation Index 2019 [8].

The rating of the countries by the number of researches in 2019 (FTE/mn pop.) is presented on Fig. 3. As we can see, in Denmark this indicator reaches the meaning 7923,2 researches, in Sweden – 7268,2 researches, in Finland – 6707,5 researches, in the Norway – 6407,5 researches, while in Ukraine – 1119,5 researches, in Romania – 890,2 researches, in the Republic of Moldova – 723,9 researches, in Kazakhstan – only 687,6 researches.

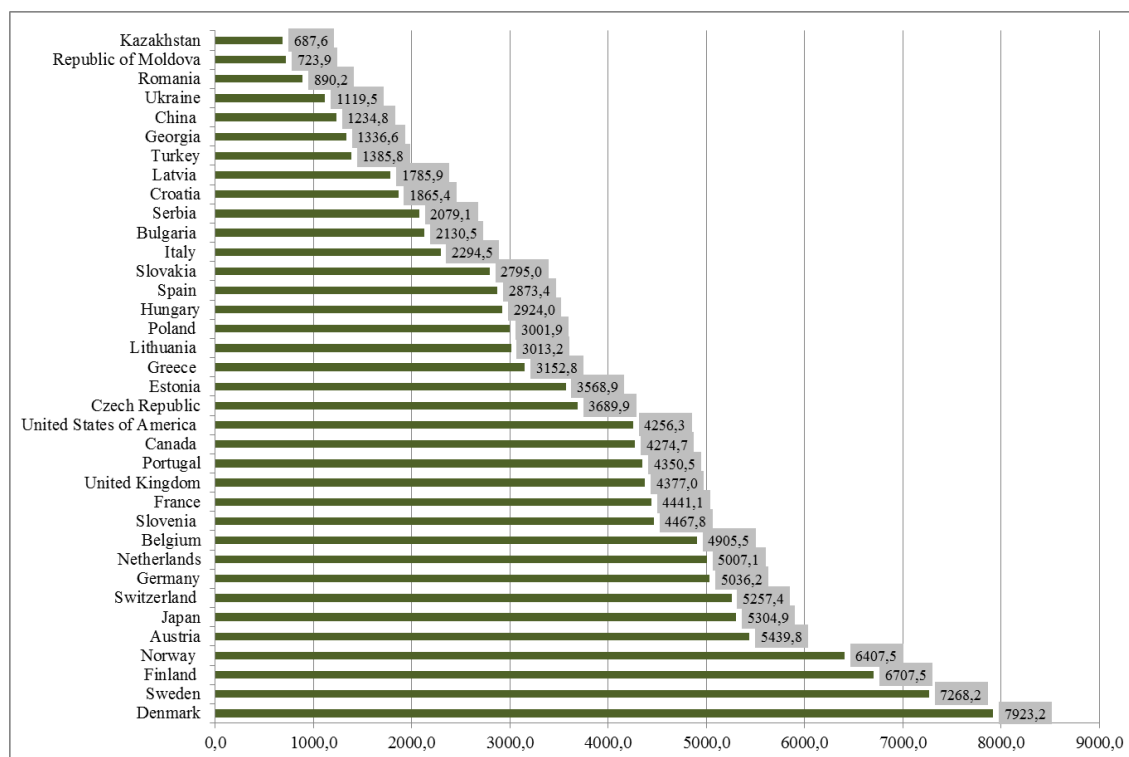


Figure 3. The rating of the countries by the number of researches in 2019, FTE/mn pop.
Source: formed by the authors at the base of The Global Innovation Index 2019 [8].

Tertiary enrolment (% of gross) among the selected group of countries fluctuates from 27,1% in Azerbaijan to 91,2% in Spain. In Ukraine this indicator is rather high – 83,4%. The weight of graduates in science & engineering reached the value 14,1% in the Netherlands (the lowest meaning among 40-ty selected countries) and 36,0% in Germany (the highest meaning among 40-ty selected countries), while in Ukraine – 24,2%.

The rating of the countries by the level of gross expenditure on R&D in 2019 (% of GDP) is shown on the Fig. 4. The lowest meanings of this indicator can be observed in Kazakhstan (0,1%), Tajikistan (0,1%), Armenia (0,2%), Azerbaijan (0,2%), Georgia (0,3%), the Republic of Moldova (0,3%) and Ukraine (0,4%). At the same time, the level of gross expenditure on R&D is much higher in Germany (3,0%), Denmark (3,1%), Austria (3,2%), Japan (3,2%), Sweden (3,4%) and Switzerland (3,4%). It's worth to highline, that the level of gross expenditure on R&D is one of the most important indicators, which significantly affects the pace of innovative development.

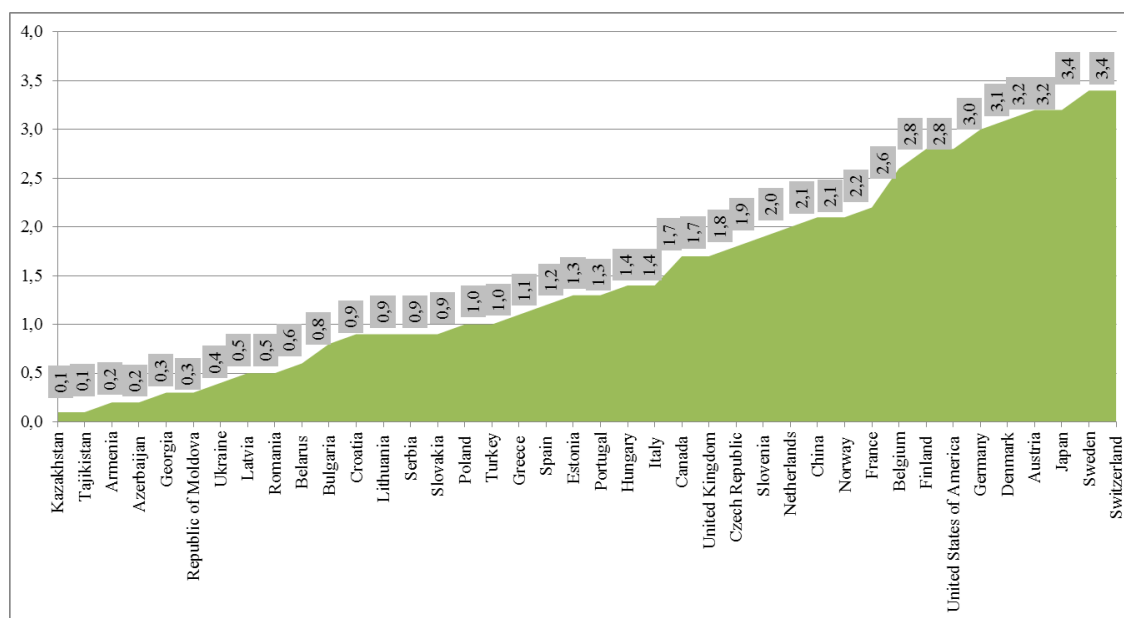


Figure 4. The rating of the countries by the level of gross expenditure on R&D in 2019, % GDP
Source: formed by the authors at the base of The Global Innovation Index 2019 [8].

The level of knowledge-intensive employment among the selected group of countries we can see on Fig. 5. The leading positions by this indicator occupy Switzerland – 52,9%, Norway – 52,5%, Sweden – 52,3% and the United Kingdom – 48,6%. The lowest meanings are observed in Azerbaijan (23,3%), Romania (23,3%), Turkey (21,0%) and Tajikistan (16,1%). In Ukraine the level of knowledge-intensive employment is 36,9%.

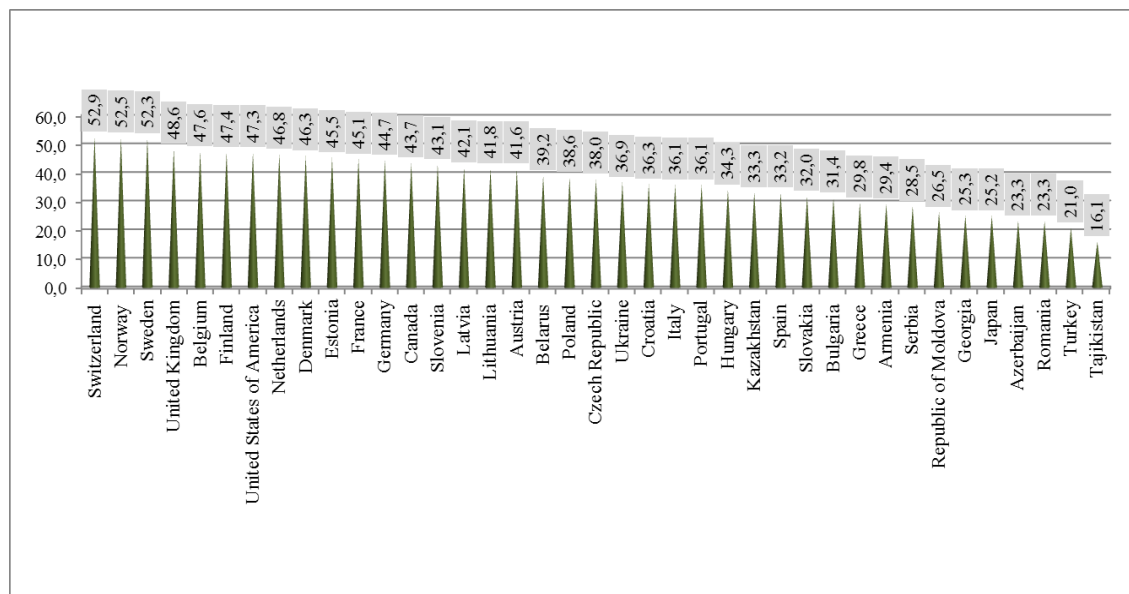


Figure 5. The rating of the countries by the level of knowledge-intensive employment in 2019, %
Source: formed by the authors at the base of The Global Innovation Index 2019 [8].

The highest level of intellectual property payments is observed in the Netherlands – 8,1% of total trade. The meanings of high-tech imports (% of total trade) fluctuate from 2,8% in Azerbaijan to 23,3% in China. The similar situation is about the

level of high-tech net exports (% total trade) – 0,1% in Azerbaijan and 27,9% in China. China is also the leader of the level of creative goods exports – 11,9% of total trade.

By using the program STATISTICA 10.0, there were calculated the pairwise correlation coefficients between the above mentioned 11 indicators (Table 2).

Table 2 – The matrix for calculating pairwise correlation coefficients between indicators

	Var1	Var2	Var3	Var4	Var5	Var6	Var7	Var8	Var9	Var10	Var11
Var1	1,000	0,472	0,341	0,041	0,857	0,818	0,745	0,463	0,217	0,289	0,118
Var2	0,472	1,000	0,510	0,276	0,578	0,392	0,700	0,134	-0,157	-0,137	-0,193
Var3	0,341	0,510	1,000	0,289	0,309	0,211	0,596	0,123	0,017	0,047	-0,071
Var4	0,041	0,276	0,289	1,000	0,050	-0,102	0,420	0,263	-0,484	-0,435	-0,412
Var5	0,857	0,578	0,309	0,050	1,000	0,882	0,703	0,384	0,139	0,278	0,065
Var6	0,818	0,392	0,211	-0,102	0,882	1,000	0,519	0,404	0,311	0,476	0,215
Var7	0,745	0,700	0,596	0,420	0,703	0,519	1,000	0,293	-0,124	-0,064	-0,199
Var8	0,463	0,134	0,123	-0,263	0,384	0,404	0,293	1,000	0,271	0,324	0,213
Var9	0,217	-0,157	0,017	-0,484	0,139	0,311	-0,124	0,271	1,000	0,825	0,802
Var10	0,289	-0,137	0,047	-0,435	0,278	0,476	-0,064	0,324	0,825	1,000	0,822
Var11	0,118	-0,193	-0,071	-0,412	0,065	0,215	-0,199	0,213	0,802	0,822	1,000

Marked correlations are significant at the level $p < 0,050$.

Var1 – GDP per capita, PPP\$; Var2 – expenditure on education, % GDP; Var3 – tertiary enrolment, % gross; Var4 – graduates in science & engineering, %; Var5 – researchers, FTE/mn pop.; Var6 – gross expenditure on R&D, % GDP; Var7 – knowledge-intensive employment, %; Var8 – intellectual property payments, % total trade; Var9 – high-tech imports, % total trade; Var10 – high-tech net exports, % total trade; Var11 – creative goods exports, % total trade.

Source: calculated by the authors at the base of The Global Innovation Index 2019 [8].

According to the results of calculating, we can make a conclusion about the presence of significant dependence between the GDP per capita with such indicators, as researchers, FTE/mn pop ($r = 0,857$), gross expenditure on R&D, % GDP ($r = 0,818$) and knowledge-intensive employment, % ($r = 0,745$). So, it can be supposed, that if the influence of other factors remains unchanged, these factors themselves have the greatest influence on the level of GDP per capita, consequently, on the pace of innovative development and the level of welfare of the population.

The main directions of innovation development and ensuring the worlds' countries prosperity, in our opinion, it is advisable to classify for four groups of actors within the Quadruple Helix Model:

(a) State (government): development of national innovation systems; diversification of sources of funding for research and development; preservation and development of human potential; international cooperation in the field of realization of innovative projects; protection of intellectual property rights; initiating the development of partnership on the basis of social dialogue; stimulating the development of entrepreneurial initiative; promoting the formation and development of innovative-integrated structures.

(b) Universities and research institutions: improving the quality of educational services; increasing the practical orientation of vocational education; active participation in research and development, international projects and grants; increasing the academic mobility of scientists and students; teaching students entrepreneurial skills; development of information and innovation culture; training the skills of modern information and communication technologies using; formation of powerful research centers on their base.

(c) Business: participation in the financing of research and development; introduction of modern equipment and technologies; ensuring decent pay for professionals; encouraging staff to implement innovative ideas and innovations; development of the system of continuous vocational education and dual education; effective knowledge management; quality management.

(d) Civil society: active civil position; upholding the priorities of environmental friendliness, resource conservation, energy efficiency; monitoring of innovation activity, its efficiency.

Conclusions and prospects for further research. Thereby, the efforts of countries seeking to accelerate the forming of the innovative economic model should be aimed at intensifying research and development, the introduction of knowledge management, training of innovative specialists and continuous professional development of human resources. It is necessary to create favorable working conditions for researchers, establishing effective cooperation between the state, business, universities and communities. In modern conditions, availability of the qualified human resources, who are capable for generating and implementing a new knowledge, is one of the most important determinants of innovative development. This fact should be taken into account during the forming of strategies, plans and programs of innovative development.

The prospect of further research lies in the field of identifying the key growth points for each country, taking into account its external and internal innovation potential, development of measures of stimulation the effective interaction of all participants in the innovation process.

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TAXABLE CAPACITY OF BUSINESS ENTITY AND TAX PASSPORTS AS AN INSTRUMENT FOR ITS IDENTIFICATION AND ASSESSMENT

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ABSTRACT

A precondition for a successful budgetary and fiscal policy is to increase the revenue of the budget system by expanding tax capacity of the economy which implies the need to stimulate the growth of tax capacity and create a reliable information base support for its assessment. However there are significant problems related to a timely strategic and, especially, operational decisions to obtain information of the required amount and quality. The concept of determining the economic essence of the notion of "taxable capacity of a business entity" and its elements is proposed, within which the classification criteria (optimal and actual taxable capacity), the structure (resource and structural approach), functions (resource-saving, regulatory, informational and analytical), the place and role in the system of tax administration are distinguished. Using of this concept ensure the correct identification of the entity from the standpoint of its capacities to provide tax obligations to the state were outlined. The principles of forming tax passports of different business entities are laid out. The priority descriptions of key aspects of activity of different entities which allow estimating their tax potential and increasing tax incomes to the budgets have been highlighted. Taking into account the significant analytical orientation of tax passports it is proposed to include the following key indicators describing the entity, grouped into three groups: group I includes indicators that characterize the financial status of the entity; group II includes indicators that characterize the tax burden of the enterprise; group III includes indicators that characterize the tax culture of the subject and the effectiveness of the state financial control bodies, in the first place, the tax authorities. Qualitative compilation of tax passports with application of other documents on tax administration will help to determine real tax burden of a particular business entity and develop directions for its optimization, conduct rational tax policy, ensure the necessary amount of tax revenues to the state and local budget system.

Keywords: capacity, taxes, taxable capacity, taxable capacity of a business entity, information support, tax passport

INTRODUCTION

A precondition for a successful budgetary and fiscal policy is to increase the revenue of the budget system by expanding tax capacity of the economy which implies the need to stimulate the growth of tax capacity and create a reliable information base support for its assessment. There are significant problems related to a timely strategic and, especially, operational decisions to obtain information of the required amount and quality.

One of the ways to increase the efficiency of management is to provide users with information that sufficiently characterizes the impact of the tax system on the internal environment of the enterprise, allows assessing the tax potential of enterprises and making management decisions, including optimal options for financial and economic activities in the current tax system, and under the current level of tax burden. Information support of the management process is a rather complex mechanism of coordination of information resources and methods of their organization, analytical procedures, especially in the sphere of tax relations. In the process of assessing the tax potential of business entities a significant amount of information can be used and this massive of information requires systematization and evaluation. The objectivity and quality of work in this direction is determined by the degree of access to information, its completeness, and reliability.

Analysis of recent researches and publications. In recent years, special literature on budgetary and tax management has been supplemented by a number of papers by well-known scholars who outline the general theoretical problems of the formation of an effective budget and tax strategy, the experience of the formation of tax systems of different countries, the organization of tax accounting and modeling of tax processes.

Tax potential and methods of its assessment is the subject of research in various areas, which are presented in the scientific literature. First of all, it is worth noting the study of the theoretical foundations of tax potential (Besley & Persson, 2009) [Error! Reference source not found.]; (Müller, 2014) [Error! Reference source not found.]. It should be noted that these issues are actively discussed in the context of researches for a low-income country, in particular: determinants of taxable capacity and its estimation (Bassey & Efiang, 2018) [Error! Reference source not found.]; (Kwaku Amoh,

2019) [Error! Reference source not found.]; (Abdalaziz, 2012) [Error! Reference source not found.]. The study of the impact on the tax potential of particular taxes – such as VAT (Andoh, 2017) [Error! Reference source not found.] and income taxation (Ziegler Rogers & Weller, 2014) [Error! Reference source not found.] is important. Much attention is paid to the comparative analysis of the tax potential of different countries (Callan & Savage, 2012) [Error! Reference source not found.]; (Le et al., 2008, 2012) [Error! Reference source not found.; Error! Reference source not found.]). It is expedient to single out the study of the relationship between the tax potential and economy's sectors (Galimardanova et al., 2014) [Error! Reference source not found.] and regional development (Igonina et al., 2015) [Error! Reference source not found.]).

However, for the effective functioning of the budget and tax system it is not always sufficient to know the approaches and the mechanism for determining tax capacity and the essence of the indicators that form it. At present, the requirements for obtaining a more comprehensive list of indicators of social and economic development of some business entities, as well as certain industries, regions and the country as a whole, reflecting the current and prospective condition of their financial and economic potential and the overall quality of the conducted economic and social policy of the state, the effectiveness of achieving its goals. This is possible only if there is complete, reliable and unbiased information on the key aspects of the activities of different business entities and the possibility of assessment, based on this information, the tax capacity of these entities.

Main purpose of the article.

The objectives of the research are as follows: (1) to disclose the essence of the taxable capacity as an economic notion and the necessity to study it at different levels (country, region, business entity); (2) to determine the basic principles of the information support system for assessing the tax potential, its types and purposes; (3) to develop the principles for the formation of tax passports for their further use at the level of certain enterprises, branches of the economy and the region as a whole in order to form objective data that characterize their tax capacity.

Results and discussions.

In "broad" understanding, taxable capacity is a total amount of taxable resources of the territory. In "narrow" (practical) sense, taxable capacity is a maximum possible amount of income taxes and fees, calculated in terms of current tax legislation. There are many factors that influence taxable capacity of the territory, both objective and subjective. The objective factors include current tax legislation, the level of development of regional economy, regional industrial structure, the level and dynamics of current prices, volume and structure of export and import etc. Subjective factors include the state of tax policy, the number of tax benefits, indulgences and deferred payments (Kolomiets, 2000) [Error! Reference source not found., p. 12]. According to this view, the definition of taxable capacity in "broader" sense comes to the definition of taxable resources, despite the fact that such economic resources may be resources that are not taxed at a certain period of time or under certain circumstances.

Based on the interpretation of the essence of taxable capacity in "broad" sense, it is clear that taxable capacity of the country as a whole and a separate region is formed in the light of components of taxable capacity of certain business entities that operate within the limits of certain territory and taxable capacity of the population that receive income that under the current tax laws are subject to taxation. Therefore, the research should be aimed at defining the nature, essence and assessment of taxable capacity of business entities (companies, institutions).

It should be noted that taxable capacity of business entities (enterprises, institutions and organizations) are mostly identified with their tax burden (Osipova, 2006) [Error! Reference source not found., p. 9], and determined by the ratio of the total tax payments to the added value resulted in the process of production. In this case, taxable capacity of a business entity is considered as a result of the implementation of tax relations of a company with the state.

Tax relationship can not happen only through the efforts of one country; like any other relationship, they are bilateral. Thus, the formation of the state income tax, on the one hand, and tax expenses of companies as a form of implementation of taxable capacity, on the other hand, involves active participation of taxpayers in the process. This participation is realized within certain legislative tax behaviour which should be formed on the basis of not only such features as tax law and duty, but as notes (Gorskiy, 1999) [Error! Reference source not found., p. 24], on the reproducibility of tax.

Reproducibility of tax is conditioned primarily by the term of tax existence as a financial category within the state. In addition, in order to ensure reproduction of the real tax it is necessary to ensure reproduction of the tax base. The tax base, in its turn is derived from the result in the flow of capital. In this regard, any business entity will not have economic possibilities to reduce tax relations with the state to "zero" through various ways of avoiding or circumventing of the taxes if there is no regulation of process by the state.

Thus, tax relations are bilateral with one party as a taxpayer (business entity: company, institution, organization) and with the other party as the state. The basis of the tax relations is tax obligations. Based on the theory of obligations they must also be bilateral. This means that if a taxpayer generates tax liabilities and acts as a debtor to the state, then the state should also assume the tax obligations and liabilities to be taxpayer at least for unambiguous interpretation of tax laws and be responsible for the effective use of tax revenues. In these conditions the interest for the formation of taxable capacity of

a business entity will be realized not only by the state but by the entity (company) from the position the optimization of the value of taxable capacity and using it as a factor for creating and maximizing added value.

Thus, taking into account the analysis of modern concepts defining the essence of taxable capacity at micro and macro levels we offer the authors' definition of "taxable capacity of a business entity". Taxable capacity of a business entity is a target identifying variable of the business entity's resources can be transformed into tax revenues to the budgets of different levels under certain conditions of formation and use of the resources during normal proceedings of the business entity and the creation by the entity added value and maximizing it. The concept of definition of the economic essence of "taxable capacity of a business entity" and its components are shown in Fig. 1.

An amount of the required data is not collected or evaluated by regional authorities. The solution of the problem of information deficiency in the assessment of tax capacity both at the level of territory (region) and at the level of a business entity should be the creation of the system of tax passports.

The need to use it can be explained by the following reasons. The information used in the process of planning tax payments at the micro level and assessment of tax capacity should be complete and provide possibility for comprehensive analysis and forecast calculations.

The reality of information is based on the presentation of true data concerning the activities of business entity taking into account the particularities of the impact of the internal and external environment on the results of its operation.

When forming an amount of information it is important to take into consideration the efficiency of its acquisition. The smaller the time of data passing from the moment of the economic transaction to the moment of receiving by a tax manager, the more effective the solution can be developed on the basis of their use.

It should be considered that obtaining information should not be more expensive in comparison with the usefulness of its use. In this way, the effectiveness of using the information amount is ensured.

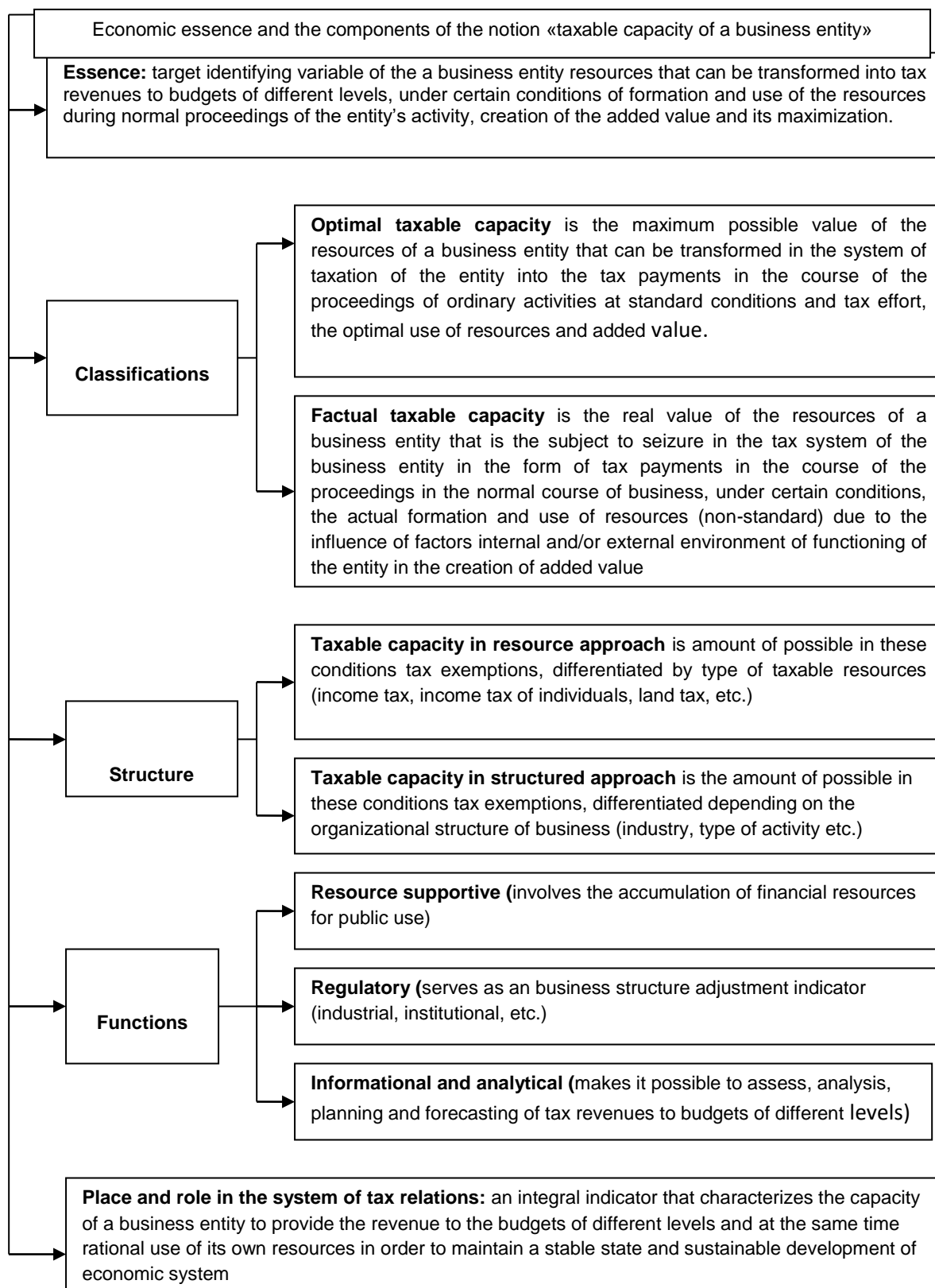


Figure 1. The concept of definition of the economic essence of the notion "taxable capacity" and its components
Source: composed by the author.

For example, the international rating "Paying Taxes" allow to assess the quality of the tax system for business. Rating of "Paying Taxes" (table 1) evaluates tax burden of an average enterprise in terms of administration and payment of corporate income tax, social contributions, taxes withheld from the income of employees, property taxes, taxes on transfer of property, taxes on dividends and other obligatory payments which have to paid by business. In addition, the analysis is made on the information on the frequency of submission of tax returns and payment of taxes, as well as the time required to perform tax obligations by business. The ranking also includes the assessment of the processes that follow tax payments, in particular tax audits, receiving budgetary claims, administrative appeals. Such complex of indicators allows making a detailed analysis of tax systems.

Table 1. Indicators of "Paying Taxes"

Indicator	Description
<i>the number of payments</i>	measures the frequency with which the company has to file and pay different types of taxes and contributions, adjusted for the manner in which those filings and payments are made
<i>total tax rate</i>	the measure of tax cost, the total of all taxes borne as a percentage of commercial profit
<i>the time to comply with the three main taxes</i>	three main taxes include corporate income taxes, labour taxes and mandatory contributions, and consumption taxes; time captures the time required to prepare, file and pay each tax type;
<i>post-filing index</i>	based on four equally weighted components: 1) time to comply with a VAT refund (hours); 2) time to obtain a VAT refund (weeks); 3) time to comply with a CIT audit (hours); 4) time to complete a CIT audit (weeks)

Based on the reports of 2017 and 2020 the comparison of Ukraine with other countries and groups of countries (table 2) shows that Ukraine has favourable conditions by the indicators such as "Number of tax payments" and "Post-filing index" but too much time for calculation and payment of taxes and a relatively high overall tax rate.

Table 2. Comparison of the indicators of Ukraine and Slovenia by the indicator "Paying Taxes 2017" [Error! Reference source not found.] and "Paying Taxes 2020" [Error! Reference source not found.] with groups of countries

Indicator	Ukraine	Europe and Central Asia	OECD high income	Ukraine	Europe and Central Asia	OECD high income
Rank among all countries	84	-	-	65	-	-
Number of tax payments	5,0	17,6	10,9	5,0	14,4	10,3
Time for calculation and tax payments	355,5	221,5	163,4	328,0	213,1	158,8
Overall tax rate (% of income before taxation)	51,9	33,8	40,9	45,2	31,7	39,9
Post-filing index (0-100)	79,3	71,9	85,1	86,0	68,2	86,7

But it must be admitted that such a small number of payments was actually artificial in Ukraine. As a result of the tax reform in 2015, three property taxes were replaced by one, in which the same three types were distinguished; the same situation occurred with rental payments and social and pension insurance fees. However, it is important to avoid activities that "artificially" increase the ranking of the country without real improvement in the area as this may adversely affect the image and reputation of the country causing distrust of the governance and regulation.

To ensure control over the correctness of the calculation and payment of taxes at the enterprise level, it is expedient to apply the following registers of tax accounting: tax passport; tax card; the calculation table; a check list for reporting to the State Tax Administration; a check list of tax payments to the budget.

The most comprehensive and informative document of the indicated registers is the tax passport of the company. This document includes all types of taxes paid by the business entity in the process of economic activity. This document is necessary to control the completeness of charging and paying corporate taxes, as well as for timely adjustments of tax policy when the approaches to the activities are changed.

The initiators of introducing such a document into the information system should be state authorities. Consequently, this document should be compiled taking into account the tasks that are solved within the framework of external tax administration.

The tax passport is a document in which a comprehensive description of the tax capacity should be provided. The tax passport must be geared towards the needs of state and local government bodies. It should provide adequate assessment of the situation in the economic and tax spheres of the country and take appropriate decisions aimed at increasing the level of taxes and fees. However, it may be interesting for taxpayers in terms of financial and investment potential of the region, types of economic activity and specific business entities.

The basis for establishing such a system of tax passports should be the informational system for assessing tax capacity and planning of budget revenues at different levels in terms of tax revenues based on the informational structure of the region in the form of the corporate network of government, local self-government and state information resources that exist in different departments.

A certain system of tax passports can be created depending on the classification features (Fig. 3).

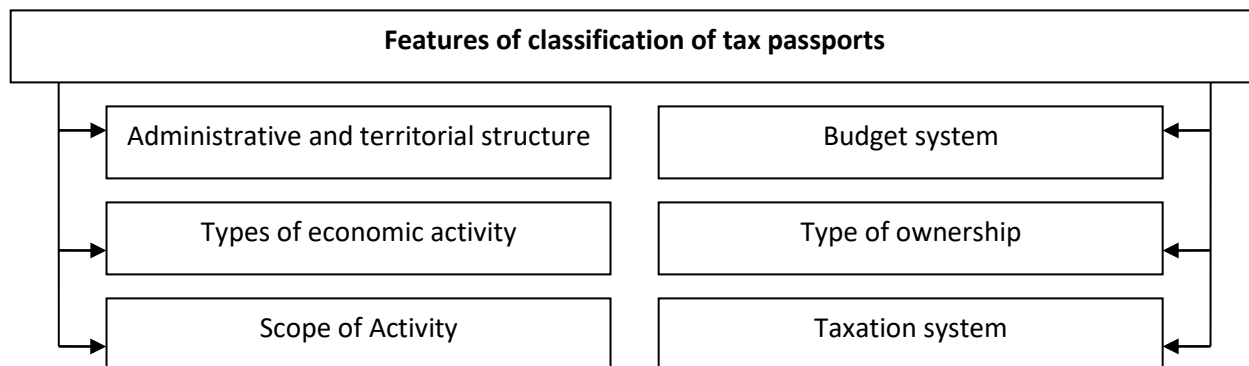


Figure 3. Classification of the information in tax passports
Source: composed by the author.

According to the administrative and territorial structure there can be created tax passports of different regions: regions, districts, cities.

The classification mark "budget system" is necessary, since the administrative and territorial structure may not fully characterize the budget needs of different regions. Thus, the budget system of Ukraine consists of the state budget and local budgets; in addition there is a complex system of consolidated budgets.

The criterion "types of economic activity" allows drawing up a tax passport for a group of companies in one sphere within different regions, budgets, etc. Depending on the needs of management the following areas of economic activity can be distinguished: industry, transport, agriculture, trade, housing and communal services, financial services, etc.

In accordance with the mark "types of ownership" tax passports can be drawn up for such groups of enterprises: state enterprises, economic partnerships (OJSC, LLC, etc.) with the authorized capital shares belonging to the state or local self-government bodies; entirely non-state-owned enterprises, private enterprises, etc. Tax passports compiled according to such groups will increase the efficiency and effectiveness of management of state property and public funds.

The criterion "volume of activity" is highlighted in accordance with the requirements of Article 63 of the Commercial Code of Ukraine. This article provides the criteria for assigning enterprises to small, large and medium enterprises: the number of employees and the amount of gross profit from sales of products per year.

Making up passports for enterprises that are grouped according to the applied tax system will allow assessing the tax capacity of different taxpayers. It is proposed to allocate the following groups of enterprises: business entities that apply the general system of taxation; economic entities that apply a simplified tax system in the form of payment of a flat-rate tax; agricultural enterprises paying a fixed agricultural tax; non-profit organizations.

Let's consider in details the principles and procedure for the formation of a tax passport of a business entity.

At the level of the entity the structure of the tax passport should be as follows:

1. General information about a business entity.
2. Main social and economic indicators of the enterprise.
3. Information on accounts in banks and other financial and credit institutions.
4. Benefits used by the business entity including the amount of subsidies received and subventions received from budgets of different levels.
5. Indicators for calculating taxable bases.
6. Tax liabilities of the enterprise to the budget.
7. System of indicators of tax burden.
8. Information on arrears of taxes and duties.

The section "General information about a business entity" should also include positions that characterize the system and features of taxation of enterprises but not only such details as data on the persons responsible for financial and economic activity, the structure of founders, activities, the nature of foreign economic activity, etc.

The section "Basic social and economic indicators of an enterprise" should contain a set of indicators in accordance with the forms of statistical and financial reporting.

In the section "Information on accounts in banks and financial and credit institutions" the relevant information is grouped, taking into account that this information is important for tracking the cash flow of the enterprise.

The section on benefits of an entity should include the following information: information about subsidies and grants received from the budget; the amount of deferred payments, tax privileges, amounts of taxes that are subject to reimbursement from the budget, in particular, VAT and amounts actually received on the current account.

All indicators of the passport should be placed in the table which will provide a complete picture of the main social and economic indicators of the legal entity, its structure, the presence of affiliated (dependent) enterprises, the indicators used to calculate the tax base, the dynamics of receipt of tax payments (fees) by the levels of the budgets, debt and tax burden.

Taking into account the analysis of the main sources of information on the activities of certain business entities we have identified the system of indicators that allow assessing their tax capacity and should be included in the tax passport.

Group I. Indicators that describe the financial situation of a business entity.

An enterprise is a complex system which consists of many subsystems, and therefore the assessment of its financial status should be characterized by the complexity of the approach, that is, the use of a certain system of indicators. A general assessment of the financial situation of an enterprise is usually presented as a system of indicators that most fully characterizes the degree of stability of its financial state.

Group II. Indicators that characterize the company's tax burden

Information on the indicators used to calculate taxable bases and tax liabilities to the budget reflect the absolute levels of financial relations between enterprises with budgets of different levels. Relative indicators include the system of tax burden indicators.

In recent years, the practice of tax authorities applies the method of identifying reserves of budget replenishment as a calculation of the average tax burden in the region and Ukraine. With this indicator, the relevant indicators are compared by calculation according to certain enterprises in a particular industry. This method is based on the assumption that for each business branch there is a certain correlation between the costs incurred by the enterprise in the course of its economic activity and the income received.

Accordingly, a certain percentage of the tax burden on one or another kind of activity is determined. Since there are many enterprises that belong to the same industry and pay much lower taxes and payments with the same gross revenues, bringing the tax burden on such economic entities to the level of the medium-scale industry would give an opportunity to increase the revenues of the state and local budgets.

This calculation is also used when distributing taxpayers according to the categories of attention. The distribution of each business entity is carried out in four categories:

1. individual tax behaviour (timeliness of presentation of tax reporting and payments to the budget, deviation from the average values of the industry, detection of violations of tax legislation during preliminary inspections, etc.);
2. riskiness of management (availability of risky activities, frequent changes in activities, etc.);
3. fiscal importance (volume of gross income, tax burden);
4. affiliation with the industry (group) in which the activity was carried out.

The procedure for calculating reserves of budget replenishment at the expense of bringing tax burden to the average industry indicator clearly allows outlining the range of enterprises that are likely to understate the amount of taxes, duties and mandatory payments. However, this method only "outlines" this circle, since each enterprise pays not one but a few taxes, the size of which is influenced by many factors. Therefore, it would be advisable to calculate the tax burden for individual taxes in order to identify:

1. specific types of taxes that are subject to deviation;
2. factors that lead to deviations (for example, for tax purposes, you can compare the structure of gross expenditures).

In this case, the taxation system applied by the enterprise is also important. For example, for agricultural enterprises, the tax burden will depend mainly on two factors: the land area (fixed agricultural tax) and the number of employees (income tax level). And since gross profit will depend on a particular cultivated crop then under all equal conditions (area of land,

number of employees), the tax burden in the form of the amount of taxes on 1 UAH of gross profit will vary considerably among different agricultural enterprises, and such fluctuations will not indicate a concealment of taxation.

In addition, the use of average tax burden across the region and the country as a whole as an external criterion of optimality causes some doubts. In general, the average is considered to be stable and can be used as a generalization characteristic of a statistical aggregate only if the coefficient of variation (the ratio of the mean square deviation to the average) does not exceed 33%. The given data shows that this condition is not fulfilled, and the average level of tax burden is not representative. This assertion is based on the fact that there are significant differences in the levels of tax burden in the region; the average level of tax burden in almost every sector is determined mainly by one enterprise which has absolute subjective advantages that allow it to pay a rather high level of taxes.

It is necessary to group enterprises according to certain features (regions, industries and branches, number of employees, capacity, types of products, etc.) in order to establish the real level of possible tax revenues based on the level of profitability of various types of resources.

In addition, the available variability of the industry in relation to the type of product and specific activities and the level of specific profitability should be taken into account.

Group III. Indicators characterizing the level of tax culture of the entity and the effectiveness of the work of the state financial control bodies, in the first place, the tax authorities.

The information about the inspections and debts to the budget should characterize the tax history of the enterprise and the effectiveness of the work of the bodies of the State Tax Service and other bodies of state financial control.

For example, various indicators derived from different sources may be used to assess the level of personal income tax payrolls, in particular, the use of information available at the State Service of Ukraine for Labor on the number and results of inspections carried out. The following indicators which make it possible to estimate the level of payment of personal income tax of certain business entities include the following:

- average number of staff members;
- the number of part-time employees;
- the amount of accrued income for all employees (for a quarter, year);
- the amount of paid income (for a quarter, a year);
- the amount of accrued income tax (for a quarter, year);
- the amount of income tax paid (for the quarter, year);
- the ratio of accrued income and accrued income tax;
- the ratio of paid income and income tax paid;
- average accrued income per worker (for a month, a quarter, a year);
- a certain amount of paid income per employee (for a month, a quarter, a year)
- an average monthly salary;
- an average salary level (in the oblast, country);
- the amount of wage arrears (at the end of the quarter, year);
- accrued but not paid wages, the expiration of which has expired (at the end of the quarter, year), including the amount of wages, delayed payment of which is more than one month;
- the amount of personal income tax payable (at the end of the quarter, year);
- the amount of income tax arrears expired (at the end of the quarter, year);
- the amount of income tax arrears exceeding one month (at the end of the quarter, year);
- the ratio of wage arrears and arrears of personal income tax;
- number of taxpayer checks of income tax accrual and income over the past three years;
- the date of last check by the tax authorities of the correctness of the calculation and payment of income tax of individuals;
- the results of inspections: financial penalties, financial penalties paid to the budget, paid by management of administrative fines;
- the amount of the accrued and paid penalty for delaying the payment of income tax for the last three years, reference is the amount of the income tax arrears, on which the penalty is calculated;
- the amount of the accrued interest for delaying the payment of personal income tax (at the end of the quarter, year); the reference amount is the amount of the tax arrears of the income on which the penalty was calculated;
- the number of inspections carried out by the State Service of Ukraine for Labor over the last three years;
- date of the last inspection by the State Service of Ukraine for Labor;
- results of inspections: fines were imposed on officials, a criminal case was initiated (in the case of closing a criminal case - the amount of arrears of wages).

The proposed indicators that reflect the main key aspects of the entity's activities can be specified depending on other classification characteristics of tax passports.

Conclusions and further researches directions. Generalization of the results of this study provides an opportunity to determine category "taxable capacity of a business entity" as target identifying variable of the business entity's resources can be transformed into tax revenues to the budgets of different levels under certain conditions of formation and

use of the resources during normal proceedings of the business entity and the creation by the entity added value and maximizing it.

Based on the place and the role of taxable capacity of a business entity in the system of tax administration it is appropriate to classify it for optimal and effective. The optimal taxable capacity of a business entity is the maximum possible value of the resources of a business entity that can be transformed in the system of taxation of the entity into the tax payments in the course of the proceedings of ordinary activities at standard conditions and tax effort, the optimal use of resources and added value. The factual is the real value of the resources of a business entity that is the subject to seizure in the tax system of the business entity in the form of tax payments in the course of the proceedings in the normal course of business, under certain conditions, the actual formation and use of resources (non-standard) due to the influence of factors internal and/or external environment of functioning of the entity in the creation of added value

Solving of the problem of information deficiency when assessing the tax potential both at the level of territory (region) and at the level of a business entity should be the creation of the system of tax passports. Proper information support of the tax planning process at the micro level serves as the basis for a qualitative assessment of the tax capacity, the study of the reasons for the deviation of the actual amounts of tax revenues from the planned indicators, the development of the basics of optimization of tactics and the strategy of tax control. The tax passport allows adequately assessing the situation in the country's economic and tax areas and make appropriate decisions aimed at raising taxes and fees. However, it may be interesting for taxpayers in terms of financial and investment potential of the region, types of economic activity and certain business entities.

It is necessary to introduce the mechanism of certification of business entities at the legislative level. The basis for establishing the system of tax passports should be the informational system for assessing tax potential and planning budget revenues of different levels in terms of tax revenues based on the information structure of the region in the form of a corporate network of government, local self-government and state information resources that exist in different departments

When developing a tax passport, it cannot be reduced to tax reporting, because it can not give full and detailed information on the tax status of a region and a particular enterprise. Taking into account the significant analytical orientation of tax passports it is proposed to include the following key indicators describing the entity, grouped into three groups: group I includes indicators that characterize the financial status of the entity; group II includes indicators that characterize the tax burden of the enterprise; group III includes indicators that characterize the tax culture of the subject and the effectiveness of the state financial control bodies, in the first place, the tax authorities.

Qualitative compilation of tax passports with application of other documents on tax administration will help to determine real tax burden of a particular business entity and develop directions for its optimization, conduct rational tax policy, ensure the necessary amount of tax revenues to the state budget system, and create a more objective system of intergovernmental fiscal relationships.

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INNOVATIVE ORIENTED DEVELOPMENT OF THE SOCIAL SPHERE OF THE REGIONAL ECOSYSTEM' SCIENTIFIC AND PRODUCTION CLUSTER

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ABSTRACT

The purpose of the publication is to determine the prospects of innovatively oriented development of the social sphere of scientific and production clusters of regional ecosystems with the preferential use of public-private partnership tools. It is concluded that the modern method of managing the development of the social sphere is the state innovation regulation of public management of public-private partnership with the use of e-Government facilities; management of virtual networks; fundraising; outsourcing; creation of social technology platforms; crowdfunding; meeting the needs of stakeholders in obtaining high-tech social services; the formation of educational production clusters, "nodes" of stabilization and development, technical, intellectual, information, social "centers of excellence"; top-priority designing on the periphery of forward-looking, innovative and technology-intensive technologies.

Keywords: innovation; innovative oriented development; social sphere; scientific and production cluster; regional ecosystem; public-private partnership

Introduction. Social sector of national economy (SSNE) is a specific environment for the direct functioning of the system of expanded reproduction of civil society in the process of implementation of the state social policy on the use of products and services of the real sector, ensuring the maintenance of life of all segments of the population, meeting social needs through the implementation of mechanisms for the appropriation of means of life and existence.

SSNE – a set of technologically interconnected entities, organizations and institutions, whose activities are aimed at the implementation of the target function of satisfying the needs of the population in labor, socio-economic activity, spiritual culture and regulated by sectoral and sectoral government and self-governance. The branches are united in the complex of social economy of the post-industrial economy, not in terms of technical and technological features and the place in the industrial cooperation of labor, but in the public value of the goods and services provided.

The modernization of scientific approaches to regulating the development of the social sector of the post-industrial economy takes place on the basis of a creative combination of the provisions of the theory of the public sector, public services and the development of sectoral / regional innovation ecosystems.

The growth of the dynamism of the development of socio-economic systems, the transition to a collaborative model for innovation at the level of mostly virtual stakeholders of the stakeholders, whose participants form networks of regional stable interconnections of growth within the framework of the deployment of the four-linked "science-business-government-society" spiral, have for as a consequence of the rapid development of the theory and practice of the ecosystem approach to the formation of an innovation policy for regulating the social sector of the national economy.

The essence of public-private partnership (PPP), is a power tool of the innovative development of social sphere, consists in functioning of a complex of partner business relations between representatives of the authorities, business, public sector of society, local communities regarding the redistribution of powers in the field of formation of innovative infrastructure of collective use, production of socially significant goods and services currently in existence in the state monopoly.

Literature review. The international practice of state regulation of the development of the social sphere of the national economy has a rather long history and involves the use of several fundamentally different models.

The generalization of the characteristic features, theoretical foundations and practical features of the implementation of the described and analyzed by the mentioned scientists of certain varieties of models of functioning of the social sphere allows them to be differentiated according to separate classification features [1].

Summarizing the essence of the processes of evolution of national models of social policy of developed countries, which takes place under the influence of external factors of the environment and internal laws of development, it is permissible to conclude that the need to study the phenomenon of Regional (Territorial) Innovative Societal Ecosystem (R(T)ISES).

R(T)ISES is a dynamic and adaptive globally networked territorially community of stakeholders in the post-industrial economy whose activities are aimed at implementing integrated, mutually beneficial actions to combine their own and other available resources in order to create knowledge flows, support technological development and commercialization of innovations in the field of creation, perception and satisfaction of needs of self-organized consumers of social services in the course of implementation of a unified social policy of the executive authorities of Ukraine state. Innovative enterprises/firms are closely interconnected elements of the ICES; innovative infrastructure; subsystem of commercialization of innovations; subsystem of innovation financing.

The peculiarity of the functioning of innovative enterprises in the structure of RISES is that their predominant majority specializes in the provision of intelligent services whose definition of substance has been thoroughly investigated in the classical publication of F. Machlup [2]. Summarizing some of the features that determine modern intellectual services, we note that their list includes:

- original nature;
- high degree of individualization;
- knowledge-intensive nature of production and consumption;
- uncertainty of the costs of the production process, minimization of the capital intensity, a significant proportion of value added in total value;
- ability to adapt to the requirements of an individual client;
- propensity for the loss of an established form, virtualization, manifestation of manifestation (specific intellectual work / goods in the case of market identification) / paid work in the case of instant commercialization);
- comprehensive character as an economic resource; diversity of social forms of production and consumption;
- presence of signs of co-production and co-service, simultaneous participation in the process of providing the consumer (information about the desired character) and the producer (creative for the provision of qualified service), obtaining under this condition the intellectual rent (monopoly, differential I and II type, absolute) both sides of cooperation;
- focusing on meeting the information needs of stakeholders of the ICES;
- availability of information systems as a prerequisite for provision;
- possibility of remote access;
- presence of network contacts.

The production of intelligent services involves the formation, at the level of the innovative organization of intellectual capital – an integrated conglomerate of human and structural elements. Its constituent elements for the innovative structure that is part of the R(T)ISES are taken as:

- human capital:
 - aggregate labor force;
 - knowledge and skills of specialists, including those whose possession is foreseen by default;
- organizational capital:
 - results of intellectual activity;
 - information resources and technologies;
 - electronics networks;
 - organizational structure and system of service management process;
- client capital (social capital, capital of relations):
 - commercial ideas and business connections;
 - commercial distribution network;
 - participation in commercial holdings, financial and industrial groups;
 - means of individualization of organization / institution (main product / business services);
 - business reputation of the organization/institution (brand).

Innovative infrastructure of RISES is a combination of facilities to provide the innovative network (IN) with the necessary resources and services – scientific, technical, natural, communicative, social, for the reproduction of human capital network participants, environmental.

R(T)ISES's commercialization subsystem provides the promotion and implementation of innovations and intellectual products, thus defining the effectiveness of the IN as a whole.

The financing subsystem, using free money for the development of the IN, is responsible not only for the financial provision of the development of the social sphere, but also for the settlement and distribution of cash flows and funds within the framework of R(T)ISES.

In general, the innovative network transformation of the process of providing social services in the post-industrial era should be updated on the following principle principles:

- use of mechanisms for ensuring the general and strategic voluntary participation of stakeholders in the IN on the basis of partnership and contract based on the results of a self-conducted comprehensive analysis of the internal and external conditions of participation;
- the legal, economic and target strategic unity of the general goals, development strategies and structure of the IN, which ensures a clear definition of the legal form of the future organization, maximizing the potential for each participant to minimize the use of general and individual resources of a single organizational system as a result of the implementation of a set of standard managerial actions, proposed in the research, which allows the IN to function as a single system that moves to a certain goal under the clear mission statement;
- definition of the scope of activity of network participants, their positioning as one of the four types of subjects of innovation activity – enterprises/institutions that carry out activities for the direct development and production of innovations (intellectual products); objects of innovative infrastructure to provide IN scientific, technical, natural and service resources/services; objects of commercialization, promotion and realization of innovations and intellectual products; objects of the subsystem of financing of innovative activity, which use the financial resources and management of the activities of IN in the external financial markets;
- legal independence in foreign markets, economic independence by the level of liquidity ratios, business activity and financial dependence, administrative independence according to the level of mobility of autonomous functioning of the independence of the participants of the IN;
- determination of interconnections between the members of the network with the priority of partnership equal rights in the defined framework;
- a clear division of rights and responsibilities between members of the network based on the principles of autonomy, voluntary participation and partnership;
- purposeful concentration of ownership in the process of identifying rights to innovations and intellectual products;
- ensuring the optimal balance between human knowledge and skills as a core capital, as well as creative teams as the main functional part of the process of creating structures and mechanisms for managing the IN;
- creation of a stable legislative framework for the development of IN of different levels;
- coordination, through state regulation of the most important processes of IN, the activity of their separate entities, establishment of price parity, regulation of their level for objects of innovation activity in order to create conditions for expanded reproduction;
- orientation on updating of professional knowledge, training/retraining of personnel, mastering of new methods, methods, means of carrying out activities through improvement of professional skills and level of education of all participants of IN;
- objective management accounting of all types of tangible and intangible resources, assets, intellectual property objects, and other elements of the resource base of the IN;
- compliance with the requirements of social justice during the functioning of the MI through the formation of high material status of members, their life support, elimination of excessive income differentiation, provision of high-level social benefits, balancing the interests of the community, the collective, the individual;
- the responsibility of each IM member for providing a qualitative final product of innovation activity [3].

The updating of the scientific approach to the solution of the problem of state regulation of the development of the SSNE of the postindustrial period appears possible on the basis of a creative combination of the provisions of the theory of the public sector of the economy, public services and the development of innovative sectoral /regional ecosystems in the context of the emergence of the digital economy.

Purpose of the study. The purpose of the publication is to determine the prospects of innovatively oriented development of the social sphere of scientific and production clusters of regional ecosystems with the preferential use of public-private partnership tools.

Results. Further development of the practice of PPP in the SSNE is based on the improvement of its organizational and economic mechanism. The content of this improvement consists in the implementation of the traditional elements of the mechanism – the goals and objectives of use, features of the functions in the process of performing the role of the control system and the special area of infrastructure management of the sectors providing individual consumer services in the social sphere of the national economy efficiency, tools and levers, specific forms and models – modernized requirements, formation of which takes place under the influence of the characteristics of adaptation by institutional actors of the national economy of the realities of participation in the sequence of formation of global value chains in the post-industrial economy, as the material basis of the social sector “glocal” regional (territorial) innovative socio-vital ecosystem.

The maximum suitable for practical use in view of specificity of domestic legislation in the area of public-private partnerships and new trends in the globalization of their funding models we believe innovative mixed model contract life cycle, that unlike a traditional contract life cycle – “modification of PFI, that is an analog of the DBFO (Design-Build-Finance-Operate) PPP provides for its use in combination with “mixed structural and investment funds”, which prevails in the European Union during the programme period 2014-2020.

According to our considerations in the process of developing models of mixed contract life cycle, it can be defined as a contract form public-private partnerships, in which the State concludes, on a competitive basis, partner with private partner agreement for the design, construction and operation of the facility throughout the life cycle, to pay for the project equal parts only after its commissioning, subject to maintenance of the private partner object in accordance with specific functional requirements. Attracting investment funds to one of the five options are governed by analogy with blending structural and investment funds with public-private partnership projects, developed by the European Centre of expertise [4].

The advantages for the Executive Authority of Public Administration (EAPA) in the implementation of a mixed life cycle contract model in the social sphere of a regional (territorial) innovative social and social ecosystem are:

- delegation of the process of charging socially significant functions to private capital;
- minimizing the risks of poor-quality design;
- avoidance of the risk of a rupture of the responsibility of a private partner for the design and construction of the infrastructure facility;
- elimination of the financial risks of improper operation and unpredictable future costs of maintaining the infrastructure.

The benefits of a private partner are the ability to obtain a large contract for the life cycle of an infrastructure facility, to be free in the process of choosing design and technical solutions; financial guarantees from the state in the process of raising funds by a private partner; avoiding the risk of demand [5-8].

From an organizational point of view, it is necessary expansion of the list of stages of implementation of PPP projects, which should include: identifying the interests of the parties to cooperation in order to select a specific mechanism; analysis of options to meet the needs of the project; preliminary examination of the suitability of the object for implementation, provides for mandatory calculations of cash flows: operating and investment activities, indicators of public project performance; operational, investment and financial activities at the stage of determining commercial performance indicators in a similar list of indicators; operating and investment activities in the case of evaluating the budgetary efficiency of the project with calculations of the total budgetary effect, discounted value, taking into account the distribution coefficient, the budget guarantee yield index, the internal budget efficiency rate [9]; technical, legal, financial, environmental analysis of the project; research its risks, profitability, availability and value for consumers; research into the value of cooperation for the market; holding a mandatory tender; calculation of public funding for non-profitable projects; providing the possibility of monitoring by the customer.

“Road maps” on the way to eliminating possible threats to the implementation of PPP projects in terms of locations during the implementation of regulatory actions by the executive authorities of the government administration must necessarily include a list of feasibility studies, legal expertise, audit of transactional pricing, formation of a system of non-financial criteria for evaluations of private partners, time management, engineering expertise, crisis management, competences’ management, operation management, management of emergency situations, the use of new financial instruments, in-depth technical analysis, management of framework agreements, providing the unpredictable impact of external risks and force majeure, constant change management. The complex nature of such an approach guarantees the realization of all the possibilities and advantages of using innovative models of PPP in the social sphere of a regional (territorial) innovative social and natural ecosystem, and in addition, it avoids the potential problems associated with those noted in Table 1 imperfections.

Taking into account the fact that the mechanism for regulating PPP operating in Ukraine is influenced by the risk factors typical for all countries and the parties failing to achieve partnerships due to prior agreements of economic interests, and the process of using the organizational and economic partnership mechanism is aimed at meeting vital needs not only so many sides of a PPP that are in commercial relations, but to the general public of stakeholders, it seems advisable to pay increased attention to this aspect of the regulation of the development of the regional (territorial) innovative social and natural ecosystem.

Table 1. Advantages and disadvantages of applying innovative PPP models in the R(T)ISS social sphere

Model PPP		Benefits	Disadvantages
Model of financing of local non-material assets development projects		Long-term focus Maximizing public sector resources Engaging private sector experience Comprehensive investment promotion Continuous monitoring of partnership development High procurement efficiency	The complexity of maintaining parity in the field of control High cost of administration and management costs Low risk transfer capability Complex accounting organization complexities
		Additional options to address the investment challenges of local EAPA: – if the level and specificity of risk, payback period, level of profitability do not meet market requirements, the viability of the project can be ensured by alternative methods; – insufficient level of financing in the public sector can be ensured by the receipt of alternative cash flows – non-availability for grant funding can be overcome by non-profit investing	
Model PFI	traditional	Ability to increase the value over the asset's lifetime High level of predictability of cost level and duration of partnership Focusing on the "value for money" problem during asset's lifetime Strong incentives for implementation Ability to be off-balance sheet	High contract value Inflexibility Excessive duration of formal procurement procedures
	with enhanced risk avoidance unit		
Integrator model		Role / responsibility allocation transparency (lower level of conflict of interest) Increasing the level of competitive pressure Attraction of a wide range of partners, including small and medium-sized businesses Lower procurement costs for the project High level of flexibility in program implementation	If the appointment of a strategic partner takes place prior to the formal procurement procedures, there is a risk of a lack of competence and service delivery skills. Lack of integrated supply chain
Model of local PPP in education / local financial trusts		An opportunity for the public sector to retain influence over the strategic direction of investment High potential for continuous improvement during the next successful phases of project implementation	Conflict of interest for a strategic partner Too high a value for money benchmarking process Strong obstacles to the ability to attract alternative providers
Model of competitive partnership		Early receipt of commercial funds from a private partner The level of competitive pressure does not decrease over time Effective benchmarking of project implementation costs	
Model extended partnership		Low procurement costs High level of flexibility to meet the adjusting requirements Relationships are formed gradually, without long-term contact Constantly maintaining a high level of competition	The model is more demanding for public sector involvement Transferring major risks to the public sector Transferring ongoing responsibility to the public sector in the negotiation and management of the PPP project
Alliance Model		Ability to continue implementing the project under uncertainty Increasing the level of cooperation and reducing the level of disputes between partners	

The life cycle of a governmental-private partnership project in the social sphere; a regional (territorial) innovative social and vital ecosystem includes the traditional stages of forming and detailing the concept of partnership, designing an innovative research component, sharing knowledge, training, collecting and analyzing data, interpreting results, developing communication channels sharing knowledge and data; identifying new information or research goals. It is also necessary to take into account the fact that the role/contribution of stakeholders differs significantly at different stages of project implementation, and the list of methods for attracting stakeholders, the skills necessary for this, coordination of methods with individual levels of involvement allows developing a detailed interaction map (Table 2).

Table 2. Map of stakeholders interaction at the stages of the PPP project on the LC' model in the SS of R(T)ISES

The role of stakeholders, scope and level of influence methods of attracting stakeholders			Level of interest			
			1	2	3	4
Stages of the project life cycle	Preparation	development of the project implementation strategy				
		development of a list of measures for the implementation of the project				
		development of a list of measures for the implementation of the project				
	Preparation / implementation	organization of the network of project stakeholders				
		development of recommendations				
		development of methodological guidelines				
		revision of the project				

	Realization	prediction / simulation				
		monitoring				
		resource provision (equipment, data, financial assets, contracts)				
	Realization/ completion	education				
		project implementation				
		identifying data users / social service recipients / beneficiaries				
	After completion	Feedback				
		communication and dissemination of project results between stakeholders				
		identification of topics for future partnership projects				

Note: level of interest: 1 – informing; 2 – counseling; 3 – attraction; 4 – collaboration

The most suitable for use in order to organize cooperation between stakeholders at different stages of the project life cycle of PPP technicians are:

- the stage of the beginning of a dialogue between the parties of cooperation - “brainstorming” (brainstorming – a method of formulating for a short time new and creative ideas that cannot be obtained by another method) meta-plan, as well as a similar method of laying out a Venn diagram – members groups followed by their association on the basis of similarity by the facilitator; technique “carousel”;
- a stage of critical analysis of previous experience in the implementation of public-private partnership projects – a technique of categorizing, rigidly sorting ideas based on predetermined criteria / similarities; mini-mapping (conceptual reflection, spray diagrams, spider diagrams) for the purpose of quick fixing and combining ideas with interested parties; analysis of the “decision tree” with the fixation of cause-effect relationships; SWOT-analysis with a detailed study of the strengths and weaknesses, opportunities and threats arising in the course of solving problems of partnership; the methodology for compiling a time period with comments from the participants in the discussion to resolve questions about the planned or expected state of the project in coordination with the interested parties of cooperation;
- the stage of making decisions on limiting the list of methods for implementing the partnership – voting; ranking – ordering ideas by degree of importance to the project; prioritization; multi-criteria evaluation of competing priorities;
- stage of integration of new results – creative techniques.

The initiators of PPP projects in the social sphere of a regional (territorial) innovative socio-vital ecosystem can adopt a significant number of other methods for attracting stakeholders, which include methods: direct promotion/proactive interactions; recording and evaluating the participation of stakeholders in the process of implementing a PPP project; tools to disseminate information about the implementation of the project and use the results of its implementation; fixation of products/services generated in the process of project implementation.

An important point in the organization of cooperation between stakeholders of PPP projects in the social sphere of a regional (territorial) innovative social and ecological ecosystem is the effective use of tools to prevent potential parties' conflicts. A clear typification of their varieties, knowledge of the level of loyalty of individual stakeholders to the goals of the project makes it possible to create a matrix of categories of project parties in terms of potential participation in direct, hidden, latent, clearly defined and blurred, cognitive, objective (interests), normative, relationships, subjective, beyond design, structural conflicts. Different attitudes to the use of project results (similar or different), degree of commitment to the project goals (high/low), critical/non-critical influence on the success of its implementation, stakeholders require the implementation of individual approaches in situations of emerging conflicts of interest.

Thus, the effective modernization of the development of governmental -private partnership projects in Ukraine is associated with the improvement of the organizational and economic mechanism of governmental -private partnership in the social sphere, taking into account the best practices of its reform in foreign countries, based on the following principles:

- clarification of the essential characteristics of partnership projects taking into account all the features of the functioning of the national economy;

- rationalization of national models of PPP development;
- updating the list of objectives for implementing the policy of PPP;
- expanding the list of the code of the type of economic activity (CTEA) covered by the practice of cooperation agreements;
- expansion of the list of types of legal registration of transactions;
- revision of approaches to the expansion of the list of business entities that may initiate the conclusion of partnership agreements;
- expansion and clarification of the content of individual stages of the implementation of PPP;
- improvement of the current legislation on the regulation of PPP;
- empowerment of parties to participation in transactions;
- improvement of risk management tools and techniques for the implementation of PPP;
- development of an effective mechanism to guarantee the return of the invested funds of the parties to cooperation agreements between EAPA and private business;
- organization of continuous monitoring of PPP projects;
- development of a mechanism for the implementation of “unclaimed projects” of cooperation in the social sphere.

Conclusions and prospects for further research. The innovative oriented development of the practice of PPP in the social sector of regional ecosystems is based on the implementation of the traditional elements of its mechanism of modernized requirements, the formation of which is influenced by the realities of the participation of institutional actors in the formation of global chains in the conditions of post-industrial economy. At the same time, localization of the vast majority of individualized socially significant services within the functioning of the socioital local innovative ecosystems takes place.

Qualitative innovation shifts in the development of a post-industrial knowledge economy, the driver of which is a steady growth in the volume of partnerships between EAPA and innovation ecosystem stakeholders, based on a substantial activation of objective and subjective factors increasing the volume of the internal fund for social sector financing.

The involvement of PPP stakeholders is based on the implementation of a set of techniques for the strategic and operational regulation of the process of cooperation between project stakeholders. The most suitable for use in the organization of cooperation between stakeholders at different stages of the project life cycle in the social sphere R(T)ISES technicians are: brainstorming; conclusions metaplan, Venn diagrams; technique “carousel”; categorization technique; mini-mapping; decision tree analysis; SWOT analysis; method of drawing up a time period; voting; ranging; prioritization; multi-criteria evaluation of competing priorities; creative techniques.

It is concluded that the modern method of managing the development of the social sphere is the state innovation regulation of public management of public-private partnership with the use of e-Government facilities; management of virtual networks; fundraising; outsourcing; creation of social technology platforms; crowdfunding; meeting the needs of stakeholders in obtaining high-tech social services; the formation of educational production clusters, “nodes” of stabilization and development, technical, intellectual, information, social “centers of excellence”; top-priority designing on the periphery of forward-looking, innovative and technology-intensive technologies.

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SPECIFIC ISSUES AND TENDENCY OF DEVELOPMENT AND FINANCING OF TRANSPORT SECTOR: REGION ASPECTS

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ABSTRACT

The transport complex belongs to the strategically important element of regional development, which includes both providing expanded access to public services for the population of remote areas, realizing the tourist potential, and strengthening industrial ties. The purpose of this article is to identify problems and growth areas of the transport sector in the region through the example of the Kirovograd's one. The tendency of priority development of land transport in the Kirovograd region, specifically automobile, has been confirmed. The key factors which influence on the transport services market development in Ukraine are given, for instance the unsatisfactory technical condition of transport, reduction of traffic during the COVID-19 pandemic, etc. The main problematic aspects of development of the transport complex in the Kirovograd region are substantiated. The main priorities for the development of transport infrastructure in the Kirovograd region are presented. In order to reduce abusive activity in the transport service market the funds transfer network implementation has been suggested. The possibility of using finance lease as a source of funding automotive maintenance during economic crisis is substantiated.

Keywords: transport, automobile, land transport, finance lease, auto financing

Introduction. It is difficult to overestimate the role of the transport complex in the economic system of the region. Transport has a special place in the development of all sectors of the economy, ensuring the promotion of material flows in macro-logistics chains. Thus, the efficiency of the production sector, the development of the tourism industry and the social sphere depend on the state of the transport system.

The efficiency of transport use depends on the technical condition of rolling stock and the transport infrastructure of the region, which require significant investment in their renewal in order to ensure the competitiveness of transport services. Despite the acknowledgement of transport as a priority area of activity, which should be supported by the state and local authorities, funded and developed, there are several problems that act as a brake in the development of transport in the Kirovograd region.

Since transport is a key factor in the development of the region's economy, this determines the relevance to study the problems of the transport complex in the Kirovograd region and the substantiation of areas for improvement.

Literature review. Problematic aspects and directions of the transport complex development have become especially relevant under the conditions of the globalization progress. This issue was raised by many domestic scientists [1] who analyzed the market of transport services of Ukraine, identified the key issues of development and integration of the transport system of Ukraine into the world transport network. Directions for further reform of the transport sector at the stage of post-crisis recovery of Ukraine's economy were suggested.

In the article Logutiva T., Poltoratskiy M. [2] the main factors of falling of volumes of transportations and the elements of a transport process are defined. The economic indicators of activity of a transport industry, that represent the necessity of reformation and updating the approach to the management of the transport industry of Ukraine. In the article Nosovska O.B., Makarenko M.V. [3] the current modern problems of development of a transport infrastructure, a well-founded role and significances of all types of transport for state economy are considered. In the article Ivanov S.V. [4] the direct correlation of transport costs with costs in other sectors of the national economy and their correspondence with the level of well-being are justified. The feasibility of creating transport service cooperatives in the regions and allocating appropriate funds from the regional budgets for the purchase of trucks for this purpose has been proved. The need to improve the state regulation of the development of river transport is established. The possibility of forming a transport and logistics cluster in the Dnipro economic region is substantiated.

However, current trends of development in the transport system of Ukraine continue, so they need constant research. Special attention needs to be paid to the range of study about special aspects of the transport system of the region, considering the territory in which it is located.

Objective. The purpose of this article is to identify problems and growth areas of the transport sector in the region through the example of the Kirovograd's one.

Results. The effective activity of all enterprises in the Kirovograd region and normal life-sustaining activity of popularity depends on providing them with quality transportation services. Expanding the supply of transport services in terms of volume and range is an important source of economic growth in the region, as it provides a certain share of revenues to the local budget, increases amount of employment and improves living standards.

The Kirovograd region has a developed network of modes of transport: railway, automobile, airline, water transport. The data given in Tables 1 and 2 indicate that the main mode of transport in the Kirovograd region is road transport. It carries the largest share of passengers (46 to 92 percent over the analyzed period) and freight (from 77 to 89 percent over the analyzed period) each year.

Table 1: Number of transported passengers by types of transport in the Kirovograd region

Year	Total	Railway		Automobile		Air		Trolleybus	
		kt	part, %	kt	part, %	kt	part, %	kt	part, %
1995	120570,1	8968	7,44	97906	81,20	2,2	0,00	13693,9	11,36
1996	147975,2	9202	6,22	114042,3	77,07	2,9	0,00	24728	16,71
1997	102024,7	5090,3	4,99	59792,9	58,61	37	0,04	37104,5	36,37
1998	103053,2	4500	4,37	53939,7	52,34	11,2	0,01	44602,3	43,28
1999	91046,6	4500	4,94	42600,8	46,79	5,3	0,01	43940,5	48,26
2000	85778,4	5101,5	5,95	39147,4	45,64	22,9	0,03	41506,6	48,39
2001	65756,3	5460,7	8,30	51036,2	77,61	44,4	0,07	9215	14,01
2002	74240,9	4658,5	6,27	57350,6	77,25	65,8	0,09	12166	16,39
2003	78571,6	5686,1	7,24	56832,4	72,33	87,7	0,11	15965,4	20,32
2004	87012,2	3856,4	4,43	66424,3	76,34	84,1	0,10	16647,4	19,13
2005	107580,9	4531,9	4,21	81983,2	76,21	72,4	0,07	20993,4	19,51
2006	91382,7	4598,2	5,03	66866,6	73,17	81,1	0,09	19836,8	21,71
2007	101311,2	5060,9	5,00	77520,6	76,52	91	0,09	18638,7	18,40
2008	113198,9	5055,5	4,47	84530,5	74,67	96,8	0,09	23516,1	20,77
2009	101827,1	4477,5	4,40	74358,3	73,02	99,6	0,10	22891,7	22,48
2010	93250,1	4794,1	5,14	85572	91,77	87,4	0,09	2796,6	3,00

2011	107897,5	4843,9	4,49	98691,9	91,47	73,2	0,07	4288,5	3,97
2012	94915,3	4877,1	5,14	85972	90,58	40,6	0,04	4025,6	4,24
2013	76688,3	5117	6,67	66965,3	87,32	60,8	0,08	4545,2	5,93
2014	58028,3	4982,3	8,59	47672,4	82,15	74,9	0,13	5298,7	9,13
2015	62851,8	4824	7,68	48487,9	77,15	63,4	0,10	9476,5	15,08
2016	58523,6	4674,9	7,99	47041,7	80,38	83,4	0,14	6723,6	11,49
2017	59882,2	2338,3	3,90	41871,5	69,92	62	0,10	15610,4	26,07
2018	70493,2	2302,4	3,27	49565,9	70,31	33,4	0,05	18591,5	26,37
2019	75970,2	2223,3	2,93	47638,8	62,71	38,1	0,05	26070	34,32

Source: compiled by the authors based on the statistical information [5; 6]

Today, all modes of transport operate in difficult economic conditions, which are associated with a decline in industrial and agricultural production, declining living standards, falling growth rates of freight and passenger traffic, deteriorating technical condition of transport.

Table 2: Number of transported freight by types of transport in the Kirovograd region

Year	Total	Railway		Automobile		Aviation	
		kt	part, %	kt	part, %	kt	part, %
1995	47340,5	5463,3	11,54	41877,2	88,46	-	-
1996	33547,7	3430,8	10,23	30116,9	89,77	-	-
1997	27127,5	2764,2	10,19	24363	89,81	0,3	0,00
1998	25937,5	3362,5	12,96	22574,6	87,03	0,4	0,00
1999	21548,4	3242,5	15,05	18305,7	84,95	0,2	0,00
2000	18871	2533,2	13,42	16334,3	86,56	3,5	0,02
2001	22237,9	3453	15,53	18779	84,45	5,9	0,03
2002	19476,3	3877	19,91	15592	80,06	7,3	0,04
2003	19467,6	4161,2	21,38	15301	78,60	5,4	0,03
2004	25139,7	5118,6	20,36	20010,3	79,60	10,8	0,04
2005	30651,2	5572,7	18,18	25068,5	81,79	10	0,03
2006	35288,9	7156,1	20,28	28125,7	79,70	7,1	0,02

2007	36953,8	8345,2	22,58	28602,6	77,40	6	0,02
2008	40197,4	8883,1	22,10	31308,4	77,89	5,9	0,01
2009	33076,1	5773,4	17,45	27297	82,53	5,7	0,02
2010	34478,7	6390,9	18,54	28081	81,44	6,8	0,02
2011	41185,6	7872,4	19,11	33308,7	80,87	4,5	0,01
2012	38537,7	7820,9	20,29	30713,8	79,70	3	0,01
2013	41906,1	7706	18,39	34196,8	81,60	3,3	0,01
2014	52103,5	6368,8	12,22	45730,4	87,77	4,3	0,01
2015	50385,5	6546,2	12,99	43835	87,00	4,3	0,01
2016	46551,4	7697	16,53	38849,9	83,46	4,5	0,01
2017	53627,6	7822,7	14,59	45802,7	85,41	2,2	0,00
2018	56380,8	7136,9	12,66	49241,8	87,34	2,1	0,00
2019	44734,6	6253,6	13,98	38479,3	86,02	1,7	0,00

Source: compiled by the authors based on the statistical information [5; 6].

At the same time, it should be noted that Ukrainian transport to a greater extent becoming uncompetitive compared to foreign ones, both as in economic terms and in terms of operation, environmental and technical safety. The situation has been compounded by deterioration of demand in passenger and freight transportation due to the COVID-19 pandemic, meaning fall of living standards, low levels of investment activity, and the disruption of many domestic and foreign economic ties.

Conducted by scientists [2, p. 13-14; 3] analysis of the dynamics of the Ukrainian transport industry shows a steady decrease in traffic. The performance indicators of the transport sector of Ukraine have ambiguous dynamics, which is related to the general economic processes in the country. These include: loss of performance of the end-production in industrial manufacture in Ukraine, decrease of domestic demand due to declining purchasing power.

The sharp decline in traffic during the COVID-19 pandemic has negatively affected the revenues of various modes of transport and the ability of replacement of fixed assets, even at the level of simple reproduction.

The main reasons for the negative trends identified in the analysis of the state and performance of the transport complex of the Kirovograd region, should be recognized as:

- high degree of obsolescence and depreciation of active part of fixed assets for all modes of transport;
- low competitiveness of Ukrainian inspections and low attractiveness of freight transfers;
- unsatisfactory environmental performance of vehicles;
- significant lag in the development of transport infrastructure, for instance, between territorial communications and facilities for the development of road, rail and mixed transport;
- unresolved problems of investment and coordination of management in the transport complex of the region;
- significant backlog of existing level of transport equipment and service from the world level, which complicates the entry of the Ukrainian transport complex into the world transport network;
- discrepancy of standards, regulations, efficiency and safety criteria, insurance principles which applies on Ukrainian transport to similar indicators used in other countries;
- irrationality of tax and customs legislation, lengthy inspection and document circulation procedures for export-import cargo transportation;
- underdeveloped of information and telecommunication infrastructure for freight transportation in the region.

The key problems of effective development of road transport, according to Logutiva T., Poltoratskiy M. (2015), are the following:

- formation of a competitive environment in the designated transportation markets;

- maintaining the stability of work in crisis conditions;
- implantation of the newest economic approaches of tariff formation for transportation;
- attracting foreign investors to state development programs on attractive terms;
- introduction of effective models of public-private partnership;
- increasing the quality of transport services provided [2, p. 12].

Solving these problems is important not only for the transport industry, but also for the whole region, for the efficient functioning of its industrial and social spheres, which is largely ensured by stable and reliable operation of transport.

To ensure the economic development of the Kirovograd region, the strategic directions of development of the transport complex should be:

- reconstruction of roads (equipment of speed change lanes, road markings, pavement repairs, barrier fencing repairs, etc.) in the directions Lviv - Kropyvnytskyi - Znamyanka, Boryspil - Dnipro - Zaporizhia, Sumy - Poltava - Oleksandriya;
- formation and expansion of the regional market of transport services;
- introduction of new equipment and modern technologies of transportation organization;
- introduction of resource-saving and energy-saving technologies, reduction of the share of fuel and energy costs;
- comprehensive solution of the problem of environmental protection;
- replacement of obsolete vehicles, purchase of new trucks, replacement of minibuses with new large-capacity buses;
- construction of new highways with preference for new high-speed highways within transport corridors;
- increasing the number of access roads to rural areas;
- improving the transport, operational and technical condition of existing roads, increasing the level of their arrangement, safety and efficiency of transportation, bringing them into compliance with modern requirements;
- increasing the capacity of nodal structures (junctions, interchanges, bridges);
- reconstruction and modernization of the infrastructure of the main railway line, renewal of their rolling stock;
- optimization of the location of the overhaul and reconstruction park of rolling stock with a concentration of repairs at enterprises with the lowest cost;
- development and introduction on the main transport routes the inspector system of freight transportation which provides increase of safety of highways and decrease in ecological pollution.

Almost all transport companies in the Kirovograd region need reconstruction, modernization, technical and technological re-equipment, but funding of the transport sector remains low. Today, the most realistic source of financing is the own resources of transport companies, but the financial situation of most of them does not allow to complete modernization of the technical park. Further development of transport depends on the improvement of tax legislation, strengthening the material and technical base of enterprises, increasing their competitiveness, improving the financial and economic condition of enterprises of all sectors of the economy and others.

Therefore, to improve the financial support of the transport complex of Kirovograd region, it can be offered:

1. introduction of an electronic ticket (e-ticket WG (E-ticket working group)) (introduction of an automated payment system for passenger transportation based on the use of electronic plastic cards, which will increase the revenues of transport companies, improve the quality of passenger service and will help address the issue of de-shadowing of financial flows in the transport-related field of the region);
2. maintaining the efficiency of the existing car and trolleybus fleet based on a system of complete overhauls performed by car repair companies, but this is not promising due to low quality of repairs, significant reduction in reliability and a sharp increase in operating costs of poorly repaired cars (trolleybuses);
3. the motor transport enterprise forms the list of equipment which must be repaired;
4. an application for repair of this equipment using leasing and a package of all necessary documents confirming the lessee's creditworthiness are sent to the leasing company (investor, bank);
5. consent to leasing is given;
6. the relevant loan agreement is drawn up;
7. the investor (bank) transfers the necessary funds to pay for the services of the repair organization.

Leasing can be used to implement the system of "branded maintenance" and technical support service of cars (branded service) at special enterprises of the automotive industry. When considering financing the repair of equipment using the leasing mechanism (figure 1) should indicate the following points of signing the lease agreement. The equipment is pledged under the lease agreement throughout the repair period, ie the leasing company is its owner until the full amount of the leasing contract is paid.

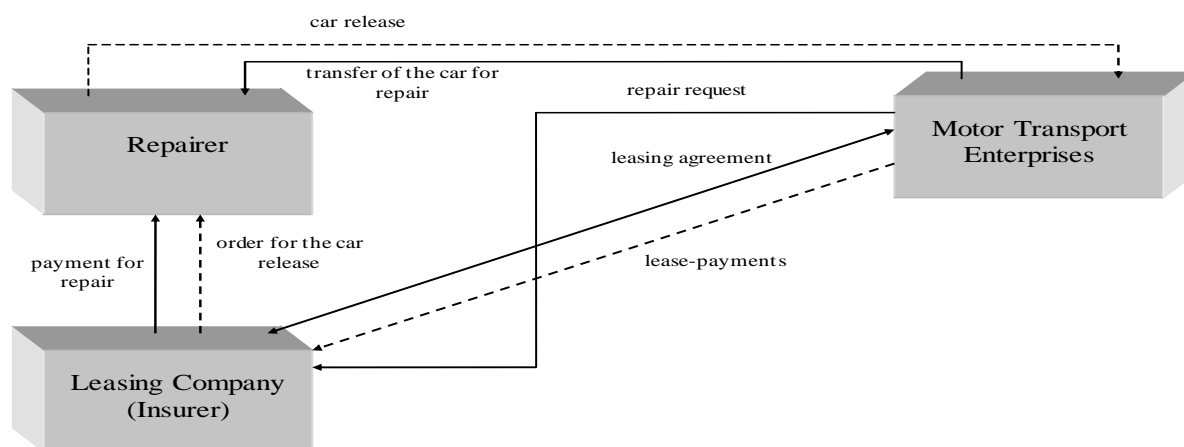


Figure 1: The scheme of leasing for the repairing of fixed assets of transport enterprises

Source: [7, p. 303].

CONCLUSIONS

Thus, we can conclude that urgent measures are needed for the transport complex of Kirovograd region, specifically for its stabilization, regulation, structural improvement and implementation of state support for priority areas of its development. The implementation of such measures involves improving the transport, operational and technical condition of existing roads, increasing the level of their equipment, safety and efficiency of transportation, bringing them into line with modern requirements, increasing the capacity of hubs, repairing pavement, repairing barriers, construction of new highways within transport corridors, which will make it possible to make effective use of the geographical location of the region.

A serious problem in the development of transport enterprises in the region is the impact of the black economy. To neutralize this negative impact, it is necessary to establish clear control in the provision of transport services by introducing a system of non-cash electronic payments, which is based on the use of electronic plastic cards. Targeted actions are also needed to increase the efficiency of the transport business, encourage the consolidation of operators and the creation of multidisciplinary transport companies that have a developed production infrastructure.

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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 подвергли 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.

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 37°C 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 37°C 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 37°C 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

No	Isolates/ Antibiotics	Class	D-1	D-2	D-3	D-4	D-5	D-6	D-7	D-8	D-9	D-10
1.	Doxylin	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 antibiotics, 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 antibiotics could inhibit the growth of bacteria strain.

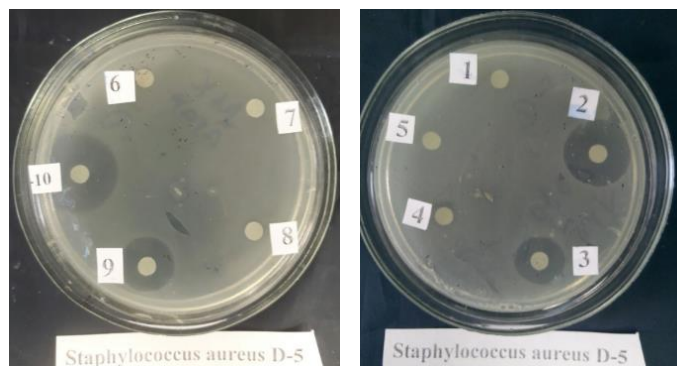


Figure1. Antibiotic resistance of *S.aureus* D-5

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

No	Strains/ Antibiotics	Class	P.aer. D-1	P.aer. D-2	P.aer. D-3	P.aer. D-5	P.aer. D-6
1.	<u>Tetracycline</u>	I	12*	12	0	9	21
2.	Chloramphenicol	II	0	20	0	0	0
3.	Rifampicin	III	9	22	12	0	9*
4.	<u>Clarithromycin</u>	IV	0	35 *	0	0	0
5.	<u>Polymyxin B</u>		20	0	0	0	0
6.	<u>Ofloxacin</u>	V	23	0	0	0	0
7.	<u>Sparfloxacin</u>		28	0	0	0	0
8.	<u>Co-trimoxazole</u>	VI	0	35*	0	0	0
9.	<u>Kanamycin</u>	VII	8	0	20*	0	10
10.	<u>Streptomycin</u>		22	0	0	0	0
11.	<u>Amikacin</u>	VIII	26	0	0	0	15*
12.	Cefotaxime		15	13	0	0	0

I. Tetracyclines II. Levomycesin III. Ansamycins IV. Macrolides V. Fluoroquinolones VI. Sulfonamides VII – Aminoglycosides VIII-Cephalosporins

“*” – Bacteriostatic activity

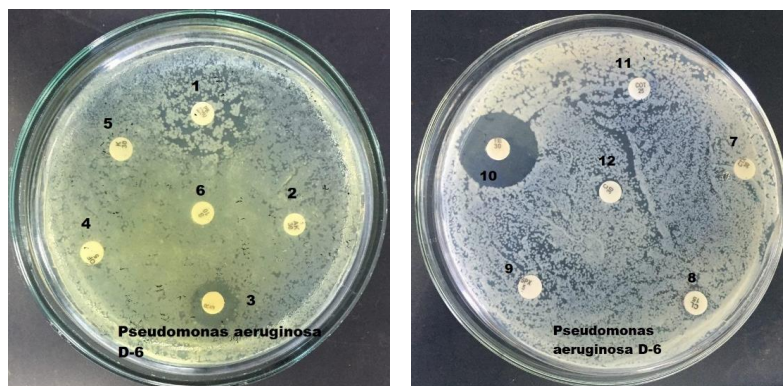
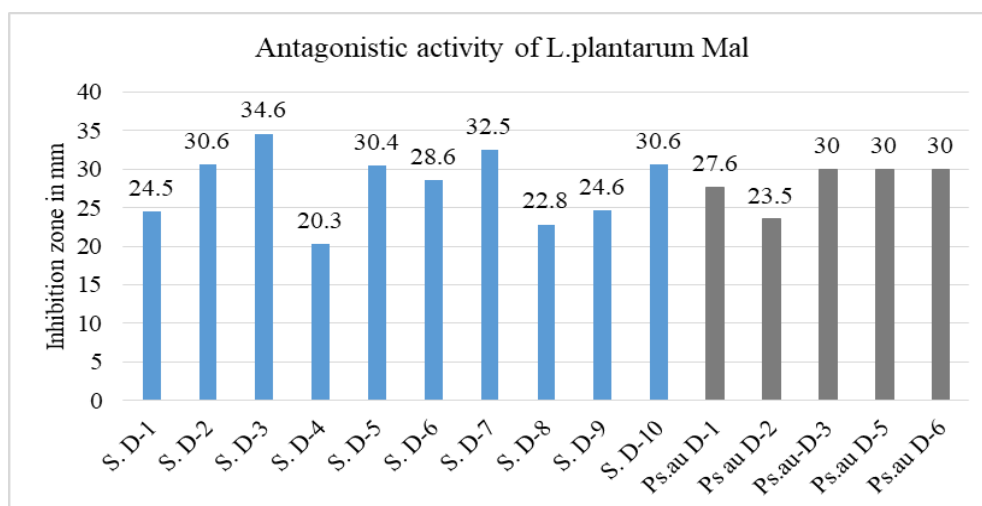


Figure 2. Antibiotic resistance of *P.aeruginosa* D-6

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).



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).

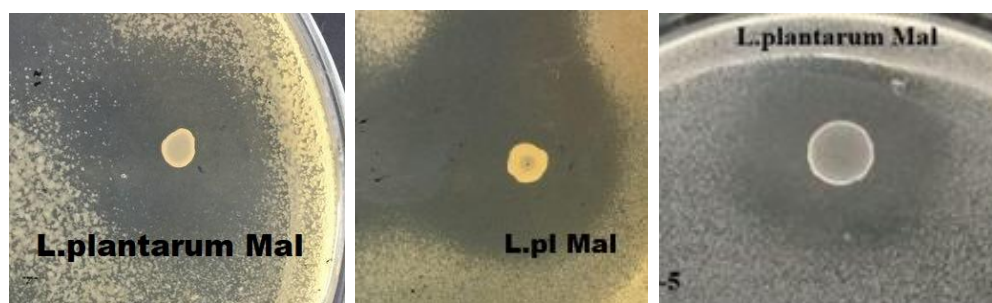
A. *P. aer* D-6B. *P. aer.* D-5C. *S. aureus* D-5

Figure 3. A. Antagonistic 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].

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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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]

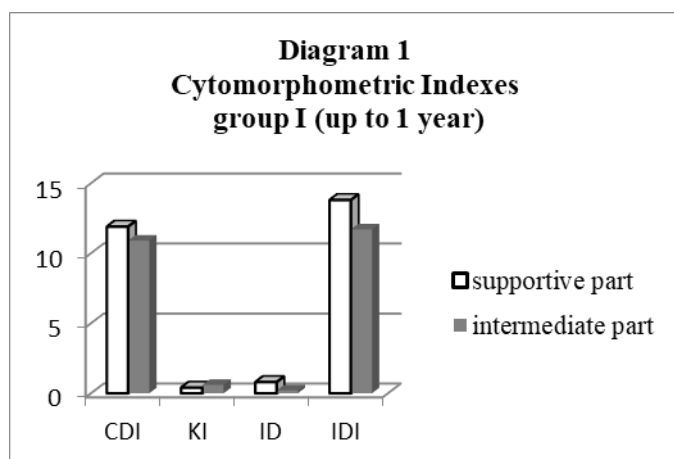
The aim of the present study is to identify the dynamics of changes of mucosa in the region of metallo-ceramic prosthesis.

MATERIALS AND METHODS

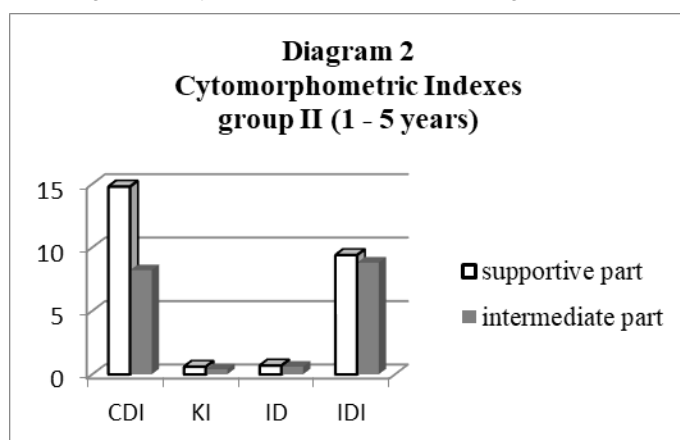
We have examined three groups of patients, according to the length of wearing time of metallo-ceramic prosthesis: I group - 1year (12 patients), II group – 1-5 years (28 patients) and III group – 6 -10 years (20 patients). Each group includes two subgroup, where was studied influence of fixed and intermediate 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

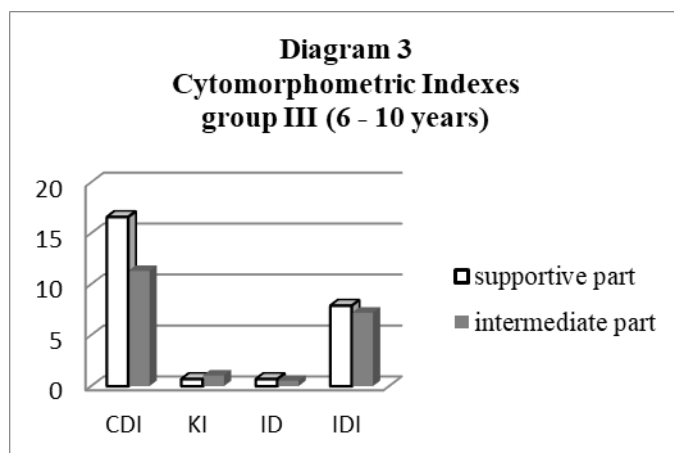
The comparative study of cytological data between supportive and intermediate parts of prostheses in group I (diagram 1) has showed that in gingival mucosa adjacent to intermediate part of prosthesis: the index of cell differentiation (CDI) is 1,1 times less ($p > 0,05$), index of keratinization (KI) 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.



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 prosthesis, 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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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 endotheliitis 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.

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The early pathogenesis in COVID-19 (Huertas *et al.*) pneumonia defined by a widespread endotheliitis 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.

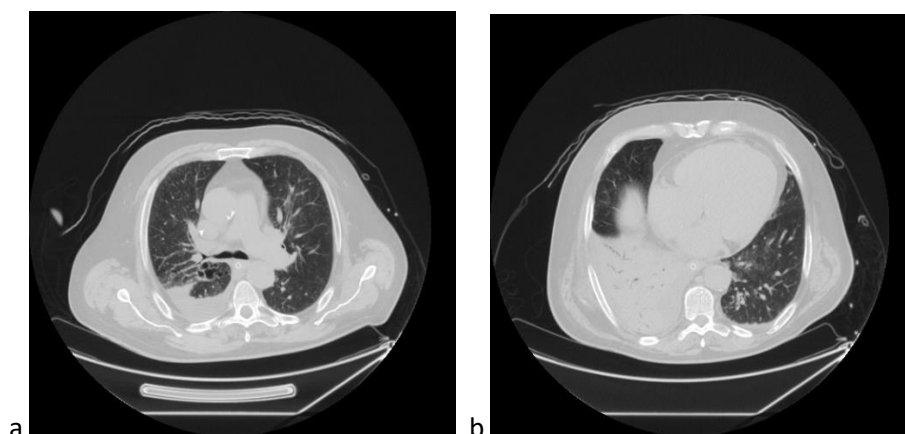


Figure 1

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

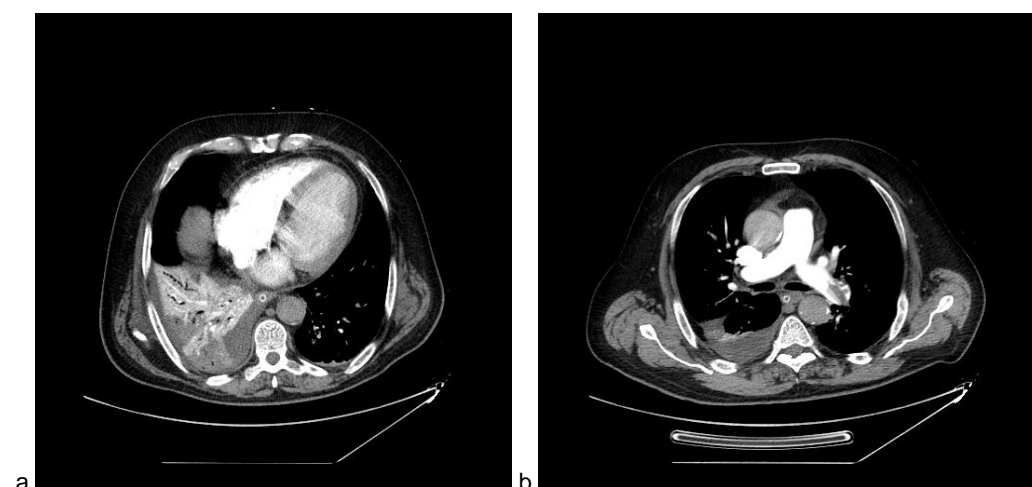


Figure 2

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 dysfunction, 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. "Bubble" 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.

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 hypodense 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.

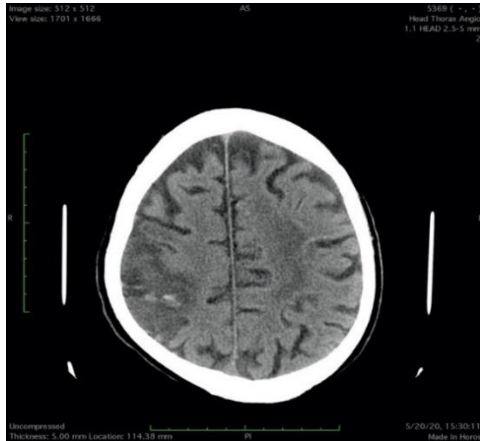


Figure 3

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 $\text{PaO}_2/\text{FiO}_2 < 150$, 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:

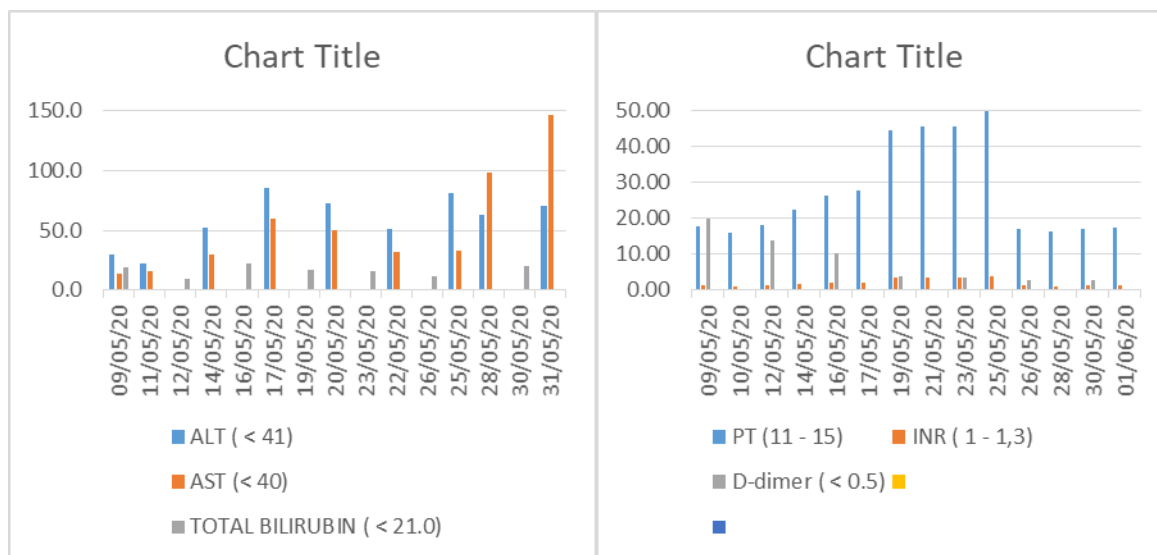


Table 1

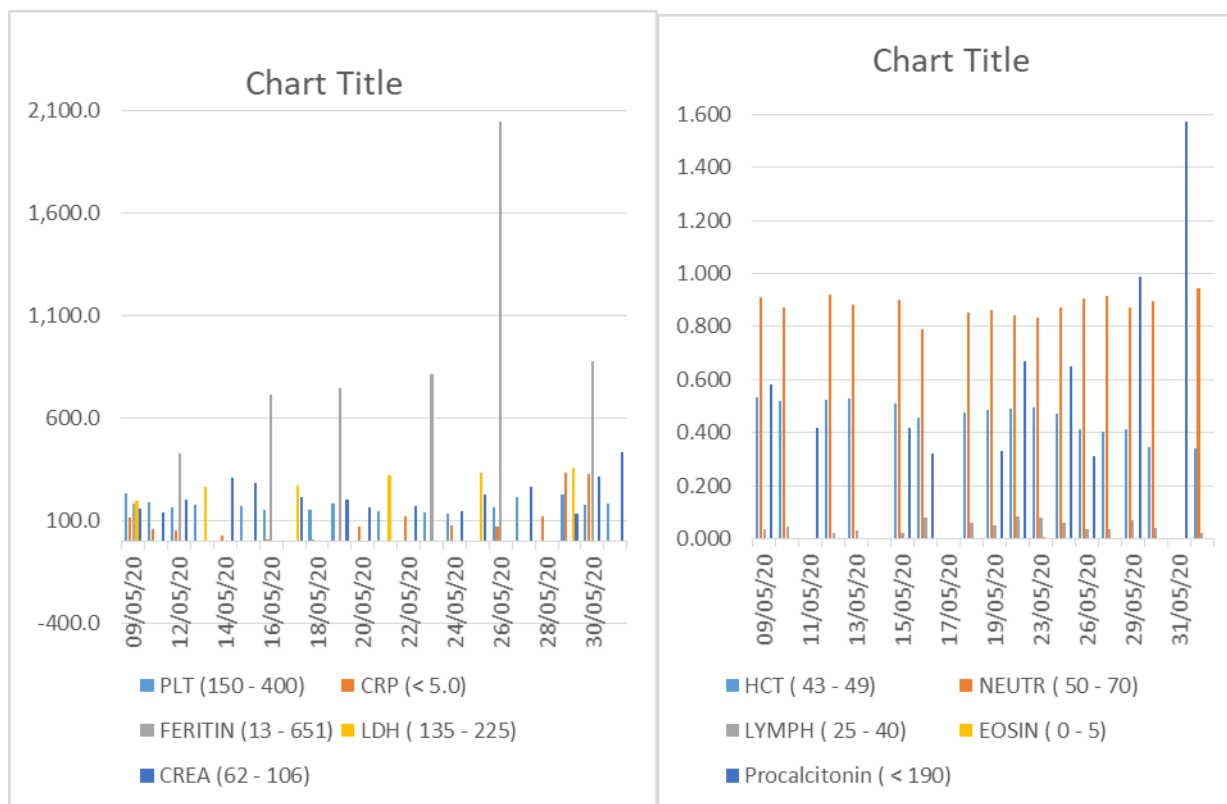


Table 2

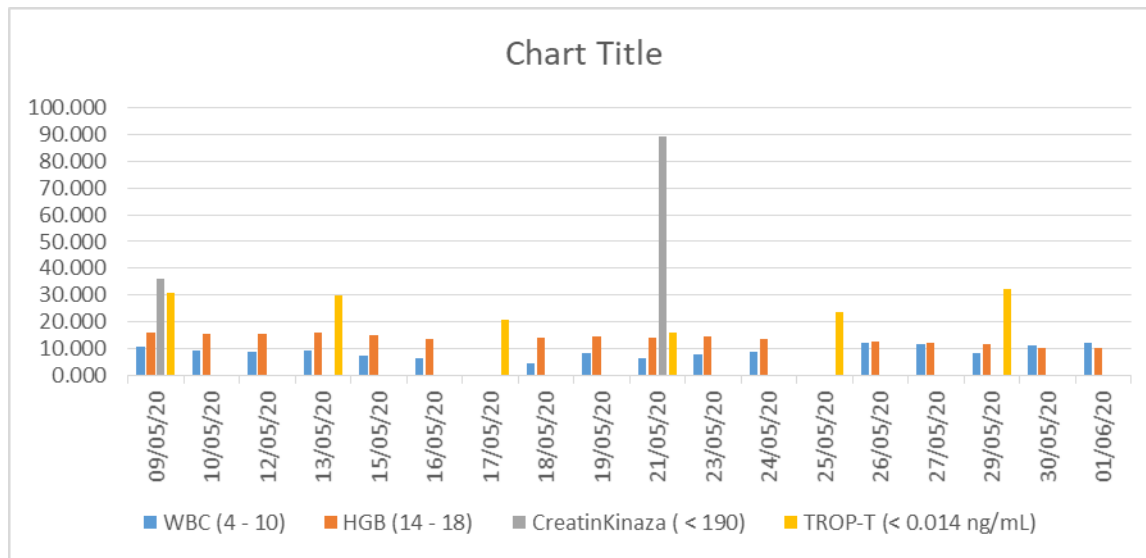


Table 3

Patient state was improved. 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

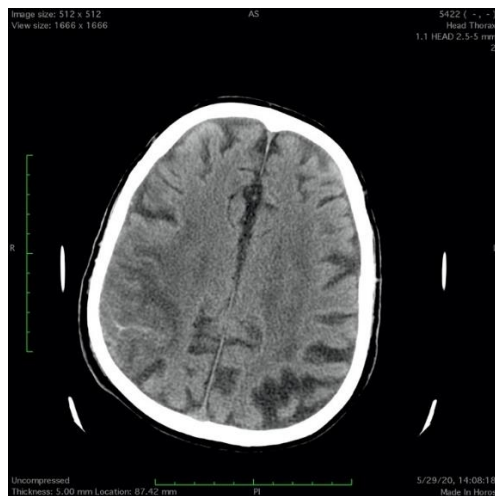


Figure 4

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

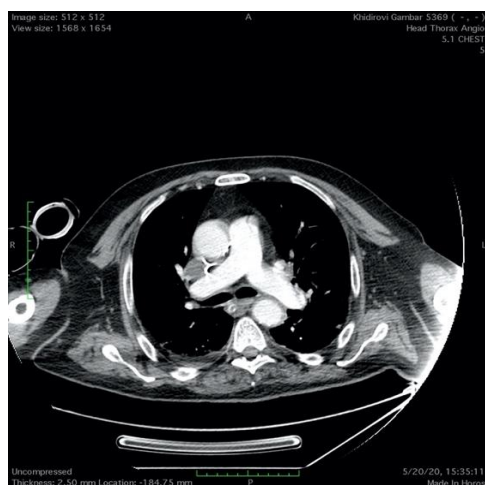


Figure 5

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)

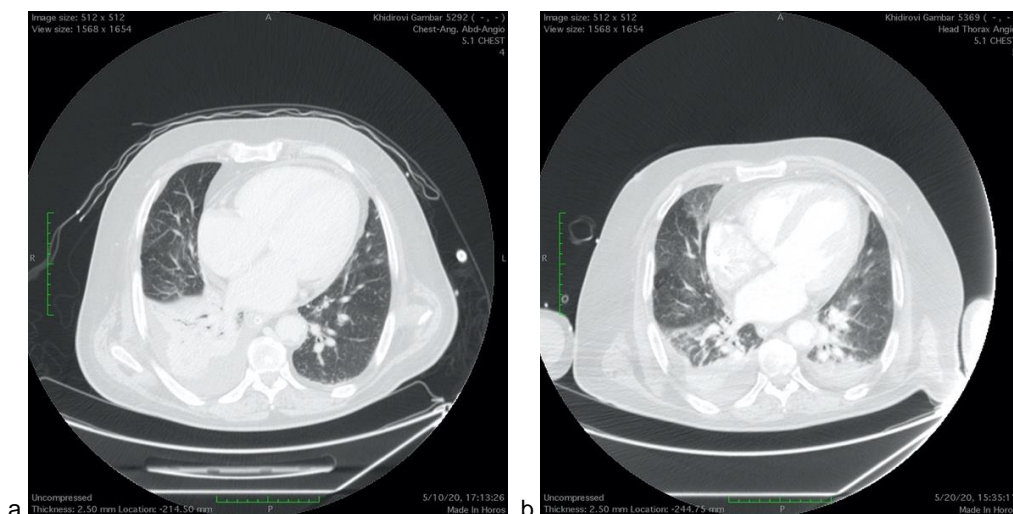


Figure 6

- In the lower part of right lung extensive inflammatory and consolidation lesions ,with airal bronchogram.
- The volume of extensive inflammatory changes is reduced with thickening of interlobar 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

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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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 O), 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. ABO 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 ABO 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 ABO 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 also 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 ABO 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	$\chi^2(0/A)$	$\chi^2(0/A+B+AB)$
Group I	N	80	25	2	0	14.11, p<0.001	24.88, p<0.001
	%	74.77	23.36	1.87	0.00		
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 \pm Std. Dev. or n(%)	Mean \pm Std. Dev. or n(%)		

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-Saharan 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 significantly 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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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 $7.4 \pm 0.2\%$ and $7.9 \pm 0.6\%$. The nondiabetic control group consisted of 82 patients (F: 48 and M: 34, mean \pm SD age 55.97 ± 0.9). Investigated the parameters of phosphorus-calcium metabolism (Ca²⁺, 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

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).

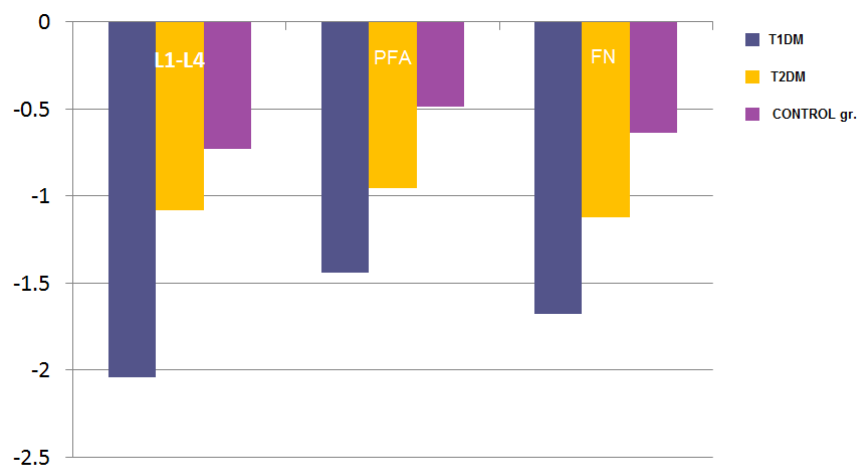


Figure 1. BMD assessment at the T-SD L1-L4, PFA and FN area in patients with T1DM, T2DM and a control group

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 PINP 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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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

Proband 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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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 (FISH) 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 (ICSI 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 χ^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 χ^2 .

Findings of Study

Mean age of females was 35.5 ± 1.0 . Infertility duration was 7.5 ± 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 B n=44		Total n=86
	Age < 35		Age < 35		
	abc	%	abc	%	abc %
Total embryos subjected to PD	52		59		220
Embryo pathologies by chromosomes, No	36	69.2	35	59.3	106
Embryo pathologies by chromosomes, Yes	16	30.8	24	40.7	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

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

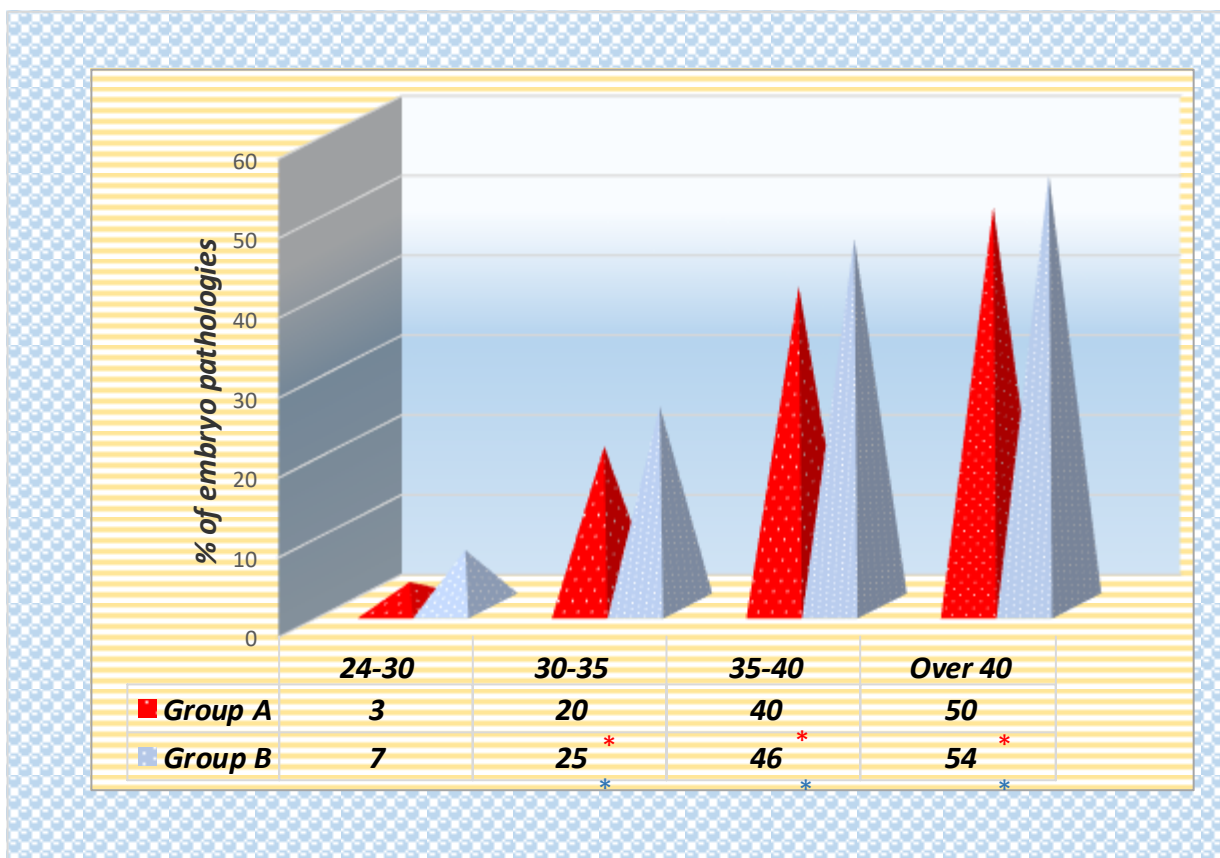
Features of embryos with pathologies detected by pre-implantation diagnosis

Value	Group A n=40		Group B n=74	
	Age < 35 abc %	Age > 35 abc %	Age < 35 abc %	Age > 35 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 ($p > 0.05$).

Table 3

Nature of chromosomal pathology in the studied pathological viable embryos

Viable embryos	Group A n=42		Group B n=44		Total	
	12 abc	%	15 abc	%	27 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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GEOPOLITICAL SIGNIFICANCE OF THE ANAKLIA DEEP SEA PORT FOR GEORGIA: A NEW STRATEGIC HUB IN EURASIA

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Georgia is a small country in the South Caucasus region. It is bounded to the West by the Black Sea, to the North by Russian Federation. To the South, the country shares borders with Turkey and Armenia and to the Southeast with Azerbaijan. The territory of Georgia is 69,700 square kilometres and the population of the country reaches about 3.78 million (**Georgia country profile, 2019**).

Georgia is situated at strategically important crossroads between Western Asia and Eastern Europe, Black and Caspian Seas; it is positioned along the shortest routes between China and Europe. For this reason, throughout history, the country attracted considerable interest of the world's greatest Empires, such as the Russian, Roman, Ottoman, Mongol and Persian Empires. Georgia was eventually annexed by the Russian Empire in the 19th century. Following the dissolution of the USSR, the country regained independence from the Soviet Union; however civil wars broke out in the country due to the two separatist regions of Abkhazia and South Ossetia.

Following the dissolution of the Soviet Union, Georgia hosts two central pipelines: Baku-Tbilisi-Ceyhan oil and Baku-Tbilisi-Erzurum gas pipelines which run from the Caspian Sea to Europe, bypassing Georgian territory and transport Caspian hydrocarbon resources to Europe (**Iomia, 2017**). In the twenty-first century, Georgia once again attracted worldwide attention since it represents a critical transport node on the new "One Belt and One Road" project between China and Europe.

According to the Anaklia Development Consortium, Anaklia Port will be the first deep water port of Georgia, and its infrastructure, equipment, and superior customer service will be the main guarantee for the productivity and efficiency of the Anaklia port. Anaklia Deep Sea Port will be designed over the course of 9 phases, with an aggregate investment of \$2.5 billion. Anaklia Port's depth will be 16 meters which enable to berth vessels up to 10,000 TEUs in capacity. Thus, ADC's fundamental objective is to establish Anaklia as a strategic hub for the new Silk Road trade route to and from Central Asia, between China and Europe. The mentioned, on the other hand, brings the country considerable economic growth and stresses Georgia's economic and geopolitical influence in the Black Sea region (**Anaklia Development Consortium, 2020**). However, big powers demonstrate a serious clash of interest to the construction of the Anaklia Deep Sea Port, which in turn, makes it harder to predict the future development of the project.

Construction of Anaklia Sea project has further worsened the U.S.-China relations, which in turn, have already been illustrated in the economic war between Washington and Beijing. As Michael Carpenter, the former assistant deputy secretary of defense and director of the Biden Center stated: "if US investors are forced out of the Anaklia project in favor of Chinese companies, this would send a chill and potentially even freeze future US and Western investments in Georgia" (**Transparency international, 2019**).

On June 11, 2019, in recognition of 10th anniversary of the joint declaration of the U.S.-Georgia strategic partnership, the U.S. Secretary of State Mike Pompeo once again highlighted the significance of the mutual partnership between the two countries and stressed the high significance of Georgia as one of the biggest contributors to global security among the NATO aspirant countries (**U.S. Department of State**). Most importantly, he expressed hope that Georgia would see the [Anaklia] project through to the end. According to Pompeo, Anaklia port would deepen Georgia's relations with free economies and help it to avoid the Russian and Chinese economic influence in the region (**Transparency international, 2019**). The Prime-minister of Georgia, in his turn, underlined the growing economic relations between the two countries and stated that the U.S.-Georgia strategic partnership will eventually lead Georgia "to a unique model of trade cooperation" (**Civil.ge, 2019**).

The People's Republic of China extended official diplomatic recognition to the Republic of Georgia on June 9, 1992. Bilateral ties have advanced gradually in the 25 years since. Cooperation is mostly confined to the economic sphere, focusing on FDI and trade. Bilateral trade has expanded significantly since trade relations were first established in 1992, and especially since 2010, as Georgia's economy recovered from the 2008 August War (**Larsen, 2017: 5**).

According to **Larsen (2017: 4)**

Georgia possesses three key features that make it attractive as a participant in China's Belt and Road initiative (BRI): Free Trade Agreements (FTAs) with both the European Union (EU) and China; an outlet to the Black Sea and overland links with Turkey, which offer platforms from which China can more efficiently conduct trade with the European Union (the second factor augmenting the first); and a flexible position at the fulcrum of two regional formats important for the BRI's

success—the Georgia, Ukraine, Azerbaijan, and Moldova (GUAM) group and the Azerbaijan, Georgia, Turkey trilateral group (AGT).

Furthermore, Anaklia Deep Sea Port became “apple of discord” between the U.S. and Russia as well, since the Black Sea and South Caucasus have always been in the special focus of Moscow. Russia has always considered South Caucasus as a “sphere of its influence”. The U.S.-Russia clashes of interests have been aggravated since the enlargement of NATO and the EU in 2004 and 2007 (**Spechler, 2007**). Kremlin strictly opposed NATO’s further expansion which had also been illustrated in Russia’s war in Georgia in August 2008. Later, the annexation of Crimea was an explicit demonstration of Moscow to show the rest of the world that it would no more compromise Western presence in the post-Soviet space (**Aljazeera.com 2019**). However, NATO continues its military exercises in the Black Sea and welcomes Georgia’s Euro atlantic aspirations. In this regard, it is significant to note that the development of Anaklia Deep Sea Port is of pivotal importance to enhance Georgia-NATO relations and eccelarate Georgia’s integration into the north Atlantic Treaty Organisation.

The U.S. is actively assisting Georgia in strengthening and deepening the Euro-Atlantic ties, building democratic institutions and supporting the country to transfer into the most developed and economically stable partner in the South Caucasus region. Georgia, in turn, is a significant ally of the U.S. in the war on terror and hugely contributes to the U.S. led anti-terrorism operations in Iraq and Afghanistan (**Lomia, 2019: 54**).

Since the early years of Georgia’s independence, the U.S. has fully supported Georgia’s democratization process and has tried to maintain stability in the region, thereby increasing the country’s opportunities for further economic progress and development. Clear illustration of the above mentioned is the great efforts made by the U.S. President Bill Clinton to construct the Baku-Tbilisi-Ceyhan (BTC) oil pipeline in the late 1990s, which was of fundamental significance for the stabilization of post-war Georgian economy. The BTC pipeline gave Georgia a new dimension since it has attracted worldwide attention as a major transit corridor in the Caucasus region for energy resources (**Ibidem, 61**).

The U.S. is supporting the “Anaklia Deep Sea Port project” (the project of a century), which on the other hand, means that Georgia will gain significant worldwide attention as a regional transport and transit hub through the development the historic Silk Road route, which is considered to be the fastest trade routes between China and Europe. As it was mentioned above, “Anaklia” is a project of key significance for the economic development of Georgia. The project will further strengthen the U.S.-Georgia business ties and stands to diminish Russian and Chinese economic influence in Georgia (**Ibidem, 62**).

It should be emphasized that „creeping annexation” is not only an act of illegal occupation of Georgian territories, Russia, on the one hand, aims at weakening Georgia’s economy, and on the other hand, tries to increase the dependence of Georgian export on the Russian market. Furthermore, Russia interferes with Georgia’s Euro-Atlantic integration and diminishes the status of the country on an international stage by showing the rest of the world that Georgia is unable to independently carry out its political course without the support of Moscow (**Lomia, 2020: 124**).

Recently, some of the U.S. senators and congressmen published official letters highlighting their concerns about the Georgian government’s close relations with the Kremlin and attempts of expulsing the U.S. companies from the Anaklia port project (**Radio Liberty 2020; Glurjidze and Dzamukashvili, 2020**.) The mentioned raised concerns about the future strategic partnership between the U.S. and Georgia; however, as it has been highlighted by the high officials of the U.S., Washington still supports Georgia’s economic development and political reforms to the way of its democratization and remains the strongest partner of the South Caucasus country.

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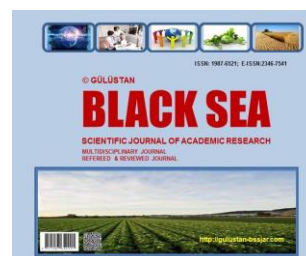
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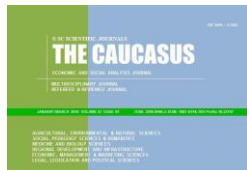
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The Caucasus Economic and Social Analysis Journal has ISSN, E-ISSN and UDC numbering: ISSN: 2298-0946 (Print), E-ISSN: 1987-6114 (Online), DOI prefix: 10.36962, UDC: 3/K-144

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ISSN: 1987-6521; E-ISSN:2346-7541

DOI: 10.36962/GBSSJAR54032020

JUNE-SEPTEMBER 2020 VOLUME 55 ISSUE 04

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