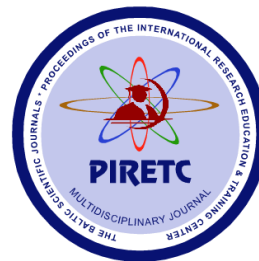


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# PROCEEDINGS

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JOURNAL OF SOCIAL RESEARCH & BEHAVIORAL SCIENCES  
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The beautiful thing about learning is nobody can take it away from you—B. B. King

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## CORRELATIONS BETWEEN GROUND-LEVEL OZONE CONCENTRATION AND COVID-19 CASES IN TBILISI

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### ABSTRACT

**Objective:** Empirical assessment shows that ambient ozone level increase the spread of COVID-19.

The aim of our study is to establish correlations between the spread of ground-level ozone in Tbilisi and the cases of infection with Covid-19.

**Methods:** From April 1, 2020 to January 1, 2021, we have been conducting between the ground-level ozone and the incidence of Covid-19 in Tbilisi

The study was conducted with a German-made ozonometer at a frequency of three to three minutes, every hour, in the Vake-Saburtalo district of Tbilisi, every day, continuously. Here is the material on how the frequency of co-infection cases in Tbilisi varied by months. Correlations were determined by Spearman correlation analysis and linear regression analysis was performed using the statistical package SPSS-23

**Results:** From April 2020 to January 2021, the incidence of Covid-19 varied from 13 to 2067 cases per day in Tbilisi, and the concentration of ground-level ozone increased from 0.67 to 94 mg / m<sup>3</sup>.

The lower the ozone concentration, the greater the number of infected. We conducted a correlation analysis to determine the relationship between these values. Correlation analysis showed that there is a significant negative correlation between these values ( $r=-0.503$ ,  $p<0.0001$ )

The regression curve shows that the distribution is close to the line and ground-level ozone change can be used to predict infection

**Conclusions:** Covid-19 frequency exhibits reliable negative correlation with surface ozone concentration. According to the ground-level ozone concentration it is possible to predict an increase in cases of Covid-19

**Keywords:** covid 19, ozone concentration

We live in the midst of a global health crisis - a similar pandemic the world has not experienced for more than 100 years.

According to modern approaches, differentiation of solid dust particles into fractions, according to their aerodynamic diameter size are used to assess and normalize the impact on human health. Namely, PM10 (particles with an aerodynamic diameter of 10  $\mu\text{m}$ ) and PM2.5 (particles with an aerodynamic diameter of 2.5  $\mu\text{m}$ ). The latter are considered the most dangerous to health because they have the ability to penetrate into the peripheral areas of the bronchioles and prevent airway into the lungs. These are carbon monoxide, lead, nitrogen dioxide, particles (very small solid or liquid particles in the air), sulfur oxides, and ground ozone (ozone does not escape directly into the air but is formed by exposure to sunlight, nitrogen oxides, and volatile organic compounds. There

are two categories of particles: 10 micrometers ( $\mu\text{m}$ ) or less ( $1 \mu\text{m} = 10^{-6}$  meters) and  $2.5 \mu\text{m}$  or less in size[1].

They adopt a 2030 emissions inventory that accounts for fully implementing anthropogenic emissions controls required by federal, state, and/or local policies, which is projected to strongly influence future ozone levels. We quantify a comprehensive suite of ozone-related mortality and morbidity impacts including emergency department visits, hospital admissions, acute respiratory symptoms, and lost school days, and estimate the economic value of these impacts. Both GCMs project average daily maximum temperature to increase by  $1-4^{\circ}\text{C}$  and  $1-5$  ppb increases in daily 8-hr maximum ozone at 2030, though each climate scenario produces ozone levels that vary greatly over space and time[2,3].

Near-term changes to the climate have the potential to greatly affect ground-level ozone. Using a 2030 emission inventory with regional climate fields downscaled from two general circulation models, we project mean temperature increases of  $1$  to  $4^{\circ}\text{C}$  and climate-driven mean daily 8-hr maximum ozone increases of  $1-5$  ppb, though each climate scenario produces ozone levels that vary significantly over space and time. These increased ozone levels are estimated to result in tens to thousands of ozone-related premature deaths and illnesses per year and an economic burden of hundreds of millions to tens of billions of U.S. dollars (2010\$)[4,5].

Air pollution, the release of various gases into the atmosphere, finely divided solids, or finely dispersed liquid aerosols at speeds that exceed the natural capacity of the environment to disperse and dilute or absorb them. O&NG emissions are predicted to affect surface ozone across a large geographical scale.

Empirical assessment shows that ambient PM<sub>2.5</sub>, nitrogen dioxide, ozone, pressure, dew, Windgust, and windspeed increase the spread of COVID-19, high relative humidity and ambient temperature have mitigation effect on COVID-19[6].

**Aim:** The aim of our study is to establish correlations between the spread of ground-level ozone in Tbilisi and the cases of infection with Covid-19.

**Methods:** From April 1, 2020 to January 1, 2021, we have been conducting between the ground-level ozone and the incidence of various non-infectious-infectious diseases in Tbilisi. Given the current unorthodox situation, when the Covid-Pandemic swept through all aspects of our lives, we wondered if we could judge the frequency of Covid-pandemics and the relationship between ozone and the troposphere ozone. We conducted an epidemiological study between the troposphere ozone level and the frequency of co-infected cases in Tbilisi.

The study was conducted with a German-made ozonometer at a frequency of three to three minutes, every hour, in the Vake-Saburtalo district of Tbilisi, every day, continuously. Here is the material on how the frequency of co-infection cases in Tbilisi varied by months.

Descriptive analysis of continuous variables including calculation of mean and standard deviations, min., max., and median. Correlations were determined by Spearman correlation analysis, and linear regression analysis was performed using the statistical package SPSS-23

**Results:** The mean values of ozone concentration and Covid 19 are given in Table 1.

From April 2020 to January 2021, the incidence of Covid-19 varied from 13 to 2067 cases per day in Tbilisi, and the concentration of ground-level ozone increased from  $0.67$  to  $94 \text{ mg} / \text{m}^3$ .

The dependence of the cases of covid-19 infection studied by us for 202 days on the ground-level ozone concentration is given in Figure 1.

As can be seen from the graph, the lower the ozone concentration, the greater the number of infected. We conducted a correlation analysis to determine the relationship between these values. Correlation analysis showed that there is a significant negative correlation between these values ( $r=-0.503$ ,  $p<0.0001$ )

Regression analysis showed that the relationship between ground-level ozone concentration and infection rate is linear (Figure 2).

- The spread of Covid infection correlates with ground-level ozone changes
- The correlation is negative
- The regression curve shows that the distribution is close to the line and ground-level ozone change can be used to predict infection

$$y=-13.04x+876.1$$

$$R^2 = 0.252$$

**Discussion:** It has been recently studied the role of environmental factors in accelerate SARS-CoV-2 spread and its lethality[7]. The time being, air pollution has been identified as the largest environmental cause of disease and premature death in the world.

The frequency increase of the new coronavirus is observed in the winter months, when the ozone concentration is minimal, which is consistent with our study.

The opposite result was shown by a study conducted in Italy in 2020, where cases of coovid-9 emissions were positively correlated with ozone concentration[8].The first study showed that there was a reliable correlation between ozone level and coovid-19 morbidity ( $p < 0.05$ ).

However, to draw final conclusions at this stage is impossible. The issue is still under investigation.

**Conclusion:** Covid-19 frequency exhibits reliable negative correlation with surface ozone concentration. According to the ground-level ozone concentration it is possible to predict an increase in cases of Covid-19.

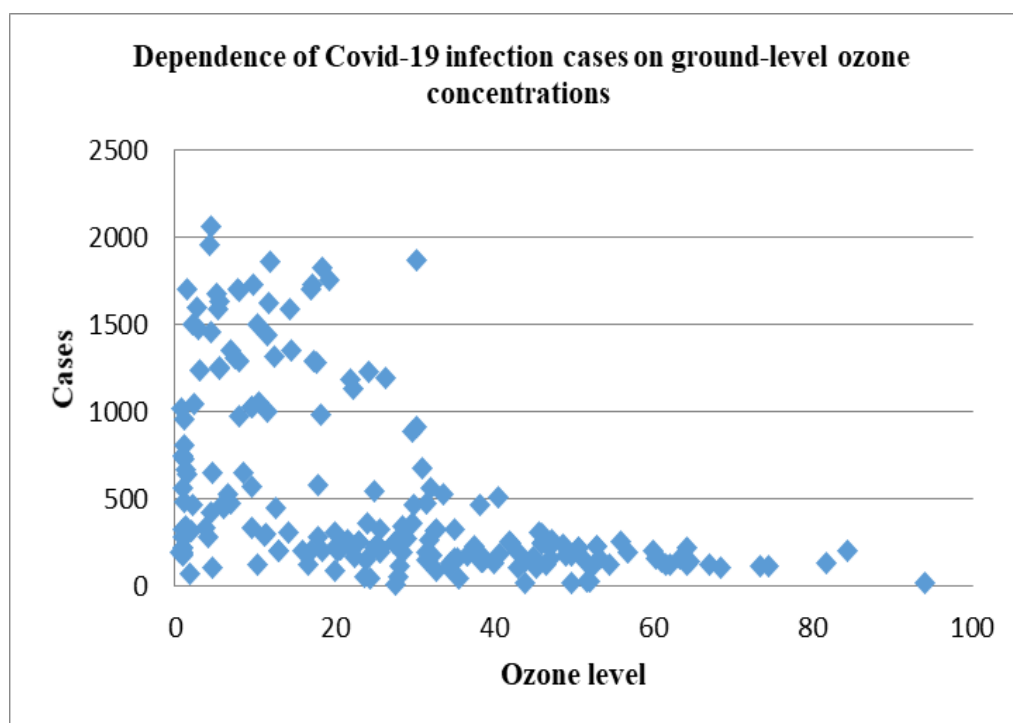
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**Table 1.** The mean values of ozone concentration and Covid 19.

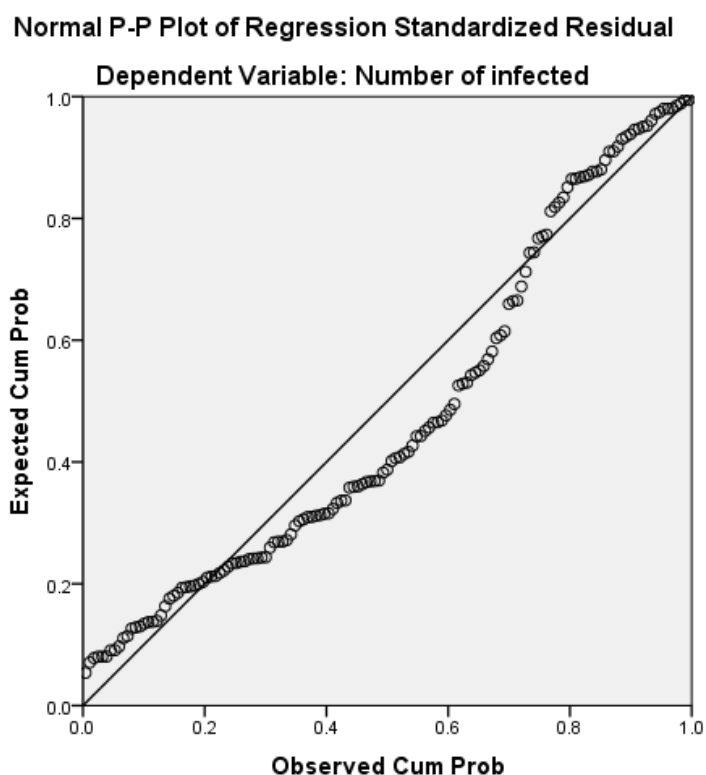
	Ozone level(n=202)	Number of infected
Mean	26.29	533.13
Median	24.05	265.00
Std. Deviation	20.43	530.30
Minimum	0.67	13.00
Maximum	94.00	2067.00



**Fig.1**

**Table 2**

	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
Ozone level	-13.045	1.586	-0.503	-5.322	<0.0001
(Constant)	876.153	52.769		14.043	<0.0001



**Figure 2**

## Description of the current state and prospects for the export of hydrocarbons by the Caspian countries

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**Keywords:** Oil, pipeline, export, energy, route

### ABSTRACT

**The problem statement:** To determine the positions of the Caspian countries in the transportation policy of hydrocarbons.

**Formulation of the problem:** Implementation of promising projects of the Caspian countries for the transportation of oil and gas.

**The purpose of the article:** To determine the role of the five Caspian Region countries as a supplier and exporter of hydrocarbons

**Presenting the main material:** One of the most significant sectors of the Caspian economy is the oil and gas sector. The presence of significant resources of oil and natural gas, an extremely favorable geographic location for the construction of pipeline transport for the purpose of export supplies of hydrocarbons make the Caspian Sea an “apple of discord” in the geopolitical interests of the Caspian countries and other states. Most of the existing Caspian hydrocarbon reserves are exported along the northern, southern, eastern and western routes. It should be noted that the export of hydrocarbons of the Caspian region, as well as the export of world oil and gas reserves, depends on various factors, which include the existing geopolitical situation, various data on raw materials reserves, demand for resources and the resulting prices of world markets, the use of modern technological equipment. difficult to develop deposits and other factors.

Oil exports of the countries of the Caspian region for the period 2004-2014 are presented in Table 1.

**Table 1.** Dynamics of oil exports in the countries of the Caspian region, 2004-2014, million tons [1]

Country	2004	2006	2008	2010	2012	2014
Iran	134,8	121,7	121,2	121,9	87,7	76
Russia	337,1	355,3	359,8	377,5	380,4	386
Kazakhstan	50	54,7	59,7	70,2	66,2	67,8
Azerbaijan	11	27,5	40,9	47,6	39,2	37,4
Turkmenistan	4,5	4,2	4,9	5	4,8	5,4

The above data indicate that the countries of the Caspian region are experiencing a steady growth trend in oil exports (the exception is Iran, which was subject to sanctions. The export quota of Kazakhstan, Azerbaijan and Russia exceeded the level of 70%). It is worth considering each country separately.

**Russia:** Russia is the country with the largest reserves of fuel and energy resources (13% of the world's oil reserves, 34% of the world's natural gas reserves). We list the main markets for Russian hydrocarbon raw materials: Great Britain and Ireland (25% in the far abroad), Eastern Europe (Bulgaria – 90%, Poland – 40-50%), the Mediterranean (Turkey, Cyprus, Greece, Italy), Austria, the Netherlands, Switzerland, Sweden, Denmark, Belgium, Finland, Liechtenstein – from 18 to 20%) USA and Canada – 7%. The main sector of Russian commodity supplies to international markets is the export of hydrocarbons (Russia controls 12-14% of the world's oil market). Exports of oil and natural gas production are increasing due to an increase in the development rates of hydrocarbon deposits.

As for the export of Caspian oil, it is necessary to consider the historical preconditions for Russia's dominance in the Caspian region, since The Caspian Sea is a traditional source of Russian interests. Until the mid-1990s. Russia has taken a clear and adamant position in relation to the Caspian Sea, which has undergone metamorphoses after the implementation of profitable projects and in the process of developing mutually beneficial cooperation with the countries of the Caspian region. Nevertheless, the target policy of Russia in relation to the Caspian Sea is based on the provisions of maintaining the monopolization of the route for the transportation of hydrocarbons in the Caspian Sea [2]. In the Russian sector, foreign companies are represented by the Russian-Cypriot company Roskaspneft, the American J.P. Kenny and EXPO as part of the CaspOilDevelopment joint venture, as well as by Halliburton and Schlumberger. Unlike the rest of the Caspian states, the positions of domestic companies (Lukoil, Rosneft, Transneft, Gazprom, Eurasia Shelf Drilling Company, PetroAlliance, Caspian Energy Group, etc.) in the Russian sector of the Caspian Sea are more stable. However, in some cases, Russian companies, together with foreign ones, form joint ventures (Caspian Pipeline Consortium, British-Russian company CaspOilDevelopment) or have a share of foreign capital (Schlumberger's capital in PetroAlliance). Nevertheless, Russian companies, such as Lukoil, over time buy out foreign shares (in the cases of Lukarko and Lukadzhip). In 1997, the Russian corporations Lukoil and Rosneft entered the consortium for the development of the Kapaz/Serdar field. At the same time, the leadership of the Chinese National Petroleum Corporation bought out stakes in oil and gas companies in Kazakhstan (for example, Aktyubinskmunai), as well as the Uzen field with reserves of 200-250 million tons. Currently, Russia is faced with the difficult task of retaining its influence in region. Russia lost its role as a transport monopoly in the Caspian (after the construction of the Baku-Ceyhan oil pipeline). Further diversification of energy transportation routes may affect the throughput of existing Russian pipeline systems [3, p. 222-239]. The oil produced in Russia (both for export and for refining) is supplied by the system of main oil pipelines of the Transneft company, which transports 93% of all oil produced in the country (more than 109.4 billion ton \* km), the remaining 7% is supplied by VIOCs and independent manufacturers. The legal basis for the activities of Transneft is the orders of the President of the Russian Federation, decisions of the Government of the Russian Federation, the Energy Strategy of Russia for the period up to 2030. All projects of the company undergo state expertise within the framework of applicable laws. The company compares favorably with its competitors in that it develops investment projects for trunk oil supply systems

with the prospective implementation of redistribution of the flow both in the eastern and western markets, taking into account the existing market conditions.

The company's activities are related to the transportation of oil and the solution of a whole range of tasks associated with this process [4].

Let's list the main projects for the development of Transneft:

- Caspian Pipeline Consortium (CPC);
- Eastern Siberia – Pacific Ocean (ESPO);
- Burgas – Alexandroupolis – Baltic Pipeline System (BPS-2);
- Tikhoretsk – Tuapse-2, the Russian part of the Druzhba oil pipeline (Russian section);
- "Purpe – Samotlor" the second stage of the pipeline system Eastern Siberia – Pacific Ocean "(ESPO-2).

The main pipelines of the company:

- Baltic Pipeline System – capacity 74 million tons / year;
- Druzhba oil pipeline – capacity 66.5 million tons / year;
- share in the Caspian Pipeline Consortium – capacity of 28.2 million tons / year;
- Baku – Novorossiysk oil pipeline;
- Grozny – Tuapse oil pipeline.

Main product pipelines:

- Severny oil product pipeline – capacity – 8.4 million tons/year;
- Yuzhny oil product pipeline.

It should be noted that the Transneft company needed a time interval of only a quarter of a century to create a reliable hydrocarbon transportation system, providing the country with an oil and oil products export system independent from other states. Of course, it is necessary to characterize the advantages of the company's export pipeline systems:

- economic advantages: creation of appropriate infrastructure around pipelines – transport interchanges, social structure, power lines, new jobs with high wages and a package of social services (social policy of PJSC Transneft);
- social benefits – manifested in a number of examples of business social responsibility – participation of companies in charitable projects or their own social projects;
- environmental benefits – despite a number of negative factors, the impact of pipeline systems on the environment, in general, the company's environmental policy is aimed at preserving the natural environment and minimizing man-made impact.

Summing up the obvious advantages, we can say that large infrastructure companies can influence the life of not only a particular region, but also the country as a whole. Thousands of kilometers of Transneft pipelines are a striking example of the above.

If we talk about the peculiarities of the export of hydrocarbons in the Caspian basin from the Russian side, it should be noted that the last decade has become a turning point for Russia as a transport monopoly after the construction of the Baku-Ceyhan oil pipeline. It is important for Russia to focus on maintaining the northern supply route (Kazakhstan and Turkmenistan) via the Atyrau-Samara oil pipeline.

Considering the issue of the prospects for the export of Caspian oil, it is worth noting that until 2023 the main increase in oil production will be carried out due to the development of the field. Filanovsky, which belongs to PJSC Lukoil and is the largest Russian field at the time of the Russian sector of the Caspian Sea (oil – 6 million tons / year, gas – 30 billion cubic meters / year).

**Turkmenistan:** State-owned companies Turkmengaz and Turkmenoil are directly involved in oil and gas production in Turkmenistan. The government of Turkmenistan is trying not to attract foreign capital to the development of hydrocarbon deposits. Nevertheless, the Irish company Dragonoil and the Italian ENI are active in the country, both participating in the Cheleken field projects. Also, Turkmenistan has entered into a number of agreements with Mobil and MonumentOil corporations regarding fields in western Turkmenistan and in the southern part of the Caspian Sea [3, p. 222–239].

The topic of the export of hydrocarbons by Turkmenistan is relevant for the reason that the role of Turkmenistan in the international arena has not only changed, but also strengthened its status as a gas supplier for countries such as China, India and the European Union (in the future).

The gross volume of exports of Turkmenistan in 2016 reached 18.4 billion US dollars, imports – 11.4 billion US dollars, thus, Turkmenistan provides itself with a high foreign trade surplus. Turkmenistan owes such a high growth rate and positive results of foreign trade to its oil and gas industry, which accounts for about 80% of the country's industrial production and also about 80% of exports. In addition, Turkmenistan exports oil and oil products, cotton and cotton products, metals and a small amount of other goods. Imports to Turkmenistan are quite diverse, although metals, metal structures, as well as equipment and technical means for various purposes prevail in it.

The export of natural gas from Turkmenistan is on average about 40 billion m<sup>3</sup>, and production is about 67-69 billion m<sup>3</sup>. Turkmenistan has favorable conditions for increasing the volume of natural gas exports, but the only available route for the export of natural gas is onshore gas pipelines. At the moment, the republic has several pipeline routes. The pipeline system "Central Asia – Center" follows from Turkmenistan through the territories of Uzbekistan and Kazakhstan to Russia and has a throughput capacity of 80 billion m<sup>3</sup> per year. The length of the gas pipeline is about 5,000 km, and it has been operating since 1967, it is one of the oldest and longest gas pipeline systems on the continent.

At the same time, at the beginning of 2016, the State Concern Turkmengaz stopped gas supplies to the Russian Federation via this gas pipeline. The official version was the change in the situation on the world energy markets and the absence of a final agreement with PJSC Gazprom on gas prices, as well as the desire of the Republic of Turkmenistan to engage not only in the production and export of gas, but also in the development of the gas processing and gas chemical industry.

The next gas supply route is the Turkmenistan-China gas pipeline, which also passes through the territory of Uzbekistan and the Republic of Kazakhstan. The throughput capacity of this gas pipeline is currently about 35 billion cubic meters. m per year. The construction of this gas pipeline began in 2007, the first branch was launched in 2009. Today, gas exports through this gas pipeline are carried out at the expense of the Samandepi field, the main operator of the field and a key investor in the pipeline project is the Chinese CNPC. Among other things, given the refusal of the Republic of Turkmenistan to export gas to the Russian Federation, today China is the main importer of gas from Turkmenistan.

**Azerbaijan:** The sale of hydrocarbons is the basis of Azerbaijan's export policy. In recent years, Azerbaijan has established itself as a reliable oil importer on the world stage of oil suppliers. Over the past 15 years, exports from Azerbaijan have grown almost 30 times. The commodity structure of exports from Azerbaijan is absolutely dominated by oil, oil products and natural gas, their share

in the value of exports in 2016 amounted to more than 90%, and in 2008 this figure reached 98%. This circumstance makes the economy of Azerbaijan extremely dependent on world energy markets. It should be noted that oil production in Azerbaijan reached a historical maximum in 2010 and since then has been steadily decreasing by an average of 3-4% per year.

It should be noted that the State Oil Company of the Azerbaijan Republic (SOCAR) participates in consortia represented in the public sector, realizing national interests. In the period from 1994 to 2001. The State Oil Company of Azerbaijan (SOCAR) has signed more than twenty agreements with foreign oil companies on exploration and production of oil in the Azerbaijani sector of the Caspian Sea. In general, about 400 companies were attracted for this goal, and the volume of foreign investments under contractual obligations amounted to \$60 billion. In total, companies from 15 countries took part in the development of the oil and gas industry in Azerbaijan. Several associations were also created, such as Azfen (Turkey, Azerbaijan), Caspian DrillingCo (USA, Azerbaijan). Oil exports by Azerbaijan are based on a network of export pipelines, opening up new possible supplies of hydrocarbons to foreign countries (Baku-Tbilisi-Ceyhan and Baku-Tbilisi-Erzurum). Transportation of oil and gas increases every year, which directly affects the success and positive assessment of Azerbaijan's strategy in the oil sector.

**Kazakhstan:** The economic, geographical and geopolitical position of Kazakhstan provides it with an extremely important role in the world economy, logistics and politics: strategically important transport routes between East and West pass through its territory.

Oil is the main export commodity of Kazakhstan. The total export volume of Kazakhstan in 2016 amounted to about 62 billion US dollars, and 85.4% fell on oil and oil products.

85% of the oil produced in Kazakhstan is exported to the following countries – the Netherlands, Italy, Austria, France, Switzerland, China.

At the same time, out of 15 regions of Kazakhstan, only 9 are supplied with gas, while the northern regions of Kazakhstan are supplied with gas from Russia, and part of the southern regions – from Uzbekistan. Moreover, according to the forecast of the Ministry of Energy of the Republic of Kazakhstan, while maintaining the current trend, gas production in Kazakhstan from 2018-2020. will begin to decline by 1-2 billion cubic meters per year, while its own consumption will grow by 0.3-0.7 billion cubic meters as a result of the implementation of a large-scale gasification program in the country. In the medium term, Kazakhstan may not only stop exporting natural gas, but also begin to experience a gas shortage [5].

Most of Kazakhstan's oil is produced in the west. The three largest Caspian fields – Kashagan, Tengiz and Karachaganak – provide about 60% of the country's total production. About 54 million tons of West Kazakhstan oil for export goes through the pipeline of the Caspian Pipeline Consortium (CPC) to the sea terminal near Novorossiysk. Last year CPC (31% controlled by PJSC Transneft) announced the completion of the project to expand the oil pipeline to 67 million tons per year. More than 61 million tons have passed through the pipeline. About 15 million tons are supplied through the Atyrau-Samara oil pipeline, from where oil flows towards the Russian ports of Novorossiysk and Ust-Luga. In addition, West Kazakhstan oil can be exported through the port of Aktau, from where it is shipped by tankers to the port of Makhachkala and delivered through the Transneft system to the port of Novorossiysk. In 2018, supplies amounted to 2 million tons against 1 million tons in 2017 [6].

Kazakh-Chinese energy cooperation has led to the creation of the Kumkol-Karakoin pipeline system. Meanwhile, 11.8 million tons were sent to China via the Atasu-Alashankou oil pipeline in

2014. It is also necessary to note the dynamic expansion of the Turkmenistan-Uzbekistan-Tajikistan-Kyrgyzstan-China gas pipeline, the total length of which will be about 7 thousand kilometers. The activity of transnational business in Kazakhstan is clearly demonstrated by the description of the contract areas of the main fields and the share participation of corporations in them. Among the main deposits of Kazakhstan, it is advisable to highlight:

1. East and West Kashagan (reserves estimate – 6.4 billion tons of oil, 1 trillion cubic meters of natural gas). Project operators – Eni, KMG Kashagan B.V. (a subsidiary of Kazmunaigas), Total, ExxonMobil, RoyalDutchShell (each has 16.81% of shares), ConocoPhillips (8.4%), Inpex (7.56%). All companies are part of the North Caspian Operating Company (NCOC) joint venture.
2. Tengiz (reserves estimate – 3.1 billion tons of oil and 1.8 trillion cubic meters of natural gas). The project operators are the national company Kazmunaigas (20% of shares), ChevronOverseas (50%), ExxonMobil (25%) and LukArco (5%).
3. Uzen (estimated reserves – 1.1 billion tons of oil). Operator of the project – the company "Kazmunaigas"
4. Karashiganak (reserves estimate – approximately 1 billion tons of oil and gas condensate). The operator of the project is the international consortium "KarachaganakPetroleumOperating B.V." (BritishGas and Eni have 32.5% shares each, ChevronTexaco – 20% and Lukoil – 15%).
5. Kalamkas (reserves estimate – 510 million tons of oil). The project operators are KazMunayGas and Mangistaumunaigas OJSC.
6. Zhanazhol (estimated reserves – 500 million tons of oil, 133 billion cubic meters of natural gas). The operator of the project is the Kazakh-Chinese enterprise CNPC-Aktobemunaigas.
7. Zhetybai (reserves estimate – 330 million tons of oil). The project operators are the companies OJSC "Mangistaumunaigas", "Zhetybaimunaigas".
8. Aktoty (estimated reserves – 269 million tons of oil). The project operator is the North Caspian Operating Company consortium.
9. Kalamkas-sea (reserves estimate – 156 million tons of oil). The operator of the project is the aforementioned consortium NorthCaspianOperatingCompany.
10. Kairan (estimated reserves – 150 million tons of oil). The project operator is the North Caspian Operating Company consortium.
11. Kenkiyak (reserves estimate – 150 million tons of oil). The operator of the project is the joint venture CNPC-Aktobemunaigas. Companies from China, Russia, Europe and the USA are mainly concentrated in Kazakhstan. Thus, the Chinese state-owned company CNPC owns more than half of the shares (the rest belongs to Aktobemunaigas) in the Aktobe project (1 billion barrels of raw materials). 1997 to 2013 the Chinese company "China National Petroleum Corporation" (CNPC) acquired 60.3% of the shares of the Aktobe Oil Company, and then in 2003 increased its share to 85.42%. Later, CNPC bought the rights to the North Buzachi fields (selling 50% of the Lukoil company), half of the shares in the Kansu and Bektas fields, 100% of the shares of the Canadian oil company PetroKazakhstan (later sold a third of the shares in Kazmunaygaz), 8.33% in the Kashagan consortium. In 2013, among the 22 largest oil companies in Kazakhstan, Chinese companies such as Sinopec and CNPC had almost 100% stake in ten of them, and in another eight – 50% and more [7, p. 41].

**Iran:** The largest oil and gas company in the country is the National Iranian Oil Company (NIOC), 100% owned by the state. NIOC (through its subsidiary NaftIran) also owns 10% in the Azerbaijani Shah Deniz gas project. However, Iran's strict foreign corporation policy may in practice prove to be incapable of opposing big business.

In 2016, exports of goods from Iran reached 66.5 billion, while imports amounted to \$40.0 billion. There is a trend towards a recovery in the growth of foreign trade indicators. Exports from Iran are dominated by crude oil, products of its processing and industrial products (mainly products of organic chemistry, as well as products made of plastic and other synthetic materials). If we exclude crude oil and petroleum products from Iran's exports, then the foreign trade balance of Iran in 2016 would become negative. Thus, the export of oil and oil products is for Iran the main source of income from foreign trade and provides the country with a positive foreign trade balance and a surplus of the state budget. The Islamic Republic of Iran produced more than 4.5 million barrels in 2016. oil per day, and domestic consumption amounted to more than 1.8 million barrels. oil per day. Among the states of the Organization of Petroleum Exporting Countries (OPEC), Iran accounted for a tenth share of production (more than only Saudi Arabia).

**Conclusions:** In general, it can be concluded that for Kazakhstan, Iran and Azerbaijan, at present, the main export commodity is oil and oil products. Turkmenistan exports natural gas; Iran and, to some extent, Kazakhstan have great potential for the development of the gas industry.

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## ROLE OF THE ASPECT SCORING SYSTEM ON BRAIN CT ANGIOGRAPHY IN ISCHEMIC STROKE

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### ABSTRACT

**Background:** The ASPECTs scoring system has been used to prognosticate, for example the score is a strong predictor of functional outcome in acute anterior circulation ischemic stroke. The effectiveness of thrombolysis and thrombectomy in patients with middle cerebral artery occlusion shows effect modification by the Alberta Stroke Program Early CT Score.

**Purpose:** Determination of the role of the aspect assessment system in computed tomography of the brain in ischemic stroke

**Materials and methods:** 81 consecutive patients with acute anterior circulation ischemic stroke treated with thrombectomy during 2019-2020 were included. Two radiologists evaluated score by using the Alberta Stroke Program Early CT methodology on CTA. Good and extremely poor outcomes at 3 months were defined by modified Rankin Scale scores of 0-2 and 5-6 points, respectively.

**Results:** Factors associated with good outcome on univariate analysis were ASPECTAS, lower NIHSS scores, and time to recanalization. On multivariate logistic regression ASPECTAS >5 were independent predictors of good outcomes.

**Conclusions:** ASPECTS scoring system on brain CT angiography ( arterial ASPECTS ) is valuable for predicting of good outcome in patients with acute anterior circulation ischemic stroke.

**Keywords:** CT, ASPECT, ASPECTA endovascular thrombectomy.

**Introduction:** Cerebrovascular disease represents a major source of global mortality, and is the second leading cause of death in all income groups worldwide, exceeded only by ischemic heart disease. In addition to being a significant cause of morbidity. Ischemic stroke is more common, representing approximately 85 % of all stroke cases . Imaging examinations play a critical role in the management of stroke patients, from establishing the initial diagnosis to determining and guiding further treatment. A non-contrast computed tomography (CT) examination, often employed at this stage, can quickly exclude the presence of hemorrhage. The imaging examination also serves to exclude other pathologies that may resemble stroke clinically, known as the “stroke mimics”. Recovery after acute ischemic stroke is improved after reperfusion – intravenous thrombolysis or ( and) with endovascular mechanical thrombectomy [2],[6] . The treatment decision depends on balancing the possibility of good clinical outcome against the risk of intracranial bleeding. The assessment has to be rapid but thorough and consists of stroke diagnosis, likely localization, assessment of severity, pre-stroke functional status, and co-morbidities. Urgent vascular imaging, typically plain CT and CT angiogram to confirm LAO prior to consideration of thrombectomy, is required [7]. In addition, the scans are useful for assessment of the collateral

circulation (patients with poor collaterals have poorer outcomes) and early ischemic changes using the Alberta Stroke Programme Early CT Score (ASPECTS). The Alberta Stroke program Early (non contrast) CT score (ASPECT) is a scoring system used to assess the extent of early ischemic changes in the middle cerebral artery territory on non contrast computed tomography [14]. An ASPECTS score less than to 7 predicts a worse functional outcome at 3 months as well as symptomatic hemorrhage. The ASPECT scoring system has been used to prognosticate for example the score is a strong predictor of functional outcome [6].

**Purpose:** Determination of the role of the aspect assessment system in computed tomography of the brain in ischemic stroke

**Methods:** The study population included consecutive patients with AIS who presented to our institution between March 2019 and June 2020 and met the following criteria: 1) time from symptom onset <24 hours; 2) anterior circulation ischemic stroke with large-vessel occlusion (intracranial carotid artery or MCA) and (ASPECTS >7); 3) baseline NCCT; 4) technically adequate pretreatment CTA ; 5) successful recanalization defined by TICI (thrombolysis in cerebral infarction) > 2b via mechanical thrombectomy. Additional inclusion criteria for this analysis was the availability of a post-treatment follow-up neuroimaging. Post- treatment follow-up neuroimaging included CT or MRI. A total of 81 patients were finally included in the study. Laboratory tests, neuroimaging, concomitant therapies, clinical course, and functional outcome were collected. Neurological status was monitored with the National Institutes of Health Stroke Scale (NIHSS) score and functional outcome was quantified with the modified Rankin Scale (mRS) score at 3 months.

**Statistical Methods:** The data were demonstrated as mean+ SD and median . Univariate associations between baseline and follow- up ASPECTS were investigated with the Spearman p analysis. A nonparametric receiver operating characteristic curve analysis and the area under the curve were used to assess the ability of CTA ASPECTS to identify patients with favorable outcomes (mRS < 2). The difference between the groups was determined by the student t criterion for quantitative data and by the chi-square criterion for qualitative indicators. We used regression analysis to determine the predictors  $p < 0.05$ . For all statistical analyses, value of  $p \leq 0.05$  was considered statistically significant.

**Results and Discussion:** The data were demonstrated in Table 1. Univariate associations between baseline and follow- up ASPECTS were investigated with the Spearman p analysis. For all statistical analyses, value of  $\leq 0.05$  was considered statistically significant. 81 patients were included in the present study. Favorable outcome (mRS < 2, n = 31) factors in univariate analysis were good ASPECTAS, baseline NIHSS and time to recanalization (Table 2). Backward stepwise regression analyses showed that ASPECTAS >5 is a significant predictor of functional outcome ( Table 3).

The initial step in the management of a suspected stroke patient is an imaging examination. A non-contrast computed tomography (CT) examination, often employed at this stage, can quickly exclude the presence of hemorrhage. The absence of hemorrhage supports the diagnosis of an ischemic event, and some evidence of ischemia may be seen in the native CT as well. The hyperdense vessel sign and signs related to the loss of contrast between the gray and white matter

(such as the insular ribbon sign and lentiform obscuration) are all examples of signs of acute ischemia on native CT. The imaging examination also serves to exclude other pathologies that may resemble stroke clinically, known as the “stroke mimics.” Additionally, the distinction between ischemic stroke following arterial occlusion and ischemia following venous sinus occlusion with secondary hemorrhage is important. Magnetic resonance imaging (MRI) is usually more sensitive and specific in distinguishing both the stroke mimics and secondary ischemic lesions. Finally, the application of a contrast agent may increase the specificity of imaging. Especially contrast-enhanced MRI can reveal a typical cortical pattern of ischemic enhancement and/or help to detect other pathologies that belong to the stroke mimics. The treatment decision in acute ischemic stroke depends on balancing the possibility of good clinical outcome against the risk of intracranial bleeding. The effectiveness of thrombolysis and thrombectomy in patients with middle cerebral artery occlusion shows effect modification by the Alberta Stroke Program Early CT Score. Those with a low ASPECTS score suggesting large MCA infarction can be excluded from futile intra-arterial treatments which are unlikely to result in patient functional independence. The clinical importance of ASPECTS is its prognostic value for determining clinical outcome after intravenous tissue plasminogen activator (i.v. tPA) and (or) thrombectomy in management of acute ischemic stroke.

There is a sharp increase in dependence and death occurs with an ASPECTS of 7 or less; attributed to symptomatic intracerebral hemorrhage. Besides that, baseline ASPECTS value correlated inversely with the severity of stroke on the National Institutes of Health Stroke Scale (NIHSS). CTP ASPECTS has been used successfully in the triage of patients with AIS with the potential added value of improving reliability and reducing variability in the assessment of early ischemic changes compared with NCCT ASPECTS, in particular in earlier treatment windows. In a study of 227 patients, Naylor et al showed improvement in the reliability of early ischemic changes using CTP ASPECTS over NCCT ASPECTS[12].

Although there are several reports supporting a favorable association between higher ASPECTS and good functional outcome [5],[13], others have debated the ability of ASPECTS to predict outcome [10], [15]. There are also some reports that showed the predictive ability of CTP ASPECTS for determination of functional outcome [8][14]. In a recent study by Pfaff et al automated ASPECTS was shown to be predictive of functional outcome[13]. Using automated ASPECTS, a recent study by Demeestere et al showed findings demonstrating a lack of association with functional outcome but significant correlation in the determination of final infarction volume [4]. Infarct extension and increased volume are possible between CT and the follow-up imaging after endovascular thrombectomy, which was used for final infarction determination. In our study 81 patients with ASPECTS >7, accurate selecting for thrombectomy were included. We hypothesized that a CTA ASPECT would also predict functional outcome. We evaluated this methodology to test our hypothesis for predicting outcome in our patients treated with thrombectomy. CTA can depict the area of ischemia (though not necessarily infarcted) much better than NCCT, especially when analyzing parenchymal CTA. Hypodensity on CTA provides greater demarcation between normal and abnormal tissue, and this finding could be explained by the ability of CTA to detect alterations in cerebral blood volume, as opposed to cytotoxic edema on NCCT, with a threshold insufficient to produce NCCT changes.

In a previous study by F.Sallustio et al, ASPECTAS was shown to be more sensitive in the early detection of irreversible ischemia and more accurate in the prediction of final infarct size [16]. Our results confirm those suggesting ASPECTAS as accurate predictor of final infarction. In our study,

as in F.Sallustio's et al study, we also to evaluate how ASPECTAS can improve prediction of clinical outcome [16]. We used receiver operating characteristic curve analysis and found that baseline ASPECTAS can also identify patients with functional independence at 3 months. We recommended a larger study to evaluate this association.

**Conclusions:** ASPECT scoring system on brain CT angiography (ASPECTA) is valuable for predicting good outcome in patient with acute anterior circulation ischemic stroke.

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**Table 1.** Patients data.

Data	value
Age >70	43(53%)
Sex (male)	41(50.6%)
ASPECTAS >5	43(53%)
Follow-up ASPECTS	3(1-6)
Baseline NIHSS	16(10-21)
Hypertension	70(86.4%)
Atrial fibrillation	21(25.9%)
Intravenous thrombolysis	61(75.5 %)
Diabetes	17(20.9%)

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**Table 2.**

Data	mRS 0-2 (n= 31)	mRS 3-6 (n= 50)	t or $\chi^2$	P
Age>70	17(54.8%)	26(52%)	0.062	0.804
Baseline NIHSS	16.9±3.1	18.73±3.7	t=4.71	<0.0001
ASPECTAS>5	23(74.2%)	20(40%)	7.949	0.005
Onset to recanalization (min)	270.9 ±86.53	320.54±80.3	t=2.60	p=0.011
Hypertension	25(80.6%)	45(90%)	1.427	0.233
Atrial fibrillation	9(29.03%)	12(24%)	0.252	0.616
Diabetes	6(19.3)	11(22%)	0.081	0.777

**Table 3.** Ignificant predictor of functional outcome

	OR	SE	95% CI	P
Onset to recanalization (min)	0.94	0.02	0.92-0.98	0.024
ASPECTAS >5	12.5	6.21	4.31-36.2	<0.001

## NEUROIMAGING IN PEDIATRIC HEADACHES: OUTPATIENT EXPERIENCE IN TERTIARY CENTER

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### ABSTRACT

**Introduction:** Headaches are common in children, with the most common cause being tiredness, short-sightedness, viral fever, sinusitis, genetic predisposition and psychosocial stressors, rarely also the presenting symptom of a trauma, an intracranial mass, a metabolic or vascular disease. Most headaches are benign primary headaches, and include migraine, tension-type headache and, less often, cluster headache. A detailed patient history and clinical neurological examination should seek to differentiate between primary and secondary headache and identify any “red flags”. Imaging studies are reported to be completely normal in most of the children with headaches. Meanwhile, is crucial for children with headache to be referred for neuroimaging if any of the known “red flags” is noted.

**Aim:** To evaluate the importance and usefulness of neuroimaging in pediatric patients with headache seen in neurologic outpatient in tertiary hospital.

**Methods:** The data were retrospectively collected from patient records (n = 98) and neuroimaging reports. Headache was classified according to International Headache Society (HIS) guidelines.

**Results:** There were 80 children with imaging studies (MRI n = 75, CT n = 10, five of which had both CT and MRI), of which 6 demonstrated an abnormal finding. Findings altering the management were obtained in 6 (8%) patients: one (n = 1, 1.3%) had headache for less than 1 month, while 5 patients had headache longer than 1 year (n=5, 6.66%), with normal neurological examination and significant MRI results affecting management. None of the children in whom the diagnosis of migraine could be made on clinical grounds (n = 11) had a significant MRI finding.

**Conclusion:** Brain MRI is the neuroimaging modality of choice and it should be performed selectively in children with headache seen in pediatric neurology clinics, especially in headache of long duration (> 1 year), abnormal neurological examination and features atypical for migraine.

**Key words:** pediatric, headache, migraine, neuroimaging

**Introduction:** Headache is defined as pain in the face, head, or neck, with prevalence ranges from 37-51% in elementary-school children and gradually rises to 57-82% in the high-school students

and reported to be more common in children with a positive family history of headaches. The classification scheme for headaches including the diagnostic criteria is provided from the International Headache Society (IHS) in three main classifications: a) Primary headaches including migraine, tension-type, and cluster; b) Secondary headaches related to head/neck trauma, vascular and nonvascular disorders, infection, or psychiatric disorders and c) Cranial neuralgias, central and primary facial pain, and other headaches. Currently accepted diagnosis of pediatric headache is based on the ICHD-II classification system. Appropriate assessment of children with headache should include characterization of the pain experienced by the child, identification of the triggers and identification of any relevant family history, a detailed patient history and clinical neurological examination that will help in narrowing down the etiology and identifying any “red flags”, signs that may indicate headache secondary to a more serious condition, such as brain tumor, subdural hematoma, a cerebral or vascular malformation or infection. An eye exam including fundoscopy can detect papilledema, a sign of increased intracranial pressure. Imaging studies are reported to be normal in most children with headache, however, neuroimaging such as brain computerized tomography (CT) scanning or brain magnetic resonance (MRI) is indicated if “red flags” are noted, including: new and dramatic onset of headache, a marked increase in headache severity or frequency over time, headache exclusively in one location, headaches that wake the child up in the middle of the night, or occur first thing in the morning, headache provoked by coughing, straining or sneezing, or headache provoked or aggravated by the Valsalva maneuver, headache that is worse when the child is in a horizontal position that may be a sign of increased intracranial pressure, papilledema, unilateral weakness or numbness, diplopia, abnormal eye movements or focal motor or sensory changes on neurological exam, imbalance, confusion, incoherent speech, and seizure. Imaging pathological findings were reported in children with abnormal signs on neurological examination. Although most headaches are relatively benign, perhaps 1% to 3% of these patients have life-threatening pathology, including subdural and epidural hematomas, that are detected on CT and MRI scans. Electroencephalography (EEG) is reported as not useful in the routine evaluation of patients with headache. White matter abnormality (WMA) have been reported on MRI studies of patients with all types of migraine, with a range from 12% to 46%.

**Methods:** In this study the data were retrospectively collected from patient records (n = 98) and neuroimaging reports (n = 80) in our hospital system. Included were children presented with headache, in neurologic outpatient in University Clinic of children disease for a period of 15 months, from January 2020 year until March 2021 year. Headache was classified according to International Headache Society (IHS) guidelines.

**Results:** There were 98 children with headache examined in our neurologic outpatient, who previously had no neurological disease, 54 of which were boys and 44 girls of age 2-14 years old. All the children included had a normal neurological examination. According to the HIS guidelines there were 11 children with primary headaches, meanwhile migraine, and the rest were classified as secondary headaches related to head trauma one patient, two patients with WMA, three with nonvascular disorders, 23 with upper respiratory tract infection such as sinusitis, rhinitis and tonsillitis, and 6 with vision disorders (myopia, hypermetropia), and the rest were related to psychosocial stressors at home and in school. The patient with secondary headache related to head trauma started having headache a few months after traumatic subarachnoid hemorrhage. Out of these children in 80 were performed imaging studies, meaning brain MRI scans was performed in

75 and, brain CT scans in 10 of them, while 5 children had both brain CT and MRI. Of patients who had at least one MRI study, six demonstrated an abnormal finding that is 8% (see Table 1).

**Table 1: Performed investigations**

	Brain MRI	Brain CT	EEG	Fundoscopy
<b>All patients (n, %),</b>	75 (93.75%)	10 (10.2%)	45 (45.9%)	55 (56.12%)
<b>Abnormal findings (n, %)</b>	6 (8%)	0 (0%)	25 (55.55%)	0 (0%)

From these abnormal findings two revealed an arachnoid cyst, one showed a subarachnoid hemorrhage due to a post traumatic contusion, another one revealed an empty Sella and two showed WMA of which one was due to a suspected neurofibromatosis and the other one due to a demyelinating disease (see Table 2). Out of 63 children with performed imaging studies, in 57 children the brain MRI revealed normal findings and all who had a brain CT (n=10) it showed normal findings.

**Table 2: Abnormal brain MRI findings**

Patient	1	2	3	4	5	6
<b>Brain MRI</b>	Arachnoid cyst in left temporal region	Arachnoid cyst	Subarachnoid hemorrhage in frontal and left temporal region	T2W and flair hyper intense lesion in left cerebral region near vermis	T2W and flair hyper intense lesions near internal capsule and basal ganglia, and in mesencephalon	Empty sella

Insignificant findings were found in brain MRI scans in 11 children which showed mucous thickening of the paranasal sinuses mostly in the maxillary sinuses due to chronic inflammation of the corresponding sinus cavity, presence of a cyst or polyp in the sphenoid or maxillary sinus, and all of them had a corresponding upper respiratory tract infection, acute or chronic sinusitis, rhinitis or tonsillitis (see Table 3).

**Table 3: Other findings**

MRI of paranasal sinuses	Patient (n, %)	ORL findings/Due to
Polycystic and polypoidal findings in maxillary, ethmoidal and frontal sinuses	1	Chronic sinusitis
Mucosal thickening of maxillary sinus	1	Allergic rhinitis
Cyst in sphenoidal sinus	1	None

Cyst in maxillary sinus	1	Chronic tonsillitis
Mucosal nasal thickening	4	Allergic rhinitis
Mucosal thickening of maxillary sinus + Mucosal nasal thickening	3	Allergic rhinitis
Mucosal polypoid thickening of maxillary sinus + Mucosal nasal thickening	1	None
Not done/none	4	Chronic sinusitis
Not done/none	5	Allergic rhinitis
Not done/none	3	Chronic tonsillitis

EEG was performed in 45 children, of which 25 revealed normal findings while the rest showed either the presence of a focal spike waves or slow high voltage waves. (See Table 4). Fundoscopy was performed in 55 children, all of which showed normal findings. From the children who had fundoscopy, four of them had myopia, one was hypermetropic and one had myopic astigmatism.

**Table 4: Normal and abnormal EEG findings**

EEG findings	Patient (n= 45, %)
Normal findings	25 (55.55%)
Focal spike waves in left hemisphere	6 (13.3%)
Focal spike waves in right hemisphere	10 (22.22%)
Focal slow high voltage waves	2 (4.44%)
Focal spike waves in both hemisphere	3 (6.66%)

Findings altering the management were obtained in 6 (8%) patients: one (n =1, 1.3%) had headache for less than 1 month. On the other hand 5 patients with headache longer than 1 year (n=5, 6.66%) and with normal neurological examination had significant MRI results affecting management. There were 11 children in whom the diagnosis of migraine could be made on clinical grounds and none of them (n = 11, 11.22%) had a significant MRI finding, while all of them had pathological elements on EEG.

**Conclusion:** Headaches are common in children. Knowledge of red flag symptoms for headaches will help one to exclude sinister causes of headaches in children. Brain MRI is the neuroimaging modality of choice, though there is a high rate of incidental findings and often does not change headache management. Meanwhile, children should be referred for brain CT scan if bleeding or fracture is suspected. In young children, the cost and the need for sedation should be taken into account when making decision of performing a neuroimaging. Therefore, neuroimaging is suggested in children with a suspicious clinical history, abnormal neurological findings especially

in headache of long duration (> 1 year) and features atypical for migraine. Pathological brain MRI findings can be found and in patients with normal neurological examination, therefore a normal neurological examination should not reassure the clinician. Further studies are needed to enrich our knowledge about the pathophysiological mechanisms that cause headaches in children and adolescents and to develop efficient strategies to alleviate their burden. EEG is not indicated unless seizures occurred or are suspected.

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## CASES OF SEVERE THROMBOSIS AND RETHROMBOSIS IN COVID-19 PATIENTS

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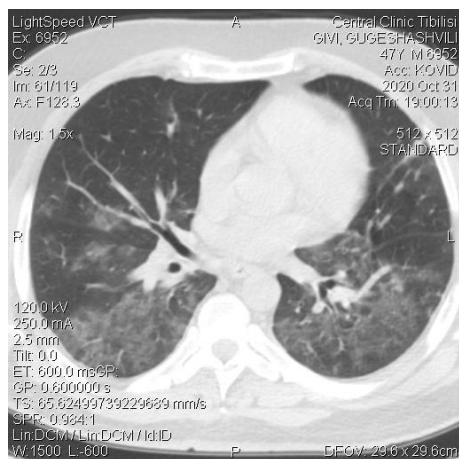
Email: gulikiliptari@yahoo.com

**Introduction:** SARS-CoV-2 infection is associated with arterial and venous thrombotic complications. Autopsy findings revealed microthrombi in multiple organ systems, that may contribute to multisystem organ dysfunction in severe COVID-19. Thrombosis in patients with COVID-19 may be due to a cytokine storm, hypoxic injury, endothelial dysfunction and increased platelet activity. Many difficult mechanisms contribute to formation of clots in vasculature of multiple organs,

We presented two different cases of pulmonary artery thrombosis complicated by severe ARDS and rethrombosis in the branches of the pulmonary artery. Both patients were treated according to PE (pulmonary embolism) management protocol (ESC)

**Conclusion:** The multisystem mechanisms: The complement system, part of the innate immune response, capable of activating the coagulation cascade, endothelial inflammation, loss of ACE2 and alteration of PAI/tPA balance, cytokine storm, high levels of the blood clotting protein factor, decreased concentrations of endogenous anticoagulant proteins increase the probability of new thrombosis, despite suitable treatment and prevention.

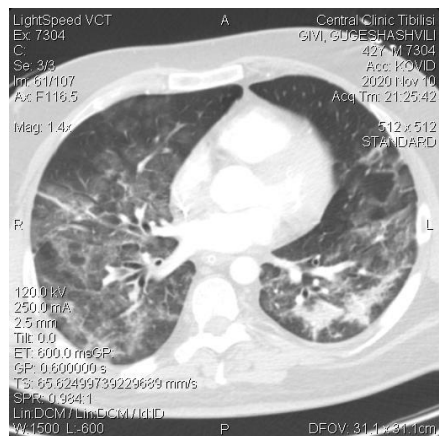
Patient N 1.



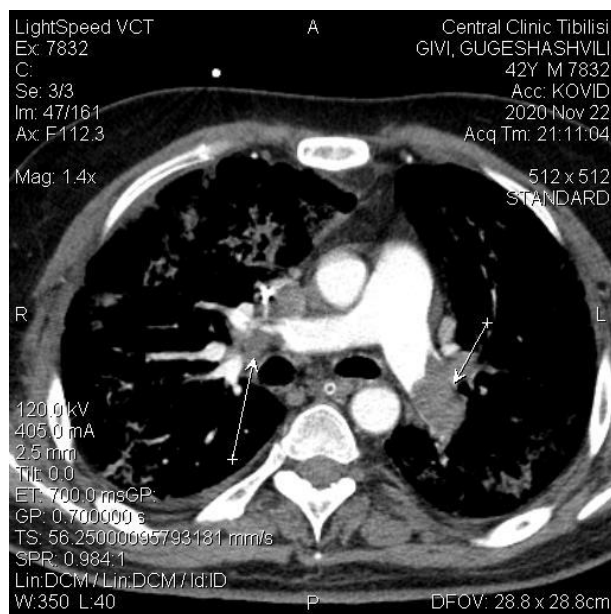
**Picture 1.** Computed tomography of the chest, axial section, pulmonary window.

On all sides, all fields are covered with foci of ground glass type infiltration and interstitial consolidation. Free fluid and air are not reflected in the bilateral pleural space. On semi-

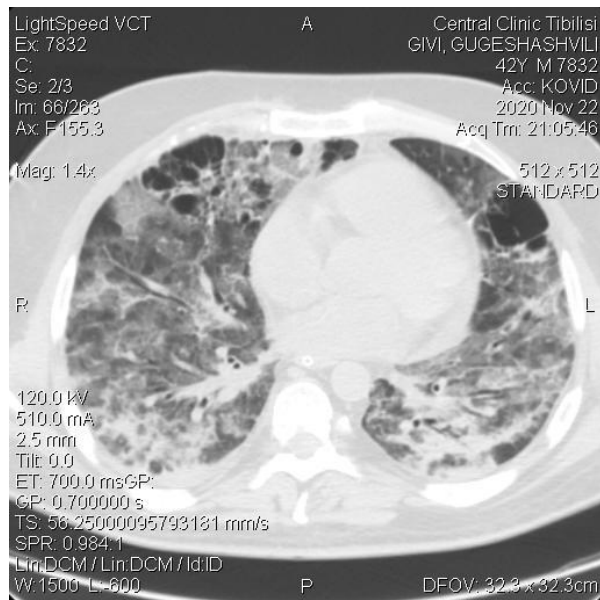
quantitative analysis of computed tomography data, the lung injury index was 18 points (0-24).[pict.1]



**Picture 2.** Computed tomography of the chest, axial section of the pulmonary window. The volume and intensity of infiltrative changes increased in all bilateral lung fields. Areas of consolidation have been identified. In a semi-quantitative analysis of computed tomography data, the lung injury index was 21 points (0-24). [pict2]



A



B

Picture 3 Computed tomography of the chest, axial section of the mediastinal window

A. On both sides, thrombotic formations are observed in the right and left main arteries of the lung, in the lumen of the parietal and segmental branches.

B. The volume and intensity of the infiltration increase. In the ventral segments, areas of lung tissue rupture were revealed. Semi-quantitative methodological analysis of computed tomography data, lung lesion index - 24 points (0-24). [pict.3]



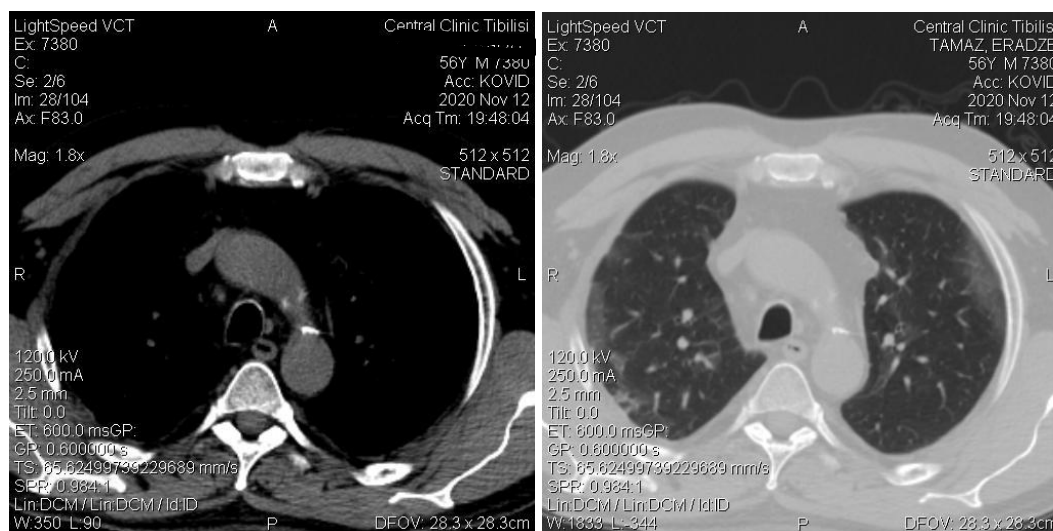
A



B  
 Picture 4

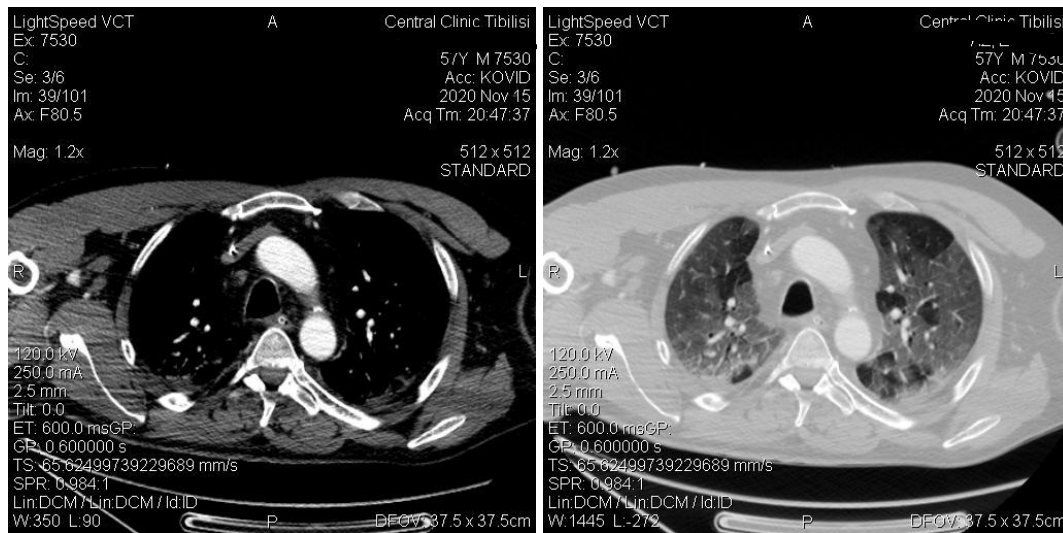
B. Angiographic examination does not reveal reliable signs of thrombosis of the lung trunk. Spreading from the level of the lung trunk bifurcation, thrombotic masses are reflected in the lumen of both large bronchi. Saddle thrombus. Thrombotic formations are reflected in the bilateral lobal and segmental arteries.

Patient N 2



Picture 1

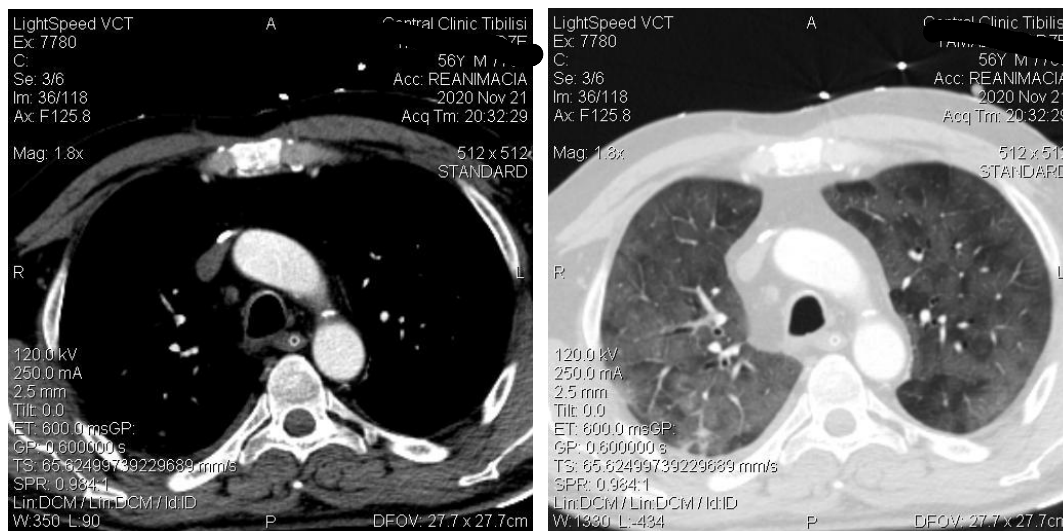
On both sides, there is an infiltrative change in the lungs in the form of a ground glass phenomenon without fluid in the pleural cavity. Semi-quantitative methodological analysis of computed tomography data, lung lesion index - 17 points (0-24).[pict1]



Picture 2

Angiographic examination does not reveal pulmonary thrombosis. The lumen of small arteries in the lower left corner is not completely contrasted, which suggests the presence of thrombotic masses. On both sides of the lung, there is a typical phenomenon of total ground glass, consolidation dorsally in the lower fields. Free fluid and air on both sides of the pleura are not detected

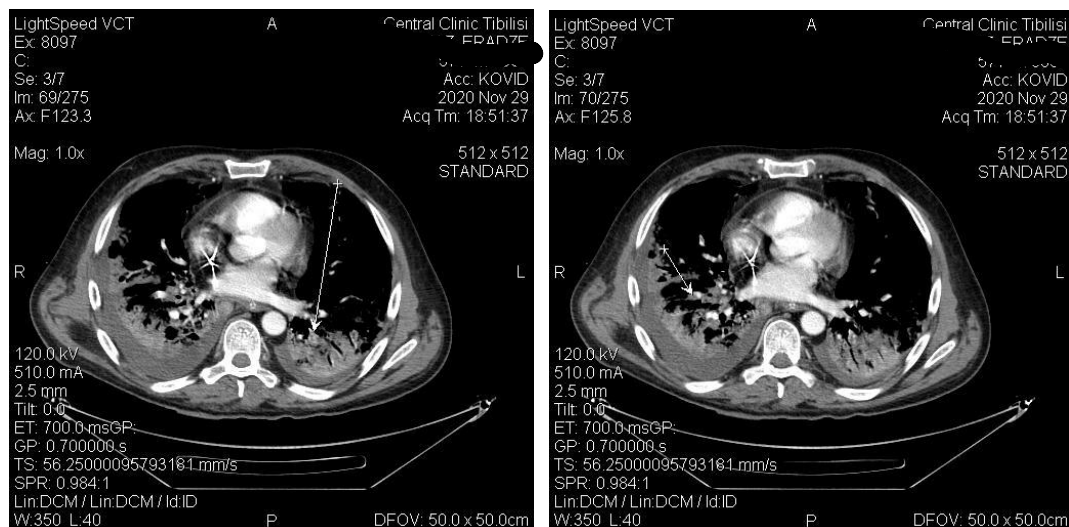
In a semi-quantitative analysis of computed tomography data, the lung injury index was 23 points (0-24).[pict.2]



Picture 3

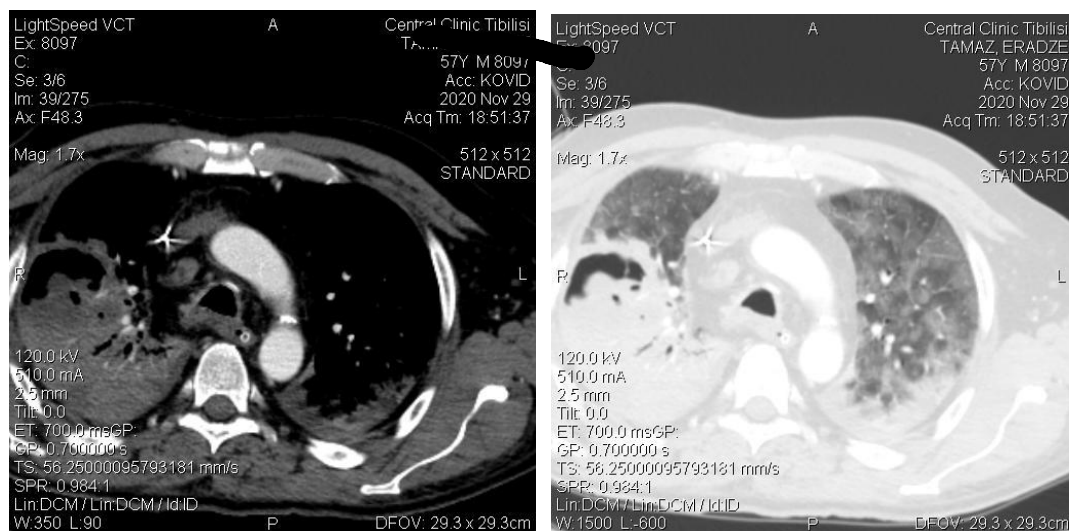
There is still lesion on both sides of the lungs, an almost entirely common ground glass phenomenon, although there is a relative decrease in intensity.

In the bilateral pleural cavity, a small liquid discharge, free air is not reflected. In a semi-quantitative analysis of computed tomography data, the lung injury index was 23 points (0-24). [pict.3]



Picture 4

Angiographic examination showed no filling defect in the lung trunk and bilateral main artery. Thrombosis in the right lower artery is increased, in the left basal thrombus masses are reduced and reflected in the lumen of the segmental arteries. Shown by arrows.[pict.4]



Picture 5

The intensity of the lesion was increased according to the type of ground glass phenomenon, which is totally widespread in both lungs; in the lower fields, extensive areas of consolidation appeared, against the background of which zones of avascular infarction pneumonia are revealed. Foci of destruction - 5.2 cm laterally in the right middle field.

The fluid is detected in the bilateral pleural cavity, the separation on the right is 2.2 cm, on the left is 1.0 cm, free air is not reflected.

In a semi-quantitative analysis of computed tomography data, the lung injury index was 24 points (0-24). [pict.5]

**Discussion:** The pathophysiology of thromboembolism in COVID-19 related to endothelial inflammation, hypercoagulability associated with increased concentrations of coagulation factors, acquired antiphospholipid antibodies, and decreased concentrations of endogenous anticoagulant proteins, loss of ACE2 alters PAI/tPA balance. High levels of the blood clotting protein factor V is at elevated risk from blood clots such as deep vein thrombosis to pulmonary embolism. Immune complex vasculitis is pathological mechanism of covid-19 pulmonary artery thromboembolism, venous sinus thrombosis, cytokine storm.

SARS-CoV-2 invasion of ACE-2 receptor expressing cells (airway epithelial cells, vascular endothelial cells, circulating monocytes), causes cellular damage, release of pro-inflammatory chemokines and chemoattractants (including C3a and C5a). The complement system is part of the innate immune response [1,2], the complement system is an important host mediator of SARS-CoV-induced disease and that complement activation regulates a systemic proinflammatory response to SARS-CoV infection, complement system is over activated and contributes to the dysregulated host immune response [3,4,5]. the complement system activates the coagulation cascade, increases tissue factor activity [6,7,8,9], increases platelet activity and aggregation [10,11,12,13], as well as stimulate endothelial cells to release von Willebrand factor and express P-selectin [14,15,16]. Complement also regulates fibrinolysis, with complement cascade inhibitors [17], and activates the fibrinolysis inhibitors PAI-1(plasminogen activator inhibitor-1) and TAFI [Thrombin Activatable Fibrinolysis Inhibitor].

Such difficult and multisystem mechanisms contributes formation clots in vasculature of multi organs, Increases probability of new thrombosis, despite suitable treatment and prevention.

**Conclusion:** The multisystem mechanisms : The complement system, part of the innate immune response and capable of activating the coagulation cascade, endothelial inflammation, loss of ACE2 and alteration of PAI/tPA balance, cytokine storm, high levels of the blood clotting protein factor, decreased concentrations of endogenous anticoagulant proteins increases probability of new thrombosis, despite suitable treatment and prevention.

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## BIOLOGIC AGENTS ROLE IN THE TREATMENTS OF PSORIASIS: UPDATE FOR THE CLINICIANS

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### ABSTRACT

The biologic agents within the past two decades has dramatically improved the treatment of psoriasis and psoriatic arthritis. Given that there now exists 11 FDA approved biologic options available for psoriasis, with more in the pipeline, the therapeutic armamentarium has been greatly enhanced. However, the fact that there are so many available options has also caused confusion for providers. Therefore, this manuscript deliberately focuses on the most clinically useful facts (such as efficacy and safety data) about each and every FDA approved biologic agent (including pipeline agents) for psoriasis.

**Keywords:** biologic therapy, psoriasis, IL-17, TNF-alpha,

**Introduction:** The great progress has been made with biologic therapy for psoriasis in terms of both the safety and efficacy of these agents. This new treatment paradigm was made possible by the continually advancing knowledge of the pathophysiology of psoriasis. Thirty years ago, psoriasis was still primarily considered a problem with the hyperproliferation of the epidermis [1]. Recent research into the pathophysiology of psoriasis has highlighted the importance of the immune system in this disease. There now exists a clear mechanism, down to the molecular level, regarding which cytokines are implicated in the pathophysiology of psoriatic disease. In the initial cascade of psoriasis pathophysiology, a variety of cell types are involved which include keratinocytes, natural killer T cells, plasmacytoid dendritic cells and macrophages. These cells secrete cytokines which activate myeloid dendritic cells and in turn, activated myeloid dendritic cells secrete IL-12 and IL-23. Both of these cytokines are integral in the cellular cascade of psoriasis pathophysiology [2]. IL-12 causes differentiation of naive T cells to Th1 cells (which produce IFN- $\gamma$  and TNF- $\alpha$ ) and IL-23 is important for the proliferation of Th17 and Th22 cells. Th17 cells produce IL-17, IL-22 and TNF- $\alpha$ . When considering all of these different signaling pathways, IL-23 [3] mediated activation of the Th17 pathway is hypothesized to be the main contributor to the inflammation seen in psoriasis. [2] Given that the IL-17 and IL-23 biologic agents are more effective may demonstrate the fact that these pathways are more [4]. In the pathophysiology of psoriasis and that psoriasis patients may, on the whole, exhibit more pathology in this specific pathway. The fact that biologic agents interact with a specific cytokine (such as TNF- $\alpha$ , IL-17 or IL-23) in a targeted manner has revolutionized the capacity to treat psoriasis [5] compared to the era of a more generalized immunosuppression reflected by the traditional oral medications. This represents an improved treatment regimen where targeted immunomodulation has resulted in a great enhancement in both safety and efficacy for biologic agents [6].

**Methodology:** The goal of this manuscript is to aid the busy practicing dermatologist in becoming more adept at using these agents with the ultimate aim of improving patient care. Each biologic

agent will be presented according to the class that it belongs, we will discuss each of them separately:

**A. TNF-Alpha Agents/ Etanercept (Enbrel®)** Etanercept is a recombinant human TNF- $\alpha$  receptor protein fused with the Fc portion of IgG1 that binds to soluble and membrane bound TNF- $\alpha$  and to tumor necrosis factor- $\beta$ . It is currently approved for treatment of moderate-to-severe adult and pediatric plaque psoriasis, psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis and ankylosing spondylitis [7].

**Adalimumab (Humira®)** Adalimumab is a recombinant, fully human, monoclonal antibody against TNF-alpha that blocks the interaction of TNF with both of its cell-surface receptors, with high affinity and specificity. For over 20 years, adalimumab has been used worldwide in more than 1 million patients for 10 different indications which are: rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, adult Crohn's disease, pediatric Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa and uveitis [8].

**Certolizumab Pegol (Cimzia®)** Certolizumab (CZP) is a monovalent, humanized Fab antibody fragment, conjugated to a polyethylene glycol (PEG) that inhibits TNF-alpha in a dose-dependent manner. This gives CZP a unique structure amongst all other biologics. There are 6 indications: Crohn's disease, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and moderate-to-severe plaque psoriasis [9].

**Infliximab (Remicade®)** Infliximab is a chimeric monoclonal antibody comprised of a mouse variable region and a human IgG1-alpha constant region which exerts its neutralizing action by binding to both soluble and transmembrane TNF-alpha molecules. It is approved in adults for the treatment of psoriasis, psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis [10].

**B. IL 12/23 Agents/Ustekinumab (Stelara®)** Ustekinumab is a human monoclonal antibody that binds with high specificity and affinity to the p40 subunit of both interleukin 12 (IL-12) and IL-23, and as a result, suppresses both IL-12 and IL-23 mediated inflammation which causes psoriasis.

**C. IL-17 Agents/Brodalumab (Siliq®)** Brodalumab is a human monoclonal antibody that binds the IL-17 receptor A and blocks the biologic activities of IL-17A, IL-17F, IL-17A/F and IL-17E (also known as IL-25). This is a unique mechanism of action as it is the only biologic in its class which blocks the entire IL-17 receptor. It is indicated for the treatment of moderate-to-severe plaque psoriasis in adult patients.

**Secukinumab (Cosentyx®)** Secukinumab is a fully human G1k monoclonal antibody, which selectively binds and inhibits IL-17A. It is currently FDA approved for plaque psoriasis, ankylosing spondylitis, psoriatic arthritis, and active non-radiographic axial spondyloarthritis.

**Ixekizumab (Taltz®)** is a high-affinity, humanized IgG4 monoclonal antibody for IL-17A, inhibiting interaction with the IL-17 receptor. FDA indications for ixekizumab include plaque psoriasis, psoriatic arthritis, ankylosing spondylitis, and non-radiographic axial spondyloarthritis.

**Bimekizumab** is a novel IgG monoclonal antibody that binds to a peptide region that is shared by IL-17A and IL-17F.

**D. IL-23 Agents/Tildrakizumab (Ilumya®)** is a humanized IgG1, monoclonal antibody designed to selectively block IL-23 by binding to the p19 subunit.

**Risankizumab (Skyrizi®)** is a humanized IgG1 monoclonal antibody selectively targeting the p19 subunit of IL-23.

**Guselkumab** is a fully human IgG1 $\lambda$  monoclonal antibody which inhibits the p19 subunit of interleukin 23 (IL-23). FDA approved indications for guselkumab include moderate-to-severe plaque psoriasis and psoriatic arthritis.

**Discussion:** Our manuscript reviews the most relevant facts about every biologic agent available for the treatment of psoriasis with a special focus on the merits and demerits of each agent. After reviewing all the available options, it has become clear that each of these agents has their own unique merits. Therefore, the more simplistic idea that several of the older The recommendation of

the authors is not to dismiss any biologic agents currently available based on just superficial assessments or a cursory glance. The authors hope that this complete characterization of all the biologic agents used by dermatologists for psoriasis proves helpful in understanding the nuanced differences between the agents, which could prove to be very important in improving patient care and patient satisfaction

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## SKIN STEM CELL THERAPY: MECHANISMS AND RECENT ADVANCES

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### ABSTRACT

Stem/progenitor cells of the epidermis are recognized to play the most essential role in the tissue regeneration of skin. In this review, we first illustrated basic stem cell characteristics and various stem cell subtypes resided in the skin. Second, we provided several literatures to elucidate how stem/progenitor cells collaborate in the process of skin repair with the evidence from animal model studies and in vitro experiments. Third, we also introduced several examples of skin cell products on the pharmaceutical market and the ongoing clinical trials aiming for unmet medical difficulties of skin.

**Keywords:** Dermatology, Stem cells, Cell Therapy

**Introduction:** Traditionally, stem cells can be categorized into two different groups, embryonic stem cells and somatic stem cells. Embryonic stem cells are obtained from the inner cell mass of blastocyst in mammalian embryos [1]. Embryonic stem cells are pluripotent; therefore, they have the potential to derive progeny cells [2] belonged to all three germ layers including ectoderm, endoderm and mesoderm [3]. Unlike embryonic stem cells, somatic stem cells are typically found in mature organs or tissues. Some somatic stem cells might be multipotent but majority of them are lineage limited, i.e. hematopoietic stem cells can only give rise to mature blood cells [4], whereas neural stem cells can only divide into neuronal and glial cells [5]. With the huge success of Professor Yamanaka's lab in Kyoto, differentiated, adult somatic cells can be reprogrammed to generate induced pluripotent stem cells (iPSCs), and now iPSCs become a new emerging group of stem cells. The reprogramming is achieved by exogenous addition of four transcription factors (Oct-3/4, Sox2, c-Myc, and Klf4) using retroviral transduction. iPSCs have been shown to be pluripotent and can give rise to a wide range of mature cell types [6]. Skin stem cells as well fall into the classification as somatic stem cells, however, due to the cellular heterogeneity of skin, various types of skin stem cells were found in past decades [7]. Recently, significant advances have been made in identifying different types of skin stem cells with the aid of molecular tools. Subgroups of skin stem cells are listed as below. 1. Epidermal stem cells, 2. Follicular stem cells, 3. Melanocyte stem cells, 4. Sebaceous gland stem cells, 5. Mesenchymal stem-cell-like cells, 6. Neural progenitor cells, 7. Hematopoietic stem cells located at the follicle dermal papillae, might divide into erythroid and myeloid lineages, shared similar cell markers as counterparts in other organs or tissues. Among all these distinct skin stem cell subgroups, epidermal stem cells are the most deeply correlated to tissue repair and skin regeneration. Scientific reports supported that stem cells of epidermis are rare, infrequently dividing, and generate short-lived, rapidly dividing cells that carry out the regeneration of the epidermis. The same infrequently dividing stem cells of epidermis are assumed to be the major epidermal cell population responsible for repairing skin injury. Most epidermal stem cells reside in the basal layer of epidermis, some might also be found in the bulge region of the hair follicle and the base of the sebaceous glands [8]. Throughout its

whole life cycle, epidermal stem cells are circulated between two different cell phases. Under the slow cell phase, epidermal stem cells are quiescent. While entering transit amplifying cell phase, they are quickly divided and the number of skin cells is amplified for the replenishment of skin tissue. Finally, they undergo numerous cell divisions before becoming terminally differentiated to accomplish skin regeneration[9]. To our understanding, several mesenchymal stem cells or progenitor cells have the capacity to release immunomodulation factors, and this might be the reason that different engrafted cell types have different efficacy upon skin repair[10]. Although the precise molecular mechanism of skin repair is still not clear, those studies already depicted an outline how epidermal stem cells participating in tissue regeneration and provided future strategies for skin cell products development. Toward skin injury, both epidermal stem cells and follicular stem cells contribute to the re-epithelialization of wounds. In the full-thickness wound, epidermal stem cells and progenitor cells from the hair follicle initially migrate toward the wound site. Epidermal stem cells have been reported to be reactivated in response to skin injury and contribute to skin regeneration on the cellular level. Further clinical evidence also suggested that epidermal stem cells and follicular stem cells participate in the re-epithelialization of wounds by evaluating the potential healing capacity.

**Methodology:** stem cell therapy on skin, although initially most clinical trials were mainly designed as autologous engraftment, nowadays already some of them aimed for allogeneic indications. Similar to the topical formulations applied in the dermatological fields, reviewing policies should be more dedicated on potential safety concerns, especially on ethnic bridging issues as mentioned above. Based upon the differences in morphology and physiology between different races, the possible variation in efficacy and/or safety of allogeneic skin cell products should not be ignored. Moreover, allogeneic skin cell/tissue engraftment might be in high demand under specific occasions with mechanic explosions or accidents. This technology was originally developed by Professor Howard Green of Harvard Medical School in the 1970s, and later been transferred to J-TEC by Professor Minoru Ueda of Nagoya University. By isolating keratinocytes from a 1-cm<sup>2</sup> skin sample from the patient and culturing them on the fibroblast feeder, a sheet of cultured epidermis measuring around 1000 cm<sup>2</sup> can be produced in around two weeks. In the event mentioned above, total five patients were benefited by JACE®, however, facing massive amount of burn patients, both autologous and allogeneic skin products will be considered to facilitate skin repair under highly demanding circumstances. Therefore, both regulatory bodies and pharmaceutical companies should work together to set the standard bridging criterion for skin stem cell products, especially those of allogeneic indications.

**Results:** The best solution will be always to enroll adequate numbers of non-Caucasian subjects into future clinical trials. For developing ideal medications, we definitely have to verify the characteristics of proposed skin stem cell products and clarify the differences in efficacy and safety across different races, hence to actually promote public health.

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## VITILIGO, FROM PHYSIOPATHOLOGY TO EMERGING TREATMENTS: A REVIEW

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### ABSTRACT

Chronic inflammatory skin disease Vitiligo leading to the loss of epidermal melanocytes, treatment options for vitiligo patients are limited, lack sustained efficacy, and are mainly based on off-label use of immunosuppressive agents, such as systemic or topical steroids or topical calcineurin inhibitors, in association with the use of ultraviolet light. However, recent insights into the understanding of the immune pathogenesis of the disease have led to the identification of several therapeutic targets and the development of targeted therapies that are now being tested in clinical trials. In this review, we summarize emerging targets that could be developed for the treatment of vitiligo and discuss recent and ongoing developments of drugs for the management of the disease.

**Keywords:** Cytokines; Disease progression; Emerging treatments

**Introduction:** Vitiligo is a common chronic inflammatory skin depigmenting disorder with a worldwide prevalence of 0.5–1% [1]. The occurrence of white patches results from a loss of epidermal melanocytes [2]. While vitiligo does not affect life expectancy, the color dissimilarity has a serious impact on patients' quality of life and mental well-being, with patients often enduring stigmatization and social isolation, as well as being more subject to psychiatric morbidities [3, 4]. To date, available treatments for vitiligo remain limited, and therapeutical strategies rely on nonspecific therapies targeting the inflammatory and immune responses, such as topical or systemic steroids or topical calcineurin inhibitors, both associated with ultraviolet (UV) light to promote melanocyte regeneration. This limitation in treatment possibilities highlights the need to improve vitiligo management. Therefore, early aggressive treatments can now be considered that would inhibit the consequences of the immune response against melanocytes to prevent their loss. Once the exaggerated immune response is controlled the regeneration of melanocytes from hair follicles or interfollicular compartment is an important to consideration, as is a maintenance therapy to prevent the recurrence of the disease In this review, we discuss the current concepts for managing vitiligo and summarize future innovative strategies and ongoing clinical trials [5]. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

**Methodology:** A. Targeting Innate Immunity Danger Signals from Epidermal Cells Epidermal cells in vitiligo, especially melanocytes, exhibit metabolic defects that contributed to increased levels of reactive oxygen species (ROS) [6]. These changes, in the context of a susceptible genetic background, are associated with the release of pro-inflammatory cytokines and damage-associated molecular patterns (DAMPs, or endogenous danger molecules). B. The Type I IFN Pathway Several data link vitiligo to a type I IFN signature [7]. First, variants of INF induced with

the helicase C domain 1 (IFIH1) gene, associated with a loss of function, could provide Emerging treatments in vitiligo. Development of vitiligo is associated with skin inflammation. Strategies targeting the innate and adaptive immune response will be important to control skin inflammation in vitiligo [8], to stabilize and prevent the progression of the disease. Therapies aiming to promote melanocyte regeneration will also be important to consider to induce repigmentation. Lastly, a maintenance therapy will be of utmost importance to prevent the recurrence of the disease [9].

**C. Targeting the Adaptive Immune Response-Resident Memory T Cells** The recurrence of vitiligo on previously affected anatomic sites demonstrate the role of a memory response in vitiligo [10]. Indeed, resident memory T (TRM) cells have been identified in vitiligo.

**D. T Helper Type 1-Skewed Immune Profile in Vitiligo** Vitiliginous skin is consistently associated with the infiltration of immune cells confined to the vicinity of the remaining melanocytes, characterized by the presence of CD8 T cells with a type 1-skewed immune profile and producing elevated levels of IFN- $\gamma$  and TNF- $\alpha$ . These T cells are characterized by the expression of the chemokine receptor CXCR3 and can respond to CXCR3 cognate ligands CXCL9 and CXCL10, which are highly expressed in vitiliginous skin.

**E. Cytokines and their Signaling Pathways** Cytokines are key mediators of melanocyte loss in vitiligo and participate at every step of the pathogenesis of this disease. The IFN- $\gamma$  and TNF $\alpha$  immune pathways are the most extensively studied to date in vitiligo and appear to be critical for disease initiation and progression.

**F. Immune Tolerance** As a chronic inflammatory disorder, vitiligo is associated with disruption of immune regulation systems. In this line, GWAS identified a polymorphism of forkhead box protein 3 (FOXP3), the master transcription factor of regulatory T cells (Tregs), in vitiliginous skin. However, it is still not clear whether the defect is due to a decreased migration of Tregs into the skin and/or a loss of function.

**Intrinsic Abnormalities of Melanocytes** Several in vitro and in vivo studies have demonstrated the presence of intrinsic abnormalities in vitiligo melanocytes. Vitiligo melanocytes are characterized by an altered redox status, with the presence of oxidative stress coupled to an increased susceptibility to prooxidant agents.

**J. Stimulating Melanocyte Stem Cells** The differentiation and proliferation of melanocyte stem cells is induced by several soluble factors targeting the melanocortin 1 receptor (MC1R), endothelin receptor, and/or Wnt receptors. The use of platelet-rich plasma that contains several growth factors has received attention as a treatment for stable vitiligo.

**Maintenance Therapy To Prevent Recurrence Of The Disease** As previously discussed, vitiligo is a chronic inflammatory skin disease that needs a careful follow-up for optimal maintenance therapy. Recurrence of the disease is mediated by autoreactive TRM cells located close to replenished melanocytes. To date, a prospective randomized study showed that a twice-weekly application of topical calcineurin inhibitors is an effective treatment strategy to prevent vitiligo relapses by supporting the need to continuously inhibit the immune system to maintain repigmentation. Therefore, with the development of targeted therapies, the use of topical JAK inhibitors could be a reliable treatment in this context. As TRM maintenance in the skin is dependent on IL-15, targeting IL-15 could be another potential treatment strategy. We have recently shown that matrix metalloproteinase (MMP)-9 released by keratinocytes in vitiligo lesional skin could induce the cleavage of E-cadherin, leading to the detachment of epidermal melanocytes. Consequently, MMP-9 inhibition could also be an interesting strategy for stabilizing melanocytes in the basal layer of the epidermis and prevent their loss.

**Conclusion:** Recent research advances in our understanding of the pathogenesis of vitiligo has led to the development of targeted therapies for this disease, which has a high impact on patients' quality of life. JAK inhibition is showing promising results, and ongoing clinical trials could lead to a first approved treatment for vitiligo. However, research needs also to remain focused on the development of strategies to prevent the loss of melanocytes and/or promote their regeneration, especially for localization of vitiligo that will not respond to the treatment.

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## CHALLENGES FACING THE CURRENT STATE OF EXPORT POTENTIAL (IN THE CASE FOR AZERBAIJAN)

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### ABSTRACT

The purpose of the study is to identify the importance of increasing export activity in ensuring economic development and the main conditions for increasing the country's export potential, to stimulate exports based on an assessment of the current state of export operations. Moreover, the study determines the directions for increasing the country's export potential and improving the legal framework for its use, furthermore, compile the adequate suggestions and recommendations. The report identifies the importance of export activities in the modern system of economic relations; The main conditions for increasing the export potential in the Republic of Azerbaijan and the stimulated means of using the export potential have been studied; the need for legal regulation of state intervention to increase the export potential of Azerbaijan and promote its implementation was substantiated; the system of legislative acts regulating the implementation of export operations was analyzed; the mechanisms of realization of the existing state support in the field of export stimulation in our country have been studied; The directions of improving the legal framework to increase the export potential and stimulate exports have been identified in our country.

**Keywords:** export, foreign relations, economic development, growth, international trade.

**Introduction:** Observing the rapid growth dynamics of economic development in the country over the past 10 years, directing revenues from the successful oil strategy to the modernization of production infrastructure, the implementation of certain measures to diversify the non-oil sector in the economy, as well as GDP growth and social welfare elevation has occurred. The sharp declines in oil prices on world commodity markets, as well as the crisis of foreign trade partners, have led to a slowdown in economic growth.

In response to the challenges facing the economic development of our country, it is necessary to make a number of institutional and structural improvements. The balance of payments deficit, the negative impact on the financial and banking sector and the non-oil budget deficit have shown the need for the country's transition to a new model of development. For sustainable economic development, it is necessary for the avant-garde sectors to be the locomotive of economic development in our economy, for the trade sector, processing industry, private entrepreneurship, high-tech sectors, as well as highly skilled labor-intensive and value-added sectors to have a special share. It is planned that the improvement in the structure of the economy will be a positive impetus for the development of the business environment, the strengthening of the financial and banking sector and the introduction of a floating exchange rate monetary policy to create conditions for access to international markets. The application of new technologies in industry, management, communications, finance, information and other areas in our country, both in the private sector and in the public sector, can give impetus to the creation of high benefit.

Along with the import of new technologies, it is possible to increase the export potential and achieve a substantial development in exports by bringing new technology in the labor force that manages the process. Because of the analysis of economic growth, we can see that the oil factor has a significant impact on macroeconomic stability and social welfare. With the implementation of procyclic economic policy, the dependence of economic growth on government demand has increased. One of the main challenges is to replace the role of public demand in economic growth with sustainable private demand.

**Modern challenges review:** As a measure adequate to the modern challenges facing the Azerbaijani economy, it is especially important to minimize dependence on exports of hydrocarbon resources, increase non-oil exports and close the non-oil import deficit. As a result of the development of the non-oil sector, the volume of exports per capita is planned to reach \$ 1,000. To achieve the set goals, it is necessary to carry out effective government regulation that creates a healthy competitive environment and transformation into an export-based economy that generates high value added. The application of a flexible exchange rate policy can increase the solvency of our country by creating positive impulses in export activities. One of the main challenges facing our country is to improve the mechanisms to protect the rights of investors, eliminate shortcomings in competition law and create a working system.

The raw material orientation of the economic development of the republic leads to the fact that the main part of exports is accounted for by hydrocarbon resources, which are products of the extractive industry. In our opinion, the application of the innovation-technology model can minimize the dependence of the national economy and exports on energy carriers. The low and voluntary nature of commodity prices compared to the products of the processing industry in world commodity markets leads to sharp fluctuations in foreign exchange inflows into the country when exports are based on raw materials, as well as negatively affects the solvency of low foreign exchange earnings. The creation of low added value in a commodity-oriented economy has a negative projection on wages. In developed countries, the use of advanced technologies and the application of innovative technological innovations in production, as well as the high value added created by the participation of highly skilled labor in the production process play a positive impetus in socio-economic development.

One of the modern global challenges is for all mankind to strive to use environmentally friendly alternative energy sources. In OECD countries, this process is faster. Renewable alternative energy sources currently account for 17.5% of the EU's energy supply. Europe's energy roadmap for the future sets energy efficiency, renewable energy, nuclear energy, carbon retention and storage as key principles for the transition to a sustainable, competitive and secure energy system by 2050. In order to protect the environment and increase the brand value of companies, companies are switching to alternative energy, and investors are interested in investing more in these companies. Studies show that by 2040-2050, the energy supply of the European Union will be almost entirely using alternative energy sources (<https://cleantechnica.com>). The use of alternative energy in production can reduce carbon emissions into the atmosphere as a result of the production process. By choosing renewable energy, companies can address carbon emissions, meet energy security targets, and pursue sustainable development goals and science-based priorities. When looking at the structure of the republic's export products, we can see that there are only a few types of refined oil products.

In our opinion, despite the use of alternative energy sources in the future, in the military industry, especially missiles, military aircraft, etc. In the future, the use of oil obtained from oil refining in the fuel supply can be considered as one of the challenges that will allow the country to specialize in the export of oil products.

**Estimation of annual investments in the oil industry:** However, in order to achieve high results in oil refining, first, the technical base of Azerbaijan's oil industry needs to be updated. The basic means of production can be used more than once in the production process, not just once, but several times. If the means of production are used repeatedly in the production process, productivity decreases. This process is called the depreciation of fixed assets. As a result of obsolescence of equipment and machinery, the quality of the product decreases, but the natural shape of the production assets does not change. Depreciation is included in the cost of production because it is incurred during production. Thus, fixed assets are funds that, by repeated participation in production activities, transfer their value in parts to the final product, but do not change their natural form. From the physical point of view, the technical base of the oil industry of the Republic of Azerbaijan needs 70-80% depreciation of fixed assets. From a moral point of view, the main production assets are completely obsolete. Insufficient investment in the oil industry also plays a role in this situation. Annual investment in the oil industry should make up 25% of the value of fixed assets in the current year. "While the value of fixed assets in the oil industry in 2017 was 95,307.9 million manat, investment in fixed assets amounted to 8,400.1 million manat, ie 8.81% of the total value of fixed assets. As a result, the depreciation rate in 2017 was 28.9%. In 2018, SOCAR has allocated AZN 10,083,000 for the renewal of fixed assets"(SOCAR, International Financial Reporting Standards Consolidated financial statements, 31 December 2017).

The low rate of renewal of fixed assets has a number of negative consequences:

- production performance falls.
- accidents often occur in the production process.
- profitability decreases.
- causes loss of time and traumatic injuries to the workforce.

One of the main reasons for the accidents at SOCAR's overpasses is the lack of transparency, as well as the inefficient and unfair use of funds allocated for the repair and construction of overpasses. If SOCAR's overpasses need to be renewed, as well as if oil companies use floating platforms in the international arena, the lack of renewal on expired overpasses can lead to accidents.

SOCAR's newly built and soon-to-be-commissioned Gas Processing Plant at the Gara-Dag Oil and Gas and Chemical Complex has a production capacity of 10 billion cubic meters, as well as a refinery with a production capacity of 10 million tons, as well as 1 petrochemical plant. , Is planned to be 8 million tons. Thus, it is expected that it will be possible to produce fuel that meets Euro 5-6 standards. Along with A-92, A-95, A-98 gasoline, it is planned to produce jet and diesel fuel. The commissioning of the complex can create conditions for increasing the export of refined oil products of our country ([www.socar.az](http://www.socar.az)). It should be noted that despite the sufficient production capacity of refineries, the small volume of refined oil products is due to the use of only part of the production capacity of refineries. Incomplete utilization of plant production capacity can be considered as one of the important factors influencing the low share of processed products in exports. Maximizing the production capacity of oil refineries is one of the main challenges facing the oil industry's exports.

**The analysis of the export potential of agricultural products:** It is possible to note some agricultural products of our republic, which have a large export potential. These products include pomegranates, figs, potatoes; natural honey, grapes, saffron, walnuts, hazelnuts, etc. can be attributed. It should be noted that saffron products might have promising export opportunities in the future. At present, the demand for saffron in the domestic market is met by products imported from Iran to our country, which negatively affects local production and hinders the development of saffron. In addition, the Cabinet of Ministers on export-stimulated products

The absence of saffron in Resolution 103 has a negative impact on the use of its promising export opportunities. The unique quality of saffron products produced in our country can create conditions for sufficient foreign exchange inflows from the export of this product to our country in the future. The high price of saffron in the world commodity markets will also encourage the development of the saffron industry as a priority agricultural sector, making it one of the main agricultural products exported in the future.

Even saffron products can be found in foreign markets as an Azerbaijani brand. In the future, our country can get large foreign exchange reserves from the export of viticulture and wine products, which have great export potential. However, the lack of competitiveness of wine products in European markets is due to its low quality, as well as the fact that the packaging and advertising of wine products do not meet modern market requirements. Due to the fact that our country is not a member of the WTO, the small export quota for wine and wine products of national origin by different countries also has a negative impact on the use of its export potential.

The establishment of fertile national regimes based on the principle of free access to WTO markets, which creates favorable conditions for free competition by eliminating quantitative restrictions on trade operations and prioritizing the impartiality and transparency of trade policy, by doing important work to maximize the liberalization of international trade, creates conditions for compliance with the rules, as well as the effective organization of trade turnover through the abolition of quantitative restrictions on imports, as well as increased transparency in the conduct of foreign trade operations by members of the organization (Bayramov V., 2010).

**Prospects for accession to WTO:** Our country's membership in the WTO is one of the important directions of economic policy and one of the main global challenges facing it. The main goals of our country's membership in the WTO and the main issues to be considered during the membership process are as follows:

- rapid integration into the global economy;
- the benefits of reciprocal concessions of member states gained;
- creation of conditions for conducting trade activities on more favorable terms by organizing trade operations on the basis of general rules;
- access to assistance from international organizations and member states in the process of economic reforms;
- to attract large amounts of foreign investment to our country;
- to be able to benefit from WTO dispute resolution mechanisms;

Our country's membership in the WTO requires the harmonization of the country's legislation with international legislation and the improvement of laws that do not meet international standards. In the field of regulation, the protection of intellectual property, as well as the improvement of laws

on foreign investment are important. The benefits that the Republic of Azerbaijan will gain from joining the WTO can be grouped as follows:

- the export potential of our country will increase and the opportunities for exporters to realize their export potential will increase.
- no ban on trade relations may be imposed on our country by the members of the organization.
- procedures applied in both domestic and foreign trade activities will be simplified.
- monopolies will be reduced, monopolies will be eliminated and a competitive market environment will be created.
- customs tariffs will be reduced; prices for imported goods will be reduced.

There are also criticisms that the application of low tariffs as a member of the organization has weakened local production, which is protected by protectionist methods, and that these producers are unable to maintain their position in the market. However, trade liberalization does not mean the complete abolition of customs barriers, and 7-8 WTO instruments can be used to protect domestic production. It should also be noted that the actual customs duties are in the range of 0% -15%, and in international practice there are import rates that are 1.5-2 times higher than the actual rate on the basis of bound rates of the CIS countries. During the negotiations, the Azerbaijani side proposed to impose import customs duties at a minimum of 0% and a maximum of 25%. In the worst case, even if the bound rates proposed by the WTO are adjusted to the actual rates, our domestic production will have the same negative impact on imports today as it did after accession. In our opinion, even if the status quota is maintained, domestic production will not have a significant negative impact. The increase in imports can be limited by regulatory tools. If the necessary legislation and institutional framework are in place, it is possible to protect domestic production from adverse effects.

Some economists believe that WTO membership will have a negative impact on the country's agricultural sector. According to these economists, certain limits will be applied to state subsidies to agriculture. In many countries around the world, such as the United States, the European Union and Japan, the development of the agricultural sector is possible with state support. State support for the agricultural sector in our country is at a lower level, mainly through subsidies. In the process of joining the WTO, the most controversial issue is the subsidization of agricultural exports.

**Constraints in local market:** Membership is expected to help lower domestic prices by strengthening the fight against low-quality products in the domestic market and strengthening food security, low tariffs and transparency, rapid productivity growth, and the establishment of a competitive market conductor.

After our country becomes a member of the WTO, Azerbaijani exporters can benefit from the following advantages in export activities:

- To use rich information resources with the help of WTO institutions and to achieve a fair settlement of disputes arising in the course of trade activities;
- possibility of guaranteed access to the domestic market of the member countries of the organization;
- to act as an equal member in multilateral trade negotiations, as well as to gain opportunities to influence world trade (Ibadoglu G., 2017, p. 13);

Azerbaijani importers will have the following advantages:

- minimization of import duties is expected to increase competitiveness in the domestic market;
- possibility for consumers to get higher quality and lower price products and services.
- low tariff rates lead to a mini-mummification of the final cost of goods and materials, as well as semi-finished products and complexes, as well as the final cost of the work (service), resulting in lower prices for products (Ibadoglu G., 2017, p. 13);

In the process of integration into the world economy, WTO membership is planned to create the following losses for our Republic:

- low competitiveness of products and services is expected to leave the market.
- tax and customs revenues of the state budget may be reduced.
- due to the use of patents in the import of advanced technologies, the presence of commission costs may increase the costs of the industry and reduce revenues.
- the gradual abolition of state support for the development of local industry over time may create conditions for an adequate adaptation crisis (Ibadoglu G., 2017, p. 14).

Identifying the challenges facing the current state of export potential can be done by studying the use of foreign experience in the field of export stimulation.

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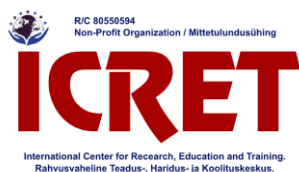
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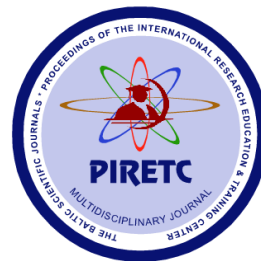
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