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Section 1
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THE ROLE OF SOCIAL MESSAGING IN THE HEALTH PROMOTION AGAINST COVID-19 IN UZBEKISTAN

During the Covid 19 pandemic, according to health guideline, the people of Uzbekistan maintain social distancing along with the rest of the world. A special republican commission «To prepare a program of measures to prevent the import and spread of the type of coronavirus into Uzbekistan» has been created on the territory of the Republic of Uzbekistan. The social network is a media by which we can spread a message to many people as most people use it today. Social media and the health care system are a special combination. It is one of the most important ways to raise public awareness of new, emerging and emerging health problems. Through Telegram messenger, a health information platform was created and spread regarding Covid 19 by the Uzbekistan government. People were attached to this platform initially very rapidly, but by the time the subscribers were reduced. Survey explored Covid 19 and updates for the same was gripped by the people very fast through social sites. The study enlightened the area of coordination between the internet and health and shows how we can utilize eHealth more and more in low- and middle-income countries.

Key words: Covid 19, pandemic, messenger, social network.

Introduction

COVID-19 has become a serious global public health problem that has affected most countries worldwide and is characterized by a steady rate of spread, leading the World Health Organization (WHO) to classify it as a pandemic. COVID-19 is transmitted from person to person through respiratory droplets and /or direct contact. [1,2] Worldwide, as of July 27, 2020, there were more than 16,249,165 confirmed cases of COVID-19 and 649,208 deaths. [3,4]

A special Republican Commission was created on the territory of the Republic of Uzbekistan to «Prepare a program of measures to prevent the import and spread of a new type of coronavirus in the Republic of Uzbekistan».[5]The first case of Covid 19 infection was registered on March 15, 2020 in Tashkent.[6] At the end of March 2020, public transport in Tashkent was temporarily stopped; special disinfected buses are provided by the Department of Transport of Tashkent for the transportation of medical personnel of medical institutions of the city based on the number of employees.[7]

The number of cases of coronavirus as of April 1, 2020 in Uzbekistan reached 173. Since April 1, a self-isolation regime has been introduced, and people over 65 years of age are prohibited from leaving their homes. Restrictions on cargo transportation were introduced on April 2, 2020. As of April 3, 2020, the number of confirmed cases reached 223, of which 25 were cured. [8,10]

During COVID-19, social media is a perfect way for individuals and communities to stay connected, even when they are far apart. For

example, when a third of the world's population became infected during the 1918 flu pandemic, according to the Centers for Disease Control and Prevention (CDC), people did not have the same sources of communication that we have now to exchange various news and relevant information quickly.

In modern times, artificial intelligence methods can be used almost not only in all areas of medicine but also in all our lives. Due to its ability to analyze complex medical data, artificial intelligence can be used to diagnose, treat, and predict the outcome of many diseases. [11] Many people are publicly sharing their opinions about various diseases, including COVID-19, on various social platforms. In recent days, it has been possible to see how people, organizations, and businesses use social media to spread COVID-19 and public actions. [12]

Research shows that currently, more than half of the world's population uses social networks. [14] Social media and the healthcare system are a specific combination. This is one of the critical ways to raise public awareness of new, emerging and annual health issues. Nowadays, more people are getting news from social networks. As for the elderly, almost 90% of them use social networks to search for medical information and share it. Facebook, Messenger, Twitter, Whatsapp, Telegram, Tik Tok, Viber, Skype, etc. are all accessible social media platforms for people to communicate and exchange ideas on all issues, including health issues. [14]

A broad set of Internet communications called «participatory Internet», as online communications provide more accessible and more cost-effective access to many people from different distances of the world. Social networks that allow people to connect, create blogs, platforms that are easily accessible for mobile phones are becoming popular day by day, especially in the health sector. This is very helpful for people to communicate about a particular state of their health with medical professionals, despite the long distance between them. [15-17]

According to research, currently, about 40% of social media consumers between the ages of 18 and 24 say that social media significantly influences their health care decisions. As the Google / Complete Hospital study shows, information technology has a significant impact on healthcare, the results of this study showed that more patients used both online and offline sources to study medical facilities; about 80% of patients used to search before making an appointment; almost 30% of patients who watched online videos made an appointment. [18]

Methodology

Tools Used: Telegram Messenger.

Telegram Messenger is an instant messaging application that requires a phone number (or user name) to connect to Telegram, users can send messages, photos, videos, audio, etc.

Telegram is available for Android, Windows, iPhone, Linux, Windows Phone, OSX. As of October 2013, Telegram had 100,000 daily active users. Moreover, on April 24, 2020, the number of active users of the Telegram app reached 400 million per month. [19-21]

In September 2015, channels were added to Telegram. Channels are one-way messaging, where not users but only administrators can send messages. However, any user has the right to create channels and subscribe to them. Users who join the channel can see the entire message history. Users can join and leave channels at any time. Administrators can grant permission to post comments on the Telegram channel using bots. The channel administrator can get general information about the channel. Each message has its view count, showing how many users have seen the message. [22]

There are now many verified telegram channels from health authorities around the world with official news about COVID-19. Currently, such channels are available in many countries, including Uzbekistan.

myGov Corona Newsdesk (official channel of the Government of India in Telegram for communications and citizen engagement, myGov homepage: mygov.in, myGov, covid19 page: corona.mygov.in, myGov Hindi Newsdesk: https://t.me/MyGovHindi) - A telegram channel created in India about COVID 19 has a more significant number of participants than other channels dedicated to coronavirus cases. It has 2,914,648 members, average post coverage ~209.7 k daily coverage ~4.4 m posts per day ~21 ERR % 7.2% citation index 85.1.[23]

Telegram as a social messenger for health promotion in Uzbekistan: The COVID-19 pandemic has led to a global health crisis that greatly impacts quality of life. People began to look for all sorts of reliable sources of information about the coronavirus, its spread and prevention, in order to provide themselves and their loved ones with reliable protection.

There are more than 30 Telegram channels about Covid 19 and related cases in Uzbekistan. The most popular and well-known telegram channel is «Koronavirus Info / stay home!» (Koronavirus Info | Uyda Qoling! @ koronavirusinfouz).

Data collection method:

An official Telegram channel with information about the coronavirus has been created for the citizens of Uzbekistan. The messages were published in Uzbek and Russian.

The authors of the initiative were the Ministry of Health, the Agency of Information and Mass Communications under the President of the Republic of Uzbekistan, and Uzbekistan's Youth Union.

The new channel was viral among the country's citizens: in just four hours of operation, the number of subscribers has reached 30 thousand people and continues to grow. The channel had more than 1 million members. This channel is in second place among all the most popular Uzbek telegram channels. Average post reach ~400.1 k daily reach ~5.2 m, posts per day ~15, delude % -35.4%, citation index -798.92. The channel was dedicated to all current events related to the pandemic and coronavirus at the national and international levels. This fast-growing channel publishes daily the number of new coronavirus cases in Uzbekistan and around the world. In addition, channel participants can get reliable information on the coronavirus, how this virus is transmitted, how the clinic of this disease manifests itself, how to carry out prevention, and where to go in the case of a coronavirus clinic, and so on.

This channel was rapidly growing in comparison with similar channels and gaining popularity at the national level. For example, compare with the channel of the same name created in Ukraine (Coronavii @ Covid19_ukraine), where the channel had 707,943 subscribers, the average post reaches ~ 282k, daily coverage ~ 840.1 k, posts per day ~ 4, ERR % -39.8% and citation index-149.52, then you can see the good popularity of this channel in the Telegram messenger.

This application contains a set of frequently asked questions and answers prepared by qualified professionals by category. In addition, citizens can correspond with operators, send them questions and receive answers from them. The operators of the online consulting module work 24/7. In addition, the official website of the Ministry of Health has created an opportunity for COVID-19 to pass a preliminary test for coronavirus infection. Qualified virologists formulate control questions. [24] A team of 85 experienced doctors, professors and teachers answers all the population questions around the clock. The chat rooms of the consultant are available in Uzbek and Russian.

Ethical issue:

The data was anonymously collected. The system has no identity of the respondent. As per Uzbekistan rules, the study does not need ethical permission.

Figure 1

Result & Discussion

Within a month after its creation, the channel actively published posts about the coronavirus, its spread in Uzbekistan and worldwide, and ways of infection, possible symptoms, prevention measures from COVID 19, changes and news related to the pandemic and quarantine in Uzbekistan. The number of posts in March and April was about 1500-2000 per month; then, it decreased in May and June (Fig.1). This is because, at the beginning of the pandemic and quarantine, people began to take an interest in this situation and look for sources where they can get reliable information about the coronavirus. Since the appearance of many other sources of information (TV, other channels in Telegram, Internet, etc.), posts in this channel fluctuate and there were not as many as there were in March and April.

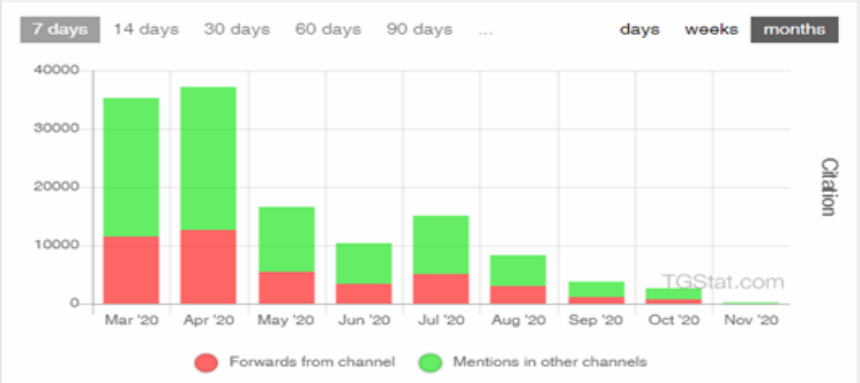

Figure 2

As posts, there were also many citations – about 40,000 per month at the beginning of the channel's creation, and then from May month, they began to fall (Fig. 2).

Figure 3

Subscribers continued to grow, mainly until April and July, just during the peak of quarantine in Uzbekistan. Further, the number of subscribers only began to drop (Fig. 3), possibly because the quarantine ended in Uzbekistan and people began to receive information about the pandemic and coronavirus at work, on the street, in public places, etc. Therefore, it shows that COVID 19 cases are declining according to the statistics and users leave the channel. However, many people still have a wariness and interest in COVID 19. This means that many people were interested in these questionnaires and searching for reliable information, so many of them remain in this channel.

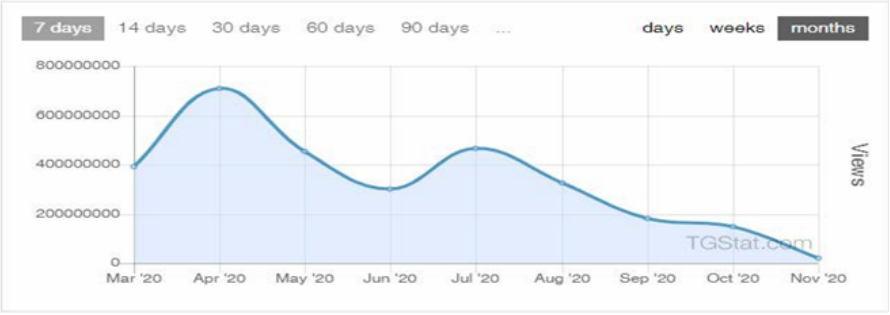

Figure 4

Accordingly, the views began to decrease in this channel (Fig. 4). [25]

Besides the posts, general information about the coronavirus, pandemic and everything related to COVID 19, the channel conducted a questionnaire among the subscribers in order to know to what extent the necessary and reliable information covers people, what they know about the coronavirus and what they would like to learn about this disease and pandemic.

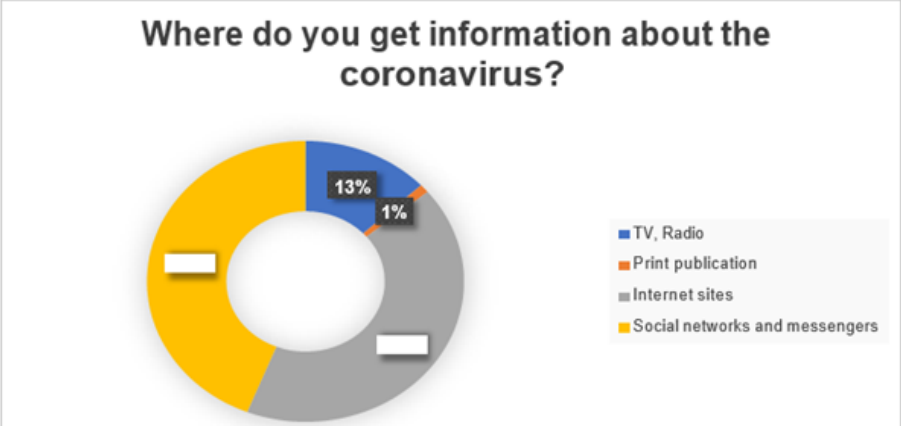

Figure 5

For example, the questionnaire of March 25 asks where people get information about the coronavirus from 323.3 K people responded to this questionnaire by leaving their vote, and 1.3 M subscribers watched it. Thus, almost a quarter of all subscribers replied to this question (Fig. 5).

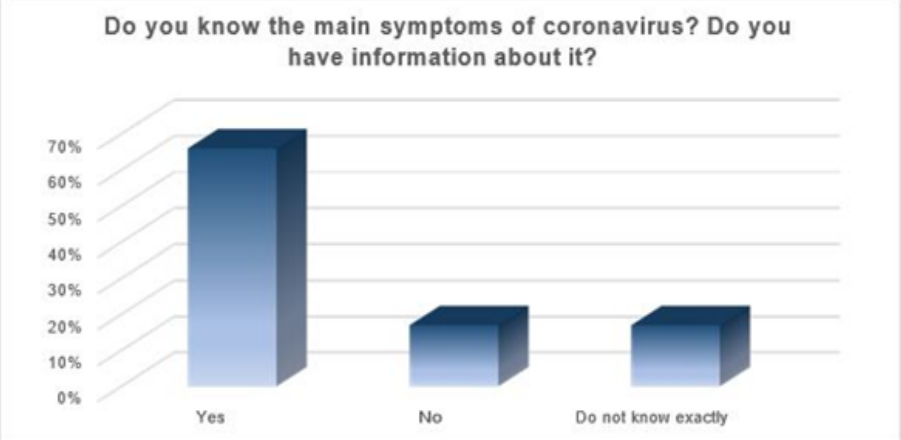

Figure 6

Another survey from March 26 asks whether people know the main symptoms of coronavirus and whether they have information about it. This question was viewed by 921.8 thousand and answered by thousand people. [26]

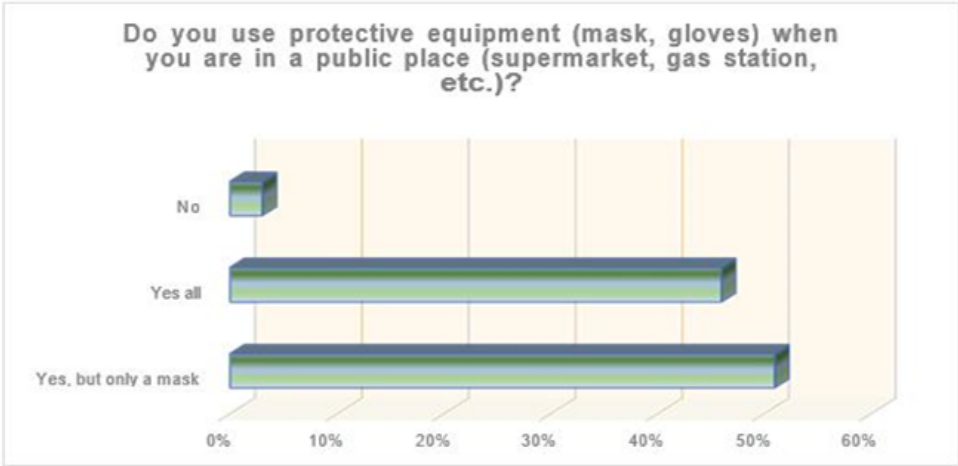

Figure 7

In another survey, subscribers are asked if they use protective equipment (mask, gloves, etc.) when they are in a public place (supermarket, gas station, etc.)? People also responded actively to this questionnaire and showed their interest in this topic. [25]

Conclusions

Social media and the healthcare system are a great combination. Many people are now publicly sharing their opinions about various diseases, including COVID-19, on various social platforms. Social networks that allow people to connect, create blogs, platforms that are easily accessible for mobile phones are becoming popular day by day, especially in the health sector. Telegram Channels are one of the perfect ways for sending messages to unlimited audiences. An official Telegram channel with information about the coronavirus called Koronovirus Info has been created for Uzbek citizens is very popular among the country's citizens. It has more than 1 Million members—this channel in second place among the most popular Uzbek Telegram channels. The channel is dedicated to all current events related to the pandemic and coronavirus at the national and international levels, which help the subscribers to receive reliable information on coronavirus questions, how this virus is transmitted, how the clinic of this disease manifests itself, how to carry out prevention, as well as where how to contact in case of a coronavirus clinic and so on.

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DETERMINING THE QUALITY OF LIFE IN CHILDREN KYZYLORDA REGION

According to the results of the survey, sanitary and educational work is carried out at a low level and children are motivated to improve their dental health. The high dental morbidity was also influenced by the child's nutrition. We found out that the diet of children mainly consists of easily digestible and soft food. On the contrary, in the use of hard food, which requires careful chewing, there are difficulties in 86.0% of cases. Undoubtedly, the high incidence was influenced by bad habits in 54.0% of cases and somatic pathology in children of the studied region. When determining the quality of life, it turned out that the material and housing conditions of students ' stay were partially satisfactory-34 (68.0%) and satisfactory - 15 (30.0%), there was not always hot water, toilets were outside the house, but 98.0% of cases almost had cold water in the house.

According to the results of the survey, the quality of life scores of children in the region were calculated, which amounted to 28.6 points for boys and 30.3 points for girls, which corresponds to a low level of quality of life. It follows from the above that it is necessary to carry out large-scale preventive work, which consists in observing and improving the basics of hygiene literacy among children and parents, increasing motivation to carry out therapeutic and preventive measures.

Key words: quality of life, dental morbidity, hygiene, housing and living conditions, nutrition.

Introduction Relevance of the problem

The World Health Organization defines quality of life as «the perception by individuals of their position in life in the context of the culture and value systems in which they live, and in a state with their own goals, expectations, standards, and concerns» [1,3].On the other hand, the «quality of life» is a set of traits and properties of the individual and society, living conditions, health, work, nutrition, recreation, and the state of the external environment [3, 6,13,14,15]. Thus, the quality of life – this concept is subjective and multidimensional, covering physical and professional functions, psychological state, social interaction and somatic sensations [4, 9,10,11,12].

Currently, various indexes and questionnaires have been developed and widely used abroad to analyze and evaluate the state of quality of life and dental health of both children and adults. These indices are objective measurement tools that evaluate dental health in terms of its impact on the quality of life. Each of these indices is designed to measure the frequency and degree of influence of dental problems on functional and socio-psychological well-being [1,2,3,4,5,6, 8].

In Kazakhstan, to date, the tools for assessing dental health have not been developed, and to solve this problem, we have developed a questionnaire to determine the quality of life of the child population in relation to dental health.

The purpose of our study was to study the influence of social and psychological factors of a person on the pathological state that occurs in the oral cavity in various dental diseases, which was the beginning of the development and implementation of various tools for measuring the quality of life in relation to dental health.

Materials and methods of research

The basis for the clinical material was the Children's Dental Clinic in Kyzylorda. Our group of researchers developed a questionnaire for the quality of life of a child, in which the answers to

the questions are built on the type of the Likert scale, ranked by 5 points, respectively, according to the answers: «never» – 0 points, «extremely rarely» – 1 point, «often» – 2 points, «very often» – 3 points, «constantly» – 4 points. The procedure for calculating the index involves summing up separately on the scales (per-scale indicators) and in general on the questionnaire (integral indicator OHIP-14 RU) (from 0 to 56 points).

The assessment of the quality of life corresponded to the following number of points: - 0-14 points – «good» quality of life; - 15-28 points – «satisfactory» quality of life; – 29-42 points – «unsatisfactory» quality of life; – 43-56 points – «poor» quality of life in accordance with the figure (Figure 1,2).

The questionnaire table includes age, gender, knowledge of how he spends his free time, and the state of his health, and this is a purely subjective indicator of objectivity (Table 1). We set the following requirements for the quality of life questionnaires: multi-dimensionality, simplicity and brevity, acceptability, and applicability in various linguistic and social cultures. One of the important requirements in the study of children for the quality of life was the presence and assistance of parents in filling out the questionnaire, regardless of age, in order to monitor the degree of loss of dental health.

It should be noted that the questions concerned how problems in the mouth affect the physical well-being of the child, his ability to fully eat, communicate with other people, perform social functions. The assessment of the quality of life in this work was based on filling out special questionnaires. Correct and honest filling out of the questionnaire allowed us to make an objective picture of periodontal disease, as well as to find out the child's attitude to his health, the reasons that led to this pathology.

The survey involved children from 7 to 13 years old, a total of 50 children. Of these, by gender: 27 (46.0%) boys and 23 (54.0%) girls, according to the figures (Fig.1,2).

Table 1 – Questionnaire (corresponds to the tableEXELL) OHIP-14 RU

1. numbering
2. inspection day
3. month of inspection
4. Gender 1-male 2-female
5. birthday
6. month of birth
7. year of birth
8. How often do you visit the dentist in the last three years
1. never
2. extremely rare
3. often
4. very often
5. constantly
9. How often do you eat soft food?
1. constantly
2. very often
3. often
4. extremely rare
5. never
10. If there are concomitant diseases, how often do they bother you?
1. constantly
2. very often
3. often
4. extremely rare
5. never
11. How often do you brush your teeth?
1. Never
2. extremely rare
3. often
4. very often
5. constantly

12. Do you use a mouthwash?
1. Never
2. extremely rare
3. often
4. very often
5. constantly
13. Do teeth bleed when brushing?
1. constantly
2. very often
3. often
4. extremely rare
5. never
14. Is there any pain in the teeth?
1. constantly
2. very often
3. often
4. extremely rare
5. never
15. Are there any difficulties when eating?
1. constantly
2. very often
3. often
4. extremely rare
5. never
16. Is there any difficulty in eating hard food
1. constantly
2. very often
3. often
4. extremely rare
5. never
17. Have you noticed the following habits: sucking your fingers, biting your nails, pens, etc.
1. constantly
2. very often
3. often
4. extremely rare
5. never
18. Is there bad breath?
1. constantly
2. very often
3. often
4. extremely rare
5. never
19. What are your material and housing conditions?
1. nedovl
2. partially satisfied
3. udovl
4. good news
5. excellent results
20. Does he often drink carbonated drinks
1. constantly
2. very often
3. often
4. extremely rare
5. never
21. Does he often drink national drinks (kumis, shubat, saumal)?
1. never
2. extremely rare
3. often
4. very often
5. constantly
22. How often do you do any sport?
1. Never
2. extremely rare
3. often
4. very often
5. constantly
23. Is there a lack of adequate nutrition?
1. constantly
2. very often

3. often
4. extremely rare
5. never
24. Do parents have a paid job?
1. Do not have
2. seasonal
3. from time to time
4. 9-10 months a year
5. permanent
25. Does the house/apartment have cold tap water?
1. never
2. extremely rare
3. often
4. very often
5. constantly
26. Does he often consume dairy products?
1. Never
2. extremely rare
3. often
4. very often
5. constantly
27. Do you have difficulty pronouncing consonants and vowels?
1. constantly
2. very often
3. often
4. extremely rare
5. never
28. Is there a feeling of constraint in communicating with peers?
1. constantly
2. very often
3. often
4. extremely rare
5. never

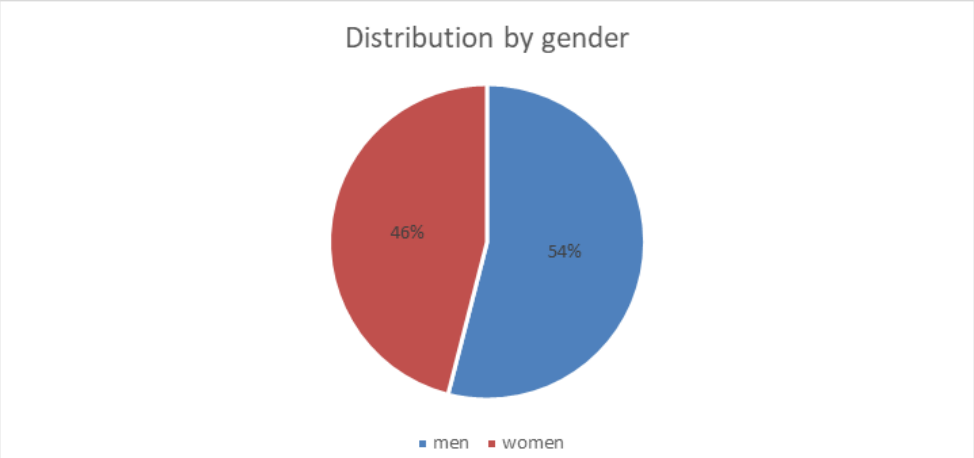

Figure 1 – Distribution of children by gender Figure 2. Distribution by age and gender

Results and their discussions

The study provided answers to the following questions in accordance with Table 2. According to the results of the questionnaire, the question: «How often do you visit the dentist in the last three years?» in 42% of cases, children did not visit the dentist, because of fear of dental manipulations, extremely rarely visited the doctor-22% of children.

At the same time, 34% of children visited the dentist's office «often» and «very often». We believe that the region is conducting low-level sanitary and educational work, there is no motivation for oral cavity sanitation either for parents or children.

Table 2 – Questions and answers asked

№	Questions	Never	Extremely rare	Often	Very often	Constantly
1	How often do you visit the dentist in the last three years	21 (42,0%)	11 (22,0%)	17 (34,0%)	1 (2,0%)	
2	How often do you eat soft food?	6 (12,0%)	40 (80,0%)	4 (8,0%)		
3	If there are comorbidities, how often do they bother you?	4 (8,0%)	2 (4,0%)	37 (74,0%)	7 (14,0%)	
4	How often do you brush your teeth?	3 (6,0%)	38 (76,0%)	9 (18,0%)		
5	Do you use a mouthwash?	45 (90,0%)	5 (10,0%)			
6	Do teeth bleed when brushing?		13 (26,0%)	23 (46,0%)	14 (28,0%)	
7	Is there any pain in the teeth?		23 (46,0%)	8 (16,0%)	19 (38,0%)	
8	Is there any difficulty in eating?	9 (18,0%)	11 (22,0%)	23 (46,0%)	7 (14,0%)	
9	How often do you eat hard food		11 (22,0%)	32 (64,0%)	7 (14,0%)	
10	Have you noticed the following habits: sucking your fingers, biting your nails, pens, etc.	4 (8,0%)	10 (20,0%)	13 (26,0%)	21 (42,0%)	2 (4,0%)
11	Is there bad breath?	4 (8,0%)	27 (54,0%)	12 (24,0%)	7 (14,0%)	
12	What are your material and housing conditions?	1 (2,0%)	34 (68,0%)	15 (30,0%)		
13	Does he often drink carbonated drinks		3 (6,0%)	22 (44,0%)	25 (50,0%)	
14	Does he often drink national drinks (kumis, shubat, saumal)?	32 (64,0%)	13 (26,0%)	5 (10,0%)		
15	How often do you do any sport?	19 (38,0%)	25 (50,0%)	6 (12,0%)		
16	Is there a lack of adequate nutrition?	30 (60,0%)	11 (22,0%)	9 (18,0%)		
17	Does the house/apartment have cold tap water?	1 (2,0%)	22 (44,0%)	26 (52,0%)	1 (2,0%)	
18	Does he often consume dairy products?	15 (30,0%)	22 (44,0%)	13 (26,0%)		
19	Do you have difficulty pronouncing consonants and vowels?			11 (22,0%)	39 (78,0%)	
20	Do you have a feeling of constraint in communicating with your peers?		5 (10,0%)	29 (58,0%)	16 (32,0%)	

The diet at the present stage has excessive softness, and the children of the studied region often use boiled, fried, cutlets, stewed food, buns, which are easier to chew and digest, from the words of the children it was clear that they prefer everything soft in 100 % of cases, answering the question: «How often do you eat soft food?», affirmatively («constantly», «very often», «often»). In turn, often when eating soft food, the teeth are not cleaned naturally and everything remains in the interdental spaces, causing tooth decay. It is well known that crushed and soft food does not give a full load on the dental system of the child, including on the periodontal tissue.

It should be noted that a number of scientific studies have been devoted to determining the impact of adverse environmental factors on the child's body in the Aral Sea region. These studies were conducted in 4 major independent research centers in Sweden, Luxembourg, Germany and Japan [9]. The studies included a comprehensive examination of

the children of the Kyzylorda region: general clinical, functional, and enzymological studies of urine, assessment of physical development and puberty, determination of hormone levels, determination of immunity indicators, accounting for small developmental abnormalities, and study of the gene apparatus. Also, many researchers have established «rejuvenation of pathology», i.e. the presence of such diseases as atrophic gastritis, urolithiasis, chronic bronchitis, which are not typical for young children. Thus, it was found that there are no healthy children in this region, and 89 % of children have several chronic diseases at the same time[9,11]. And so it is not surprising that the question: «If there are concomitant diseases, how often do they bother you?» was answered in almost 86% of cases as follows: «constantly» – 4 (8.0%),» very often «- 2 (4.0%),» often «- 37 (74.0%) and only» extremely rarely « in 7 (14.0%) cases.

Among the diseases of a somatic nature, according to parents, diseases of the organs of vision, hearing, gastrointestinal tract, hypertension syndrome are noted. This factor is undoubtedly one of the reasons contributing to the development of many dental diseases, including periodontal diseases.

Oral hygiene is the basis for the prevention of caries and periodontal diseases. And to the next question: «How often do you brush your teeth?» children of this region 3 children answered that they do not like to brush their teeth at all, and in 76.0% of cases they «extremely rarely» brush their teeth, which explains the high prevalence of caries and its complications, periodontal diseases.

According to our survey results, mouth-washers are a «curiosity» for children of the studied region, because 90% of children answered «never» to the question: «Do you use a mouthwash?», and only 5 children of teenagers «extremely rarely» use it. This also indicates a low level of sanitary and educational work.

One of the first symptoms of periodontal diseases is bleeding when brushing your teeth, when eating. And to the question: «Do teeth bleed when brushing?» in 72% of cases, they answered:» very often « - 13 (26.0%), «often» - 23 (46.0%). A common cause of bleeding was: poor oral hygiene, improperly applied filling. The danger of periodontal diseases lies in the fact that it is asymptomatic.

According to the results of the answer to the question: «Is there any pain in the teeth?» in 62% of cases, children answered in the affirmative, which is associated with a high prevalence of caries and its complications, especially complicated forms of caries. Pain in the teeth also explains the fact that children are not interested in brushing their teeth. The question «Is there any difficulty in eating?» was answered positively by 86% of children. This issue was associated with the presence of carious cavities, periodontal diseases, and dental anomalies.

It should be noted that the results of our research have established the prevalence of sub - and decompensated forms of caries, and especially the deplorable condition in the Aral Sea region with the first and second permanent teeth. Caries damage to these teeth begins at the age of 7 and is 61%, then after 10 years, the incidence of caries of these teeth is 100 %. Starting from the age of 14, children begin to lose these teeth in 46.4 % of cases. The absence of chewing teeth or the presence of pain in these teeth causes difficulty eating.

One of the ways to prevent periodontal diseases, we consider the mandatory use of hard food, which requires careful chewing. Such as carrots, apples, cabbage, kurt, meat with bones, greens. As a result of active chewing movements of the maxillofacial area, the surface of the teeth is cleaned, there is a rush of blood to the dentoalveolar papillae, which provides nutrients and oxygen, thereby strengthening the entire dental apparatus. But the children of this region, according to the results of the survey, experienced difficulties in eating hard food in 86% of cases, and were limited only to soft and easily digestible food.

A lot of scientific research works are devoted to the harm of bad habits .They contribute to the development of parafunction of the muscles that surround the tooth and dentition, cause violations of the position of groups and individual teeth, displacement of the lower jaw, and changes in the bite. They also subsequently cause the development of periodontal diseases. It should be noted that with age, these habits are fixed to automatism and involuntariness. Therefore, the elimination of these habits is a difficult task, it requires a very long patience on the part of parents and dentists. To the question: «Have you noticed the following habits: sucking fingers, biting nails, pens, etc.» our respondents answered in the affirmative in 54.0 % of cases, which indicates a high risk of changes in the dental apparatus during the growth of the child. They mostly noted: finger sucking, sucking and biting their lips, biting their nails and pens, chewing on one side, sleeping with their mouth open.

Halitosis (bad breath) in children of the studied region was determined in 86% of cases, the causes of which are waste products of bacteria that multiply in the mouth, nasopharynx and gastrointestinal tract. The main etiological factors for the development of halitosis in children of this region were: poor oral

hygiene, caries and its complications, periodontal diseases, rhinitis, sinusitis, frequent consumption of carbohydrates, etc.

The material and housing conditions of students ' stay play an important role in dental health. Unfavorable living conditions lead children to a depressive state, an increase in the risk of developing dental caries and periodontal disease, when there are no conditions even for simple oral hygiene. To the question: «What are your material and housing conditions?» there were the following answers: partially satisfactory-34 (68.0%) and satisfactory-15 (30.0%), total -98% of students. This question included: what is the area of the apartment (house), whether there is hot and cold water in the apartment(house), whether there is a sewer, whether the child has his own desk, etc. According to the responses of the respondents, it was possible to judge that the apartment (house) did not always have hot water, the toilets were outside the house. And only in 2 % of cases there was a small area of the dwelling and they had to bring or buy cold water.

It is well known that carbonated drinks contain dyes, a large amount of sugar, artificial sweeteners (aspartame), which cause allergic conditions, headaches, depressive states, diabetes and constant use causes tooth decay. According to many researchers, carbonated drinks were the cause of obesity in 20% of children in the United States [11,14]. According to our research, the attitude to carbonated drinks in all children of the studied region is positive. In 6.0% of cases, it is consumed constantly, in 44.0 % - they drink these drinks «very often». Half of the students surveyed answered «often», meaning drinking drinks 4-5 times a week. It should be noted that this is also one of the factors of the high spread of caries in the region, as sweet drinks disrupt the pH balance in the oral cavity, microorganisms that are located in the thickness of the plaque absorb carbohydrates and secrete acid, which aggressively acts on the unformed tooth.

National drinks (kumis, shubat, saumal) have healing properties. Many studies have proven that they contain 10 times more vitamins than cow's milk. Among them-vitamins A and E, vitamins B and C, calcium, phosphorus, folic and pantothenic acids. This product contains 2 times less protein and 1.5 times less lactose. These drinks increase the immune system, strengthen teeth and bones, improve blood circulation, thanks to the thiamine in the drink-strengthens the nerves, improves the functioning of the gastrointestinal tract (due to pantothenic acid), normalizes the growth and development of the body. According to our research estimates, 64% have never drunk it, 26% use it once a week, and only 10% of children use it «often». Although national drinks, we think it is necessary to introduce a set of preventive measures for dental diseases.

The impact on the dental health of children of engaging in any kind of sport is not always clear. Currently, in the country, the attendance of any sports sections is put on a paid basis, which is not available to many children. This explains that 38% of children do not play sports at all, in 50% of cases - «extremely rarely» and only 12% of schoolchildren attend some kind of sports activities. But as practice shows, those children who play sports develop in the character of the child responsibility, perseverance, and, accordingly, the habit of oral hygiene and mandatory sanitation.

To the question: «Is there a lack of adequate nutritions the answer was «constantly» in 60.0% of cases and in 40% of children, the nutritional value of the diet was often reduced. The question reflects the level of quality of life of schoolchildren, the consumption of the main food groups, the nutritional and energy value of diets. The analysis showed that children are more likely to consume bread products, potatoes, sugar and confectionery. There is a restriction on the consumption of vegetables, fruits, herbs, fish, etc. Perhaps this is due to low income in the family budget and low dental culture. At the same time, a variety of high-quality food contributes to the physical and mental development of the child.

In many ways, the quality of life of a child is determined by the level of wages of parents, i.e. how fully they can improve the standard of living of their children. All parents of the children surveyed have some kind of job, but only 10.0% of parents have a permanent job. In 56.0% of cases, parents have seasonal work, 34% of parents said that they work «from time to time». More than half of parents have an average income level [15].

The presence of tap water in the house is one of the priority social tasks and the answer to the question: «Does the house/apartment have cold tap water?» was very important. The survey revealed that in more than half of the cases (54.0%), cold tap water flowed in the house, in 44% of cases the water supply was limited, and only in 2% of cases there was no tap water in the house/apartment. Consequently, most of the children were able to maintain oral hygiene.

It is known that dairy products contain protein, fats, carbohydrates, including calcium, amino acids, phosphorus, potassium, vitamins D, A, B12, B1, which are necessary for a growing body. According to the survey, 30.0 % of children do not like to

consume dairy products at all, 44.0% - consume it in small quantities, and only 26% of children have dairy products in their daily diet. This may be due to the quality of the dairy products produced, low motivation of parents in the consumption of dairy products by children, increased sensitization of the children's body to kozein, etc.

Difficulties in the pronunciation of consonants and vowels were «often» experienced in 22.0% of cases and «extremely rarely» - in 78.0% of cases in children of this region. The share of such difficulties was accounted for by children of primary school age. We believe that this was due to the age characteristics of the child, the presence of small anomalies in the development of the oral mucosa, in particular the short frenulum of the tongue. It is well known that the formation of sound pronunciation occurs gradually and some complex sounds in terms of articulation appear later.

The answer to the question: «Is there a feeling of constraint in communicating with peers?» is yes in 68.0% of cases. The main reasons for embarrassment in communicating with peers were: bad breath, swallowing some sounds, stuttering, missing some teeth, bleeding teeth, etc. From a psychological point of view, the lack of communication creates a feeling of dissatisfaction with life, such children become timid and withdrawn. Increasingly, shyness prevents children from demonstrating their cognitive abilities. We believe that the solution to this problem in half of the cases lies in improving dental culture.

Conclusion

Thus, according to the results of the survey, sanitary and educational work is carried out at a low level in the region, there are problems with the psycho-emotional state of children in this region, since in 42 % of cases they do not visit the dental office due to a negative attitude to dental manipulations. Also at a low level is the motivation of children in relation to oral hygiene, because in 76.0 % of cases it is extremely rare to brush their teeth.

The high dental morbidity was also influenced by the child's nutrition. We found out that the diet of children mainly consists of easily digestible and soft food, which does not give a full load on the dental system of the child, including on the periodontal tissue, carbonated drinks.On the contrary, in the consumption of hard food, which requires careful chewing, there are difficulties in 86.0% of cases. In relation to national drinks, 64.0 % of cases do not drink at all. According to the survey, 30.0 % of children do not like dairy products at all, 44.0% - use it in small quantities. The basic role in the spread of dental diseases, including periodontal diseases, is played by the use of food products, the nutritional and energy value of which is low. Together, these factors lead to halitosis in 86.0% of cases.

Undoubtedly, the high incidence was influenced by bad habits in 54.0% of cases and somatic pathology in children of the studied region. Therefore, there were high rates of symptoms of the disease, for example, in 72.0% of cases they had bleeding when brushing their teeth and in 62.0% of cases there were pain when eating.

When determining the quality of life, it turned out that the material and housing conditions of students ' stay were partially satisfactory-34 (68.0%) and satisfactory - 15 (30.0%), there was not always hot water, toilets were outside the house, but 98.0% of cases almost had cold water in the house. Consequently, most of the children were able to maintain oral hygiene.

All parents of the children surveyed have some kind of job, but only 10.0% of parents have a permanent job. In 56.0% of cases, parents have seasonal work, 34% of parents said that they work «from time to time».

According to the results of the survey, the quality of life scores of children in the region were calculated, which amounted to 28.6 points for boys and 30.3 points for girls, which corresponds to a low level of quality of life. It follows from the above that it is necessary to carry out large-scale preventive work, which consists in observing and improving the basics of hygiene literacy among children and parents, increasing motivation to carry out therapeutic and preventive measures.

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CERVICAL CANCER ELIMINATION PROGRAM

Cervical cancer is one of the most common types of malignant neoplasms in women. According to Globocan, in 2018, 570000 new cases of cervical cancer and 311 thousand deaths from this pathology were registered. More than 85 % of cases of cervical cancer are registered in developing countries, where a third of all women are detected in the advanced stage of the disease.

The association of cervical cancer with the chronic persistence of the human papillomavirus is unquestionable. To date, more than 200 types of HPV (human papillomavirus) are known, 12 of which are dangerous to humans and can cause the development of cervical cancer

The discovery of the link between HPV infection and breast cancer has changed the approach to cervical cancer screening in many ways. The fact that cervical cancer is primarily associated with an infectious agent has led to the development of new, more sensitive HPV-based screening tests for secondary prevention of cervical cancer and three HPV vaccines that are used for primary prevention.

The only method that prevents the development of cervical cancer is HPV vaccination and cervical cancer screening. To date, there are 3 recombinant HPV vaccines: a bivalent HPV vaccine of type 16 and 18, a quadrivalent HPV vaccine of types 16, 18, 6 and 11, and a nine-valent vaccine of types 6,11,16,18,21,33. 45,52 and 58 . HPV vaccination has entered the immunization calendar in more than 100 countries where the experience of using the vaccine is more than 10 years.

Large international randomized clinical trials have shown that HPV vaccines are safe and highly effective against persistent infection and precancerous lesions of the cervix in women (vaccine efficacy ≥93%). These vaccines target high-risk HPV types, which are responsible for the development of about 90% of cervical cancer. Countries that achieved high vaccination coverage saw a 73-85% decrease in HPV prevalence and a 41-57% decrease in high-grade lesions among young women less than 10 years after the introduction of HPV vaccination

Organized, well-designed primary and secondary prevention strategies can have a positive impact on the incidence and mortality rates caused by cervical cancer.

Key words: cervical cancer, HPV, vaccination, screening.

Cervical cancer is one of the most common types of malignant neoplasms in women. According to Globocan, in 2018 were registered 570,000 new cases of cervical cancer and 311,000 deaths from this pathology. In more than 85% of cases, cervical cancer is registered in developing countries, where one third of all women are diagnosed in an advanced stage of the disease.

With the invention of the Pap test in the 1940s by George N. Papanicolaou and H.F. Trout, cervical smear cytology has become a reliable and uncomplicated method for screening for cervical cancer [1]. This process entails the detachment of cervical cells, which are then fixed, viewed under a microscope and subsequently morphologically interpreted. The pap test allows assessing changes in nuclear chromatin, necrosis, determining the degree of cellular degeneration and distinguishing the maturity of squamous epithelial cells [2].

Screening for cervical cancer using a cytological smear is widely accepted as a public health policy in many countries. The International Agency for Research on Cancer (IARC) has determined that the incidence of cervical cancer can be reduced by at least 80% by introducing Pap-based cervical cancer screening programs every three to five years for women aged 35-64 [3,4,5]. Nevertheless, there are disadvantages of cytological examination. The main disadvantages of the PAP test are that the results depend on the quality of the sample collected during the study, the identification of morphological changes in the cells and the need to retest if the results are unsatisfactory or questionable, which has serious medical, economic and legal consequences. [6]. Despite constant efforts to improve the results of cytological examination of the cervix, its sensitivity is not optimal, and the method still gives a large number of borderline results.

The association of cervical cancer with chronic persistence of human papillomavirus is undeniable. To date, more than 200 types of HPV (human papillomavirus) are known, 12 of which are dangerous to humans and can cause the development of cervical cancer [7,8].

It has been proven that (HPV (16/18/31/3 5/39/45/51/52/56/58/66/68) are responsible for the development of more than 97% of cases of cervical cancer, while low-risk types (HPV6) / 11/40/42/43/44/54/61/72) are associated with anogenital and laryngeal papillomas [12,13]. The aforementioned HPV16 and HPV18 are the most common types of HPV and are responsible for 70% of cervical cancers worldwide (~ 50% HPV16, ~ 20% HPV18) [9,10].

It is estimated that approximately 80% of sexually active women will contact the infection during their lifetime, and in most cases (> 90%) it will be a temporary asymptomatic infection that is cleared by the immune system within the first year of infection [11,12]. Only chronic persistence of HPV infection can lead to the development of low or high grade cervical intraepithelial neoplasia, which can ultimately progress to cervical cancer [12,13,14].

The discovery of the link between HPV infection and cervical cancer has changed the approach to cervical cancer screening in many ways. The fact that cervical cancer is primarily associated with an infectious agent has led to the development of new, more sensitive HPV-based screening tests for the secondary prevention of cervical cancer and three HPV vaccines that are used for primary prevention.

Unlike screening methods based on cytology, HPV testing does not rely on morphological interpretation and is based on the detection of HPV DNA and RNA, or other viral markers. Over the past two decades, HPV testing has been recognized as an effective screening tool in developed countries [15].

The results of the ATHENA multicenter study of 47,000 women showed that 10% of women positive for HPV types 16 and 18 had severe cervical lesions (HSIL) and were not detected during cytological examination [16]. Data on false negative Pap smears indicate that the failure rate of the PAP test in developed countries is about 28-41%. [17]. The low sensitivity of the PAP test, as well as errors in the analysis and interpretation, necessitate re-screening and increases the interest in the development of more accurate and reliable screening tests [18]. Given the problems of cytological screening, researchers began to look for solutions through the introduction of liquid cytology and HPV testing [19].

A study in Mexico comparing two screening methods found that a combination of a PAP test and an HPV test was more cost effective than using a single PAP test [20]. In 2007, IARC recommended HPV testing as the primary screening.

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DETERMINING THE TYPES AND SEVERITY OF VIOLENCE AGAINST WOMEN IN AFGHANISTAN

Violence has a negative impact on various aspects of women's health, including quality of life, social functioning, physical health and is one of the most considerate human rights issues in Afghanistan. The aim of this study: to determine the anatomical parts, types and severity of injuries in cases of violence against women in Afghanistan.

This study is an Analytic Cross-sectional study. Primary data containing information referring to cases of violence against women registered from January 2019 to January 2021 were extracted from Afghanistan Forensic Science Organization. The scope of interest in this study was females over the age of 18 and they were inclusive of Afghan women.

he average age of women was 22.3 and more than 80% of them had primary and secondary education; this study shows in 2019 the most injuries were limbs and nervous injury was only one case. (table 1)

In 2020 most injuries were limbs and nervous injury was only one case. (table 1) Table 2 shows that most of injuries were moderate level and mild injuries were the next and severe injuries with 20 cases was last of this rank. In 2020 most of them were moderate level and after that was mild and severe level. In additional, Type of injuries in 2019 shows that 38.2% of injuries was blunt, 4.9% sharp, 2.2 thermal and 0.02% was unclear. In 2020 blunt injuries was the first injuries and unlike 2019 weapon reported as injures types (table 3).

With the passage of time and the civilization, the intellectual levels of individuals in society increased and the thinkers of societies became more prominent in the presence of women alongside men, so women were considered complementary to men, and this was the beginning of changing women's status.

Key words: injuries, violence against women, Afghanistan.

Introduction

Women's health impacts the overall family health and society and helps advance the goals of growth and development of the country. Numerous studies in different countries show that women are more prone to mental disorders and psychosocial problems than men for various reasons. Violence against women is any act of gender-based violence that has direct or indirect consequences, including physical, sexual and psychological harm or the suffering of women. Behaviors that impose fear and intimidation, coercion, and deprivation of liberty on women, both in women's social and private lives, include sexual, economic, verbal, and abusive threats [1]

In general, all types of violence occur as a result of severe disrespectful behaviors that have many psychological and physical effects [2]. Domestic violence is seen in four forms: psychological-verbal, economic, physical and sexual. The psychological-verbal type includes: the use of isolating methods (such as weakening women's relationships with others, preventing telephone contact or family visits, and Friends), instilling fear (such as threatening to physically harm, threatening to alienate or harm children) or cursing, humiliating, harassing and not talking to them. Economic violence includes behaviors such as refusing to pay and financing, encroaching on or seizing women's property, or harassment in the workplace; So as to lead to the loss of the woman's source of income. Physical violence includes repetitive behaviors based on physical assault in various forms (slapping, punching, kicking, etc.) or preventing the spouse from accessing health care services, as well as sexual violence from any sexual intercourse with the spouse without his or her consent, or it is a relationship with the use of force and anger and unnatural methods[3].

As stated in the Declaration on the Elimination of Violence against Women All Forms of Discrimination against Women, issued by the United Nations General Assembly, the term «violence

against women» means any gender-based violence that causes gender-based physical, mental or psychological harm to women, including any threat to such acts, coercion or deprivation of liberty, whether in public or in private[4]

There are different types of violence against women, including: verbal, psychological, emotional, economic, physical, sexual and even death. Domestic violence against women has been reported from all countries, but data is very difficult to access because in many cultures, women are socio-economically disadvantaged and violence against them, especially in the family environment, has not been identified and in some cases, it is even justified as legitimacy [5]. Studies show the widespread prevalence of this health problem in the world [6].

The World Health Organization [WHO] has classified VAW as a «significant public health problem as well as a fundamental violation of women's human rights. An autopsy on this issue is important not only because it is a violation of fundamental human rights, but also because it affects all women everywhere.

Studies on this subject (VAW) – particularly male partner ferocity – has augmented. Since 2005, when the first results of the World Health Organization (WHO) Multi-Country Study on Women's Health and Domestic Violence3 were launched, the number of intimate partner violence prevalence studies increased fourfold, from 80 to more than 300, in 2008 [7]

Violence against women is one of the most thoughtful human rights matters in Afghanistan. However, in recent years there have been significant changes in the lifestyle of women in field of education, provision of health services, their participation in political and economic issues of the country but unfortunately, deep- rooted traditional and social issues still are in contradiction of realization of and their freedom in many parts of our country[8]

Each year, 1.3 to 5.3 million women in the United States experience Intimate Partner Violence[9] National Inner Partner and Sexual Violence Survey (NVAWS) shows that 30% of women experience physical violence during their lifetime, 9% are raped, and 17% experience non-rape sexual violence. And 48% of them experience psychological aggression [10]. NVAWS reports that approximately 3 in 10 women have experienced defiance, rape, and / or physical violence by an intimate partner. According to supplementary homicide reports by the Federal Bureau of Investigation, 1,026 women were killed by an intimate partner in 2011[11]. Women and young minorities are more likely to experience IPV. People who identify themselves as racial. Native Americans are more than twice as likely to be raped or raped as other racial groups [12].

According to the 2010/2011 Afghanistan Multiple Indicator Cluster Survey, 15% of Afghan women (aged 15-49 years) were married before the age of 15, and 46% before the age of 18. Out of all 92% believe that a husband is justified in beating his wife. In March 2014, the Government published its first report on the elimination of violence against women (VAW) in Afghanistan. 2 Overall 4,505 incidents of violence against women were registered in relevant Afghan ministries in 32 of Afghanistan's 34 provinces between 2012 and 2013[13].

Violence has a great negative impact on various aspects of women's health, including quality of life, social functioning and physical health. Violent women show many problems such as depression, post-traumatic stress and anxiety [14]. Based on the assumption that the initiatives currently in place to tackle the issue of VAW are lacking in that they do not take the diversity of women into account, the aim of this thesis is to determining types of injuries in cases of violence against women in Afghanistan.

Methods and material

Research method was an Analytic Cross sectional study. Primary data containing information referring to cases of violence against women registered from January 2019 January 2021 to were extracted from Afghanistan Forensic Science Organization. The population of interest in this study was females over the age of 18 who reside in Kabul. The population of interest was inclusive of Afghan women. To ensure the research would be conducted in an ethical manner, I proposed to satisfy the ethical principles of the American Psychological Association (APA) as listed in the 1990 edition of the Ethical Principles in the Conduct of Research with Human Participants (reproduced in Palys, 1997). I selected to follow the ethical guidelines set forth by the APA because of its careful drafting and revision of the areas to consider when dealing with human participants and its applicability to research especially in the realm of the social sciences. In no way was there the idea of concealing some details of my study or deceiving the participants. Data were tabulated and analyzed using the Statistical Package for the Social Sciences (SPSS®) software, version 18.0 for Windows®. Initially, a descriptive analysis was performed, and subsequently, bivariate analysis was using the Chi-square test was applied. For this study, the significance level adopted was 5% ($p<0.05$), with a confidence interval of 95% (CI 95%).

Research

The average age of women was 22.3 and more than 80% of them had primary and secondary education;

First table shows in 2019 the most injuries were limbs (both upper and lower) and nervous injury was only one case and in 2020 the most injury were internal viscera and like 2019, table 4-2 shows in 2020 most injuries were limbs (both upper and lower) and nervous injury was only one case.

Table 1 – Area of injury in 2019 and 2020

	2019		2020	
	Frequency	Percent	Frequency	Percent
Head	36	8.8	54	8.0
Ear	6	1.5	12	1.8
Face	87	21.3	131	19.3
Neck	25	6.1	39	5.7
Shoulder	29	7.1	68	10.0
Thoracic	13	3.2	21	3.1
Abdominal	6	1.5	11	1.6
Upper limb	104	25.5	171	25.2
Anal and genital	2	0.5	4	0.6
Gluteal	6	1.5	19	2.8
Lower limb	66	16.2	121	17.8
Axial	3	0.7	2	0.3
Back	21	5.1	23	3.4
Nervous	1	0.2	1	0.1
Internal viscera	0	0	2	0.3
Total	405	-	677	-

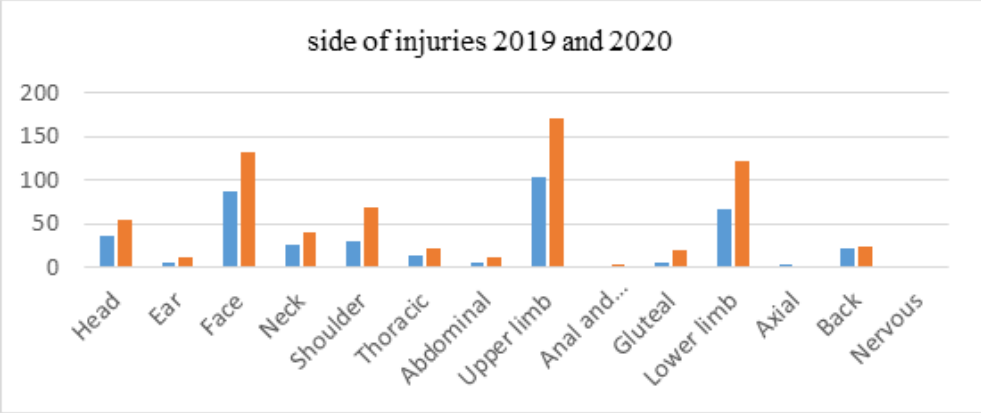

Figure1 – Side of injuries 2019 and 2020

Table 2 shows that most of injuries were moderate level and mild injuries were the next and severe injuries with 20 cases was last of this rank and in 2020 like 2019 and most of them were moderate level and after that was mild and severe level.

Table 2 – Severity of injury in 2019 and 2020

	2019		2020	
	Frequency	Percent	Frequency	Percent
Mild	35	8.6	46	6.8
Moderate	164	40.2	220	32.4
severe	20	4.9	41	6.0
Total	219	53.7	307	45.2

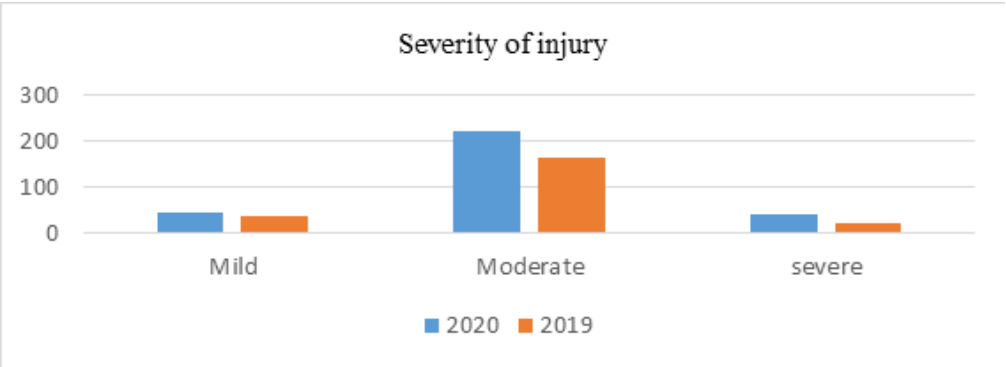

Figure2 – Severity of injuries 2019 and 2020

Type of injuries in 2019 shows that 38.2% of injuries was blunt, 4.9% sharp, 2.2 thermal and 0.02% was unclear. In 2020 blunt injuries was the first injuries and unlike 2019 weapon reported as injures types.

Table 3 – Type of injury in 2019 and 2020

	Frequency	Percent	Frequency	Percent
Blunt	156	38.2	241	35.5
Sharp	20	4.9	12	1.8
weapon	9	2.2	2	0.3
unclear	1	.2	13	1.9
chemical	0	0	2	1.9
Total	222	-	409	-

Result

The role of women in the family and society is an undeniable fact. Women have many roles in society such as the role of wife, mother and engaged in different parts of society such as marriage, health and education, however, due to different roles and responsibilities in society, they suffer from gender inequalities. (Maldonado et al, 2014). On the other hand, the family is one of the most important social institutions and is the basis of society. Interactions and patterns of interaction between family members create family performance, and a healthy practice indicates that patterns of interaction and interactions between family members are useful and effective in achieving family goals. Healthy functioning in a family environment is characterized by clear communication, clear roles, cohesion, and proper emotional regulation, while poor performance in a family with high levels of conflict, confusion, and poor behavioral and emotional control [15].

In a patriarchal attitude system, it is a form of male violence in the family and is considered a part of their normal life for women. Therefore,

for more than three decades, pro-women groups have been working with the attitudes and beliefs that Strengthens violence against women, fight extensively. Identifying the thoughts and beliefs that shape men's attitudes toward violence against women is important because identifying these attitudes in men can prevent the spread of violence against women and reduce this harm in society [16].

The issue of violence against women is so pervasive and borderless that international institutions such as United Nations and human rights organizations have been forced to respond. Although women make up more than half of the population of human society, they have been discriminated against throughout history and threaten the rights, health and well-being of women. Statistics show that most domestic abuse is directed at women and girls, who are humiliated on a daily basis. And most of them have less facilities such as the right to choose their destiny and education.

Violence against women was any act of gender-based violence that has direct or indirect consequences, including physical, sexual and psychological harm or suffering of women. Domestic violence is observed in four forms of psycho-verbal, economic, physical and sexual, which psycho-verbal type includes: using isolating methods of the person (such as weakening women's relationships with others, preventing phone calls or meeting family and friends) Inducing fear (such as threatening to physically harm, threatening to alienate or harm children) or cursing, humiliating, harassing and not talking to them. Economic violence includes behaviors such as refusing to pay and financing, encroaching on or seizing women's property, or harassment in the workplace; So as to lead to the loss of the woman's source of income. Physical violence includes repetitive behaviors based on physical assault in various forms (slapping, punching, kicking, etc.) or preventing the spouse from accessing health care services, as well as sexual violence from any sexual intercourse with the spouse without his or her consent, or sexual relation with force and anger or unnatural methods [2].

Trauma from domestic violence associated with some chronic health issues such as drug addiction, alcohol consumption, sexually transmitted diseases such as AIDS, limiting women's ability to manage chronic diseases such as diabetes and high blood pressure, leading to serious health consequences. Studies have shown prevalence of domestic violence in women is higher than other problems such as diabetes, breast cancer and cervical cancer. In the United States, more than half a million people go to hospital emergency room for domestic violence each year, and the number of outpatient visits, estimated at one million. The cost of this issue in the United States is more than eight billion dollars annually [17]

Violence against women is a latent social and worrying issue from the point of view of physical, sexual and mental health. Studies have shown that in different societies there is a range of types of violence against women and women as a special group are 5 times more likely to be abused by their husbands than men. The global estimate of violence against women is 27.2-5.2%. Domestic violence and rape in developing and developed countries account for 5 and 19% of the total health problems of women aged 15-44, respectively.

The main strength of study was that the analysis is based on data collected from all part of country. Relatively large sample size respondents were randomly selected and the data were collected by highly well-trained. As a limitation, this study uses cross-sectional data that constrained to determine causality. In addition, Violence against women is a sensitive issue that may be associated with guilt and negative stigma. As a result, women may be reluctant to disclose their experiences of intimate partner violence, which may affect the prevalence reported in this study. Therefore, the findings of this study should be interpreted in this manner.

Violence against women is a growing social problem, more epidemiological research is needed to understand the nature and extent of this frightening social phenomenon, so experts, specialists and officials involved can address this. Have serious oversight of the disaster. Educate medical students, and psychologists to become familiar with the signs and symptoms of domestic violence, the importance of screening violence against women of all ages, especially young women of childbearing age, as well as premarital education and public awareness to control and eradicate problem.

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COMPARISON OF ROAD TRAFFIC ACCIDENT DEATH BETWEEN ALMATY CITY AND NUR-SULTAN

Deaths caused by road accidents are a big concern all over the world and every year near 1.3 million people die due to it.

This study aimed to find the mortality rate due to RTA (Road Traffic Accident) based on gender, city, year and comparing the rate of RTAD (Road traffic accident death) to total death and deaths due to external cause from 2010 to 2019 in two major cities of Kazakhstan, Almaty city and Nur Sultan. And also to find the cause of death in forensic medicine to what degree of the injury whether the head or other part of the body is more to be the cause of death.

The study design was quantitative cross-sectional. The data were obtained from the demographic yearbook of Kazakhstan for 10 years. For analyzing the data, the SPSS version 22 was used.

The total number of deaths due to RTA in two major cities of Kazakhstan, Almaty and Nur sultan, from 2010 to 2019 was 2632. Among them 1732 (68.4%) were male, and 833 (31.6%) were female. In Almaty city, it was 1805 (68.6%) and in Nur Sultan city it was 827 (31.4%). The high rate among males was in between the age group of 30 – 39 while for the female it is 50 – 59 According to sex distribution males are more prone to have road traffic accident deaths comparing to females. The cause of death due to RTAD are around 65% in the head and 15% in the chest. The fracture of the femur bone is more prevalent among males and the fracture of humerus bone was more prevalent among females.

This rate study of road traffic accident deaths might contribute to reducing the numbers of deaths due to RTA in Kazakhstan.

Key words: Road traffic accident death, Rate, Kazakhstan, Almaty city, Nur Sultan, Forensic medicine, comparative study.

Introduction

The problem of high rates of road traffic accidents is now one of the most challenging health and social policy problems affecting countries around the globe. Nearly 1.3 million people die every year on roads across the world, and 20–50 million suffer from serious injuries [1], the majority of which need long-term care. One of the most dangerous situations people face on a regular basis is being killed in a car accident. When a car/vehicle collides with another car, a pedestrian, an animal, road debris, or other things, it is known as a traffic accident. Road traffic accidents often result in injury, disability, death, property harm, and financial costs for both society and the people involved, but the numbers of people killed and injured in such accidents receive less media attention than other, less common forms of tragedies [2]. This issue has been studied since the beginning of automobile production. The first scientific study on an accident involving a vehicle and a motor vehicle was published in 1902 [3]. People will suffer not just from physical injury, but also from psychological trauma following a road traffic accident that requires special attention [4].

All over the world, annually 1.35 million people die due to road traffic accidents. RTAD is the 8th leading cause of death all over the world and is the first leading cause of death among people aged 5 - 29 [1]. Nearly half (49%) of people, dying due to road traffic accidents, are pedestrian [5]. The number of RTAD in 2010 in Kazakhstan is 3381 and to compare it with 2015, it shows a decrease to 2659 and again in 2019, there is a slight increase to 2726 [6] [7] [8]. The Frequency of RTAD is 11 times higher in Kazakhstan than in Europe [9]. The rate of RTAD in all Kazakhstan according to 100,000 population is 25,0 (±2.1), while for males it is 38.2 (±3.2) and for females, it is 12.6 (±1.1). The age group of 30 – 39 had high rates in males and the age group of 50 – 59 years old had high rates in females [10].

Environmental factors play a significant role in RTAs, according to the data. To minimize and reduce RTA in a community, public awareness can

play an important role. [11]. The question always being asked is that who is the cause of the accident, which are drivers, about 95% involvement of them in having the accidents [12]. The RTAD rate increases as blood alcohol level increases [13]. Most users of alcohol while driving are among males aged 25 – 34 years [14].

The correct use of a helmet can reduce mortality by 42% and head injuries by 69% [15]. An autopsy study in forensic medicine confirms this and shows that the cause of death due to RTAD are around 65% in the head and 15% in the chest [16]. The fracture of the femur bone is more prevalent among males and the fracture of humerus bone is more prevalent among females [17]. To get a reliable forensic report from a road traffic accident death, it's better to do both the analysis and computed tomography before the autopsy, so that a forensic specialist can be more specific [18]. The correct use of child restraints can reduce the fatality of children by up to 90% [19]. The use of mobile phones has a negative impact on road traffic accident deaths [20]. The study finds that the restriction on the use of a phone while driving can reduce the RTA by 22 % [21] and also a 5% reduction in average speed can reduce the number of fatalities by 30% [22].

However, the rate of RTAD is being mostly discussed as by 100,000 population in one year which exactly we can't understand by this rate that in a year from total death how many died due to RTAD which in this study I will find this rate that is more exact to find out the real proportion of RTAD to total death in two major cities of Kazakhstan, Almaty city and Nur-sultan and compare these two cities.

Justification of the choice of articles and goals and objectives

Aim

This study aims to compare the mortality rate due to RTA in Almaty and Nur Sultan, two major cities in Kazakhstan, from 2010 to 2019.

Objectives

To study RTAD by city

To study RTAD by gender

To compare the rate of RTAD to total death in the city

To compare the rate of RTAD to deaths due to external causes

Scientific research methodology

The study was designed as a retrospective cross-sectional study, with data on road traffic accident deaths collected from Kazakhstan's Demographic Year Book from 2010 to 2019; based on gender, population, and year. For statistical analysis, the statistical package for social science (SPSS) version 22 was used. Variables were compared between Almaty city and Nur-sultan using independent t-test and one-way ANOVA Statistically, it was calculated by 95 % confidence interval, A p-value <0.05 was considered statistically significant. In this study, the two cities of Kazakhstan, Almaty city and Nur-Sultan were compared by the rates of RTAD by 100,000 population, and also it was calculated by 1000 total death and by 1000 deaths due to external causes.

The nominator for this study was considered the Road traffic accident death and the denominator was population, total death, and death due to external causes. To visualize the data more understandable; we multiply the calculation to the population by 100,000, meanwhile, the data for the calculation of the total deaths and deaths due to external causes were multiplied by 1000.\

Results and discussion

From 2010 to 2019, 2632 people died as a result of RTA in Kazakhstan's two major cities, Almaty and Nur sultan. There are 1732 men (68.4 percent) and 833 women (31.6 percent) among them. It was 1805 (68.6%) in Almaty city and 827 (68.6%) in Nur Sultan city (31.4 percent). Table (1) shows the number of RTAD in two cities of Kazakhstan by each year. The total count and the difference between the male and female for each year are also shown. To visualize better, in the last row, the total number is calculated for each column related to male, female and total numbers, and also the data are presented in percentage.

Table 1 – RTAD from 2010 to 2019 with percentages

No	City	Year	Male	%	Female	%	Total	%
1	Almaty city	2010	131	7.28%	72	8.64%	203	7.71%
2	Almaty city	2011	123	6.84%	79	9.48%	202	7.67%
3	Almaty city	2012	142	7.89%	63	7.56%	205	7.79%
4	Almaty city	2013	120	6.67%	41	4.92%	161	6.12%
5	Almaty city	2014	137	7.62%	48	5.76%	185	7.03%
6	Almaty city	2015	106	5.89%	41	4.92%	147	5.59%
7	Almaty city	2016	100	5.56%	56	6.72%	156	5.93%
8	Almaty city	2017	98	5.45%	49	5.88%	147	5.59%
9	Almaty city	2018	111	6.17%	72	8.64%	183	6.95%
10	Almaty city	2019	143	7.95%	73	8.76%	216	8.21%
11	Nur-Sultan	2010	66	3.67%	31	3.72%	97	3.69%
12	Nur-Sultan	2011	54	3.00%	20	2.40%	74	2.81%
13	Nur-Sultan	2012	58	3.22%	26	3.12%	84	3.19%
14	Nur-Sultan	2013	69	3.84%	36	4.32%	105	3.99%
15	Nur-Sultan	2014	59	3.28%	15	1.80%	74	2.81%
16	Nur-Sultan	2015	52	2.89%	20	2.40%	72	2.74%
17	Nur-Sultan	2016	56	3.11%	24	2.88%	80	3.04%
18	Nur-Sultan	2017	58	3.22%	23	2.76%	81	3.08%
19	Nur-Sultan	2018	62	3.45%	24	2.88%	86	3.27%
20	Nur-Sultan	2019	54	3.00%	20	2.40%	74	2.81%
Total			1799	68.35%	833	31.65%	2632	100%

Table (2) shows the rate of RTAD per 1000 deaths due to external causes for each year between the Almaty city and Nur-Sultan. To differentiate between the sexes, for each sex separate variables by combining city names are used.

Table 2 – The rate of RTAD per 1000 deaths due to external causes of deaths

No	Year	Almaty city (Male)	Almaty city (Female)	Nur sultan (Male)	Nur sultan (Female)
1	2010	122.9	240.8	163.8	236.6
2	2011	124.5	261.6	145.6	192.3
3	2012	162.8	254.0	156.3	250.0
4	2013	126.3	138.5	174.7	262.8
5	2014	169.3	202.5	157.3	153.1
6	2015	144.4	191.6	140.9	168.1
7	2016	155.8	213.7	152.2	233.0
8	2017	168.4	247.5	177.9	219.0
9	2018	182.9	293.9	179.7	237.6
10	2019	208.5	323.0	166.2	208.3

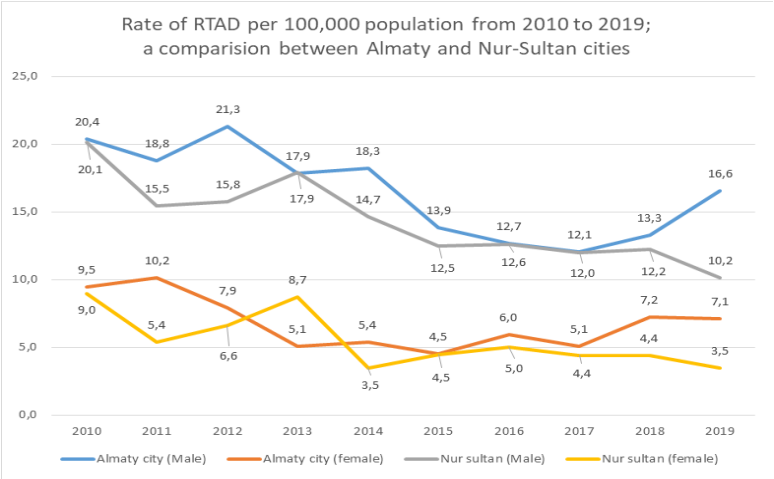

Figure 1 – Rate of RTAD per 100,000 population from 2010 to 2019; a comparison between Almaty and Nur-Sultan cities

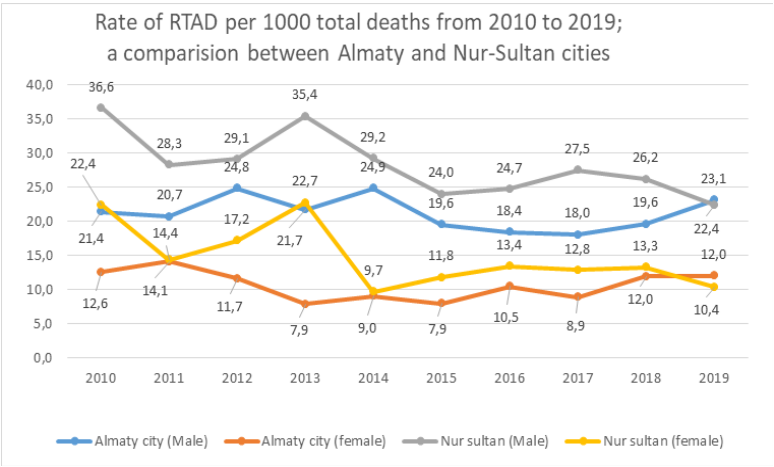

Figure 2 – Rate of RTAD per 1000 total deaths from 2010 - 2019; a comparison between Almaty and Nur-Sultan cities

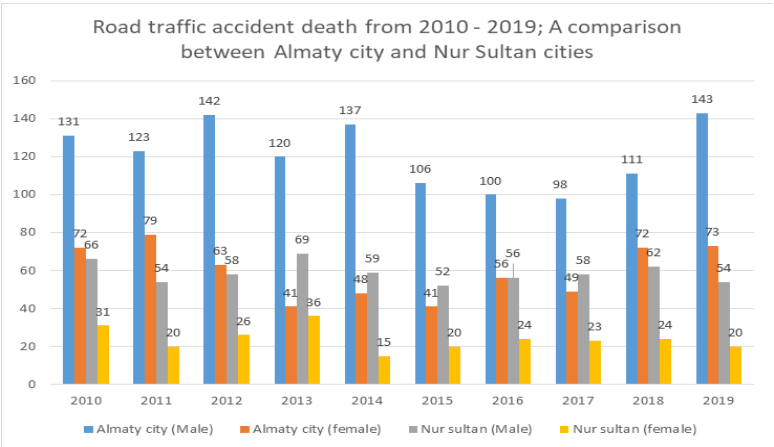

Figure 3 – Road traffic accident deaths from 2010 to 2019; A comparison between Almaty city and Nur-Sultan city

Discussion

This comparative study between Almaty city and Nur-sultan city shows that the number of RTAD is quite different and the number between both genders was higher in Almaty city than in Nur Sultan city with annual males means of 121 ± 16.9 and 58 ± 5.5 RTAD in Almaty and Nur Sultan cities, respectively. Comparison of these two values by the statistical test of an independent sample (t-test) confirms the significant difference among them with the p-value of < 0.0001. The same procedure was applied to the female group. The results showed means of 59 ± 14.2 in Almaty city and 24 ± 6 in Nur Sultan city. T-test showed a significant difference between these values with a p-value of < 0.0001. A similar comparison was also done to the first five years and second five years which confirms a decrease of numbers for the years 2015 – 2019. The mean of RTAD for each year in 2010 – 2014 in Almaty was 191 ± 18.7 and for the year 2015 – 2019 it was 170 ± 29.7, in the Nur Sultan for the first five years it was 87 ± 13.9 and for the second five years, it was 79 ± 5.6. the result of one-way ANOVA confirms the difference between these means with the p-value of >0.0001.

On the other hand, by comparing the RTAD by 100'000 population, we find out no significant difference in the rate of RTAD between the two sexes. For the first five years, The mean rate for males in Almaty city is 16.5 ± 3.3 and in Nur Sultan city it is 14 ± 3.1, which shows no significant difference. For the female in Almaty city, it is 6.8 ± 1.9, while for in Nur Sultan, it is 5.5 ± 2, which again shows no significant difference among them. The comparison among first and second five years for Almaty and Nur Sultan is 13.0 and 11.6 for the first five years, respectively, and 9.5 and 8.0 for the second five years, respectively. One-way Anova test results confirmed the difference between pairs of data and showed a decrease in the rate of RTAD per 100'000 population in the second five years.

The outcome of calculating and comparison of RTAD to total deaths is a key to know about the exact dangers of RTAD; which among male in Almaty is 21.2 and in Nur Sultan is 28.3 deaths per 1000 total death with the p-value of <0.0001, which shows higher value in Nur Sultan. For the female, this value is 10.7 in Almaty city and 14.8 in Nur Sultan with the p-value of 0.018, which similarly is higher in Nur Sultan city. The rate of the first five years in Almaty city is 17.0 and in Nur Sultan is 25.5 deaths due to RTAD per 1000 deaths; and for the second five years, the rate is 15.0 in Almaty city and 19.4 in Nur Sultan with a p-value of <0.0001, we can confirm that there is a difference among these values and the RTAD has declined in the second five years.

The comparison of RTAD to external causes of death shows that for the males of Almaty city, it is 156.6 and for Nur Sultan, it is 161.5 per 1000 external causes of death. For females in Almaty city, it is 158.9 and in Nur Sultan city, it is 216.1 per 1000 external causes of death. Comparison of the result of the two sexes shows no difference among males and females in this regard. The number of deaths due to RTAD per 1000 total deaths due to external causes of death are 158.9 and 173.6 in the first five years in Almaty and Nur Sultan cities, respectively. In the second five years, these values are 174.8 and 193.5 in Almaty and Nur Sultan cities, respectively. One-way Anova results show no significant difference between these two cities regarding this rate.

Table 3 – Comparison of mean values for both sexes in Almaty and Nur sultan cities and the result of statistical difference signification

Variable			Nur-Sultan Results	Almaty P-value	Test of difference	
Road traffic accident death (RTAD)	Sexes	Male	58	121	11.074	<0.0001
		Female	24	59	7.258	<0.0001
	Years	2010-2014	87	191	44.923	<0.0001
		2015-2019	79	170		
RTAD rate per 100,000 population	Sexes	Male	14	16.5	1.51	0.148
		Female	5.5	6.8	1.482	0.156
	Years	2010-2014	11.6	13	9.572	0.001
		2015-2019	8	9.5		
RTAD rate per 1000 Total deaths	Sexes	Male	28.3	21.2	-4.306	<0.0001
		Female	14.8	10.7	-2.596	0.018
	Years	2010-2014	25.5	17	15.702	<0.0001
		2015-2019	19.4	15		
RTAD rate per 1000 external causes of deaths	Sexes	Male	161.5	156.6	-0.5	0.623
		Female	216.1	236.7	1.024	0.32
	Years	2010-2014	173.6	158.9	1.859	0.177
		2015-2019	174.8	193.5		

Conclusion

According to the number of the RTAD, the Almaty city has a higher number comparing to Nur-Sultan city. By comparing both sexes, it can be concluded that the number of RTAD in both sexes in Almaty city is higher. The timely comparison shows that there is a total decrease in RTAD in both cities. The rate of 100,000 population didn't show any significant difference among these two cities, but for the rate which was calculated by 1000 total deaths, the Nur-Sultan RTAD rate is higher than Almaty city among both males and females. And for the rate of RTAD compared to 1000 deaths due to external causes there was no significant difference between Almaty city and Nur-sultan. The most common cause of death due to RTAD are around 65% in the head and 15% in the chest. The fracture of the femur bone is more prevalent among males and the fracture of humerus bone is more prevalent among females. Also, there is alcohol in the blood of the corpse that was more male aged 25 – 34. The high rate for males is for the age group of 30 – 39 and females it is 50 – 59. That the correct usage of a helmet and observing drivers for alcohol can reduce the fatality rate. There are some points to be considered to reduce RTAD:

Public awareness is the key to reduce the rate of RTAD. The media and social networks can play a significant role in this regard.

The leading cause of the RTAD is the speed of the driver, therefore, speed limits should be decreased and selected with more caution.

Alcohol and other drug consumption adversely affect RTAD rates. More and random control of drivers, especially male drivers, can reduce this rate significantly.

The correct use of helmets and child restraints can reduce the rate and should be considered.

Around 95% of the time, the cause of RTAD is related to the driver. Even we can no longer call this RTAD, but just an accident, maybe we could call it a careless and reckless act of the driver, which consequently affects adversely not only the driver but also pedestrians.

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Section 2
General medicine

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HCV-RELATED VASCULITIS

Up to 3% of people in the world are infected with HCV, and 75-80% of them have chronic currency of infection. In the clinical picture of HCV infection, a significant place is given to extrahepatic manifestations - more than half of patients suffer from lesions of the skin, kidneys, heart, blood vessels, autoimmune and lymphoproliferative syndromes associated with HCV. Usually, mortality from chronic hepatitis C is associated with liver cirrhosis and hepatocellular carcinoma, but in fact, more patients die from complications associated with the development of cryoglobulinemic vasculitis - chronic renal failure and cardiovascular catastrophes. 40-60% of patients with chronic HCV infection suffer from cryoglobulinemic vasculitis in a wide range of clinical manifestations: from minimal to life-threatening. The pathogenesis of mixed cryoglobulinemia syndrome is based on polyclonal activation of lymphocytes.

The systemic nature of the lesion, which is observed in HCV infection, reflects its generalized nature with the involvement of many organs and tissues in the pathological process, which complicates timely diagnosis and treatment. A variety of systemic extrahepatic pathology, which often outstrips the clinical picture of hepatitis itself, masquerading as another disease means that a specialist of any profile can meet with chronic HCV infection and its consequences.

Key words: hepatitis C, extrahepatic manifestations, cryoglobulinemic vasculitis.

Introduction

General overview

First reported in 1989, the hepatitis C virus (HCV) is an enveloped positive-stranded RNA virus that belongs to the Flaviviridae family and to one of its three genera, hepacivirus, more specifically [1]. About 9400 nucleotides and multiple regions are found in HCV genome [2].

HCV is among the viruses with the highest diversity in the genome. One of the key characteristics of HCV, which can be categorized as genotypes, subtypes and quasi-species, is its genome heterogeneity. A lack of corrective action of virus-dependent RNA-polymerase leading to the regular introduction of nucleotide substitutions into the genome of the virus is the underlying explanation for such variability. Sequences are homologous in about 95 percent within the same genotype, although they are so in just 65 percent of cases between genotypes. Continuous HCV mutation greatly threatens immune memory as the number of memory cells capable of recognizing new varieties from the first exposure is steadily lower with each new mutation [3].

HCV is a pathogen widespread globally and a significant health concern. According to the World Health Organization (WHO) more then 71 million people had chronic HCV infection in 2015 (an approximate global prevalence of 1%). These persons have a high risk of advanced liver disease, including cirrhosis and hepatocellular cancer. HCV infection is normally asymptomatic, and just 20-40% of individuals spontaneously clear the virus, so most subjects who experience the virus become chronically

infected[4]. Compared to HCV-negative people, HCV-related all-cause mortality is twice as high and extrahepatic manifestations are a significant risk factor [5]. The most prevalent extrahepatic conditions associated with HCV infection are lymphoproliferative and autoimmune disorders, from cryoglobulinemia vasculitis to malignant B-cell lymphoma [6]. Additional extrahepatic manifestations, including cardiovascular, neurological, metabolic and renal disorders, have been revealed in large cohort studies, and multiple manifestations frequently coexist in the same patient [7]. A study recorded that up to 74% of patients infected with chronic HCV undergo at least one extrahepatic manifestation [8] .

More than 50 percent of infected patients develop recurrent, sometimes steadily progressive hepatitis, which can be associated with extrahepatic skin, renal, hematopoietic, and cardiovascular symptoms, leading to an elevated risk of atherosclerosis, cardiomyopathy, peripheral artery disease, and stroke, thus increasing mortality[9].

Around 130-170 million individuals are infected with the HCV chronically, which is 3 per cent of the world's population. It is a significant public health challenges, with an estimated 3-4 million individuals worldwide infected every year. One of the most important causes of liver-related death and the most common indication for liver transplantation in the United States of America, is chronic hepatitis C (CHC)[9]. Around 30,500 new cases of HCV in the United States have recently been identified by the Centers for Disease Control and Prevention, and the number of chronic cases has been estimated to be 2.7-3.9 million[10].

It is understood that chronic hepatitis C can cause cirrhosis and hepatocellular carcinoma. The key site of replication of HCV is in hepatocytes, which illuminates the substantial damage it does to the liver. It is stablished, however, that the virus is not hepatotoxic, and that most liver injuries are caused by a cell-mediated immune response to infected liver cells. Likewise, the production of extrahepatic manifestations can include immune defects resulting in autoimmunity. The affected organ, system, or pathological process may be categorized by the extrahepatic manifestations of chronic hepatitis C. The strength of available evidence that link them to CHC, however, differs [11]. The clinical appearance varies from subclinical cases to very severe immunological disorders in CHC patients. Indeed, autoimmune symptoms linked to hepatitis C virus infection often contribute to the diagnosis of infection with this virus [12].

HCV vasculitis

Of all the extrahepatic Hepatitis C Virus (HCV) manifestations, vasculitic manifestations merit special attention. Since they include blood vessels, they have a multisystem appearance. The existence of cryoglobulins (CGs), a material with unusual physicochemical properties and substantial morbidity and mortality, is mainly due to cases [13].

The tale of revealing the association between HCV and mixed cryoglobulinemia (MC) is a noteworthy scientific success story in which an infectious agent could be traced to an autoimmune disorder. The final act of investigating the effect on patients with cryoglobulinemic vasculitis of the application of recently presented antiviral agents will provide us a vision into the management of autoimmune phenomena when they are related to microbial pathogenic factors. Centered on the ascription of vasculitis to the existence or absence of serum cryoglobulins as a pathogenic factor that involves HCV vasculitis in the existence of cryoglobulins and HCV vasculitis in the absence of cryoglobulins, HCV vasculitic syndromes will be addressed under two key topics [13].

Cryoglobulins (CGs), first termed in 1947 by Lerner and Watson, are immunoglobulins that, when exposed to temperatures below 37°C, precipitate or produce a gel and re-solubilize when re-warmed [14].

Cryoglobulinemia refers to the presence of cryoglobulins in serum (qualitative test positive findings and/or >0.05 g/L in cryocrit quantitative test concentrations). There may be no clinical symptoms of cryoglobulinemia, but it can additionally lead to a broad range of clinical presentations, including skin lesions, arthralgia, peripheral neuropathy, single or multiple organ injury. Symptomatic cryoglobulinemia is referred to as cryoglobulinemic vasculitis (Cryo Vas) or cryoglobulinemic disease[15; 16 ;17 ;18 ;19]. Three subtypes of cryoglobulinemia occur based on the immunoglobulin composition, according to Brouet's classification [20].

Single monoclonal immunoglobulins (most commonly immunoglobulin M (IgM), sometimes IgG or IgA) include type I cryoglobulinemia. Cryoglobulinemia type I accounts for 10% to 15% of cases. Mixed cryoglobulinemia is known as type II and type III since it involves two types of immunoglobulins (normally IgG and IgM) that account for 50 to 60% of cases. Form II mixed cryoglobulinemia includes a mixture of monoclonal and polyclonal immunoglobulins (usually IgM plus IgG c or IgG c), while IgM and IgG, both polyclonal, constitute type III mixed cryoglobulinemia. Oligoclonal IgM or

mixed polyclonal and monoclonal IgM along with polyclonal IgG can also be detected. An intermediate evolution from type III to type II mixed cryoglobulinemia may be this unique serological branch, referred to as type II-III mixed cryoglobulinemia. Notably, the cryoglobulins present in mixed cryoglobulinemia are autoantibodies with action of the rheumatoid factor (i.e. an antibody with the ability to bind another antibody) that allow the formation of immune complexes, which is essential for the pathogenesis of cryoglobulinemic vasculitis [17; 18]. In addition, it was occasionally reported that mixed cryoglobulins were not composed of IgM-IgG, but of other immunoglobulin combinations, like IgG-IgG, IgA-IgG, or IgM-IgG-IgA[21; 22].

Aberrant autoantibody development by B cells and B cell proliferation is the basic mechanism leading to cryoglobulinemia. By interfering with normal B cell function, many underlying diseases may promote this. A lymphoproliferative disorder of B cells is often associated with the involvement of type I cryoglobulins. By comparison, systemic autoimmune conditions, lymphoproliferative disorders and chronic infections are related with mixed type II or type III cryoglobulinemias, with hepatitis C virus (HCV) infection producing 80-90 percent of mixed cryoglobulinemia events [23; 24 ;25]

HCV-related cryoglobulinemic vasculitis

Hepatitis C virus (HCV) is noted for its hepatic and extrahepatic manifestations (25). Extrahepatic complications are mainly immunologically induced by chronic hepatitis C virus infection. Of such, the greatest correlation is cryoglobulinemia and its clinical sequelae. In 40-60 percent of HCV-infected patients, cryoglobulins are easily detectable, while cryoglobulinemia vasculitis occurs in just 5-10 percent of cases [26; 27 ;15; 28; 29]. The involvement of autoantibodies and T cells in vascular infiltrates and the discovery of the susceptibility of particular HLA alleles to cryoglobulinemic vasculitis in patients infected with hepatitis C virus support the autoimmune existence of this virus-associated pathology [30 ;31] .

Cryoglobulinemic vasculitis is a serious small vessel vasculitis mediated immune complex that mainly involves the skin, joints, kidneys, and peripheral nerves, if untreated, caused end-stage organ/tissue injury. It may be of infectious origin, with the most common cause being infection with the hepatitis C virus (HCV) [32 ;33] . cryoglobulinemia is the result of the persistent proliferation of B cells, which generates pathogenic isotypes of IgG and IgM immunoglobulin (Ig) with rheumatoid factor activity[34;35;36] .

Mixed cryoglobulinemia is one of the most serious problems in which vasculitis (mixed-cryoglobulinemic vasculitis) can be produced by deposition of cryoglobulins and cause palpable purpura, arthralgias, glomerulonephritis or neuropathy [25].

The most important etiology of mixed cryoglobulinemia type II and type III is chronic hepatitis C virus infection, which accounts for 80-90% of mixed cryoglobulinemia cases [37 ;26 ;38; 39; 24 ;23 ;40]

Pathophysiology of HCV-related cryoglobulinemic vasculitis

For HCV-related mixed cryoglobulinemia, the mechanism of cryoglobulin pathogenicity is best identified. Due to the widespread expression of the hepatitis C virus entry receptor CD81 on the plasma membrane of both cell types, HCV is capable of simultaneously infecting B cells and hepatocytes [24 ;40;41;42;43]. Active hepatitis C virus replication has been shown in CD19positive B cells; hepatitis C virus RNA and core and nonstructural NS3 proteins can be found in CD19positive, but not CD19negative, peripheral blood mononuclear cells[44;45]. In monocytes, peripheral dendritic cells, and 36,37 macrophages, HCV replication has also been identified [46,47].

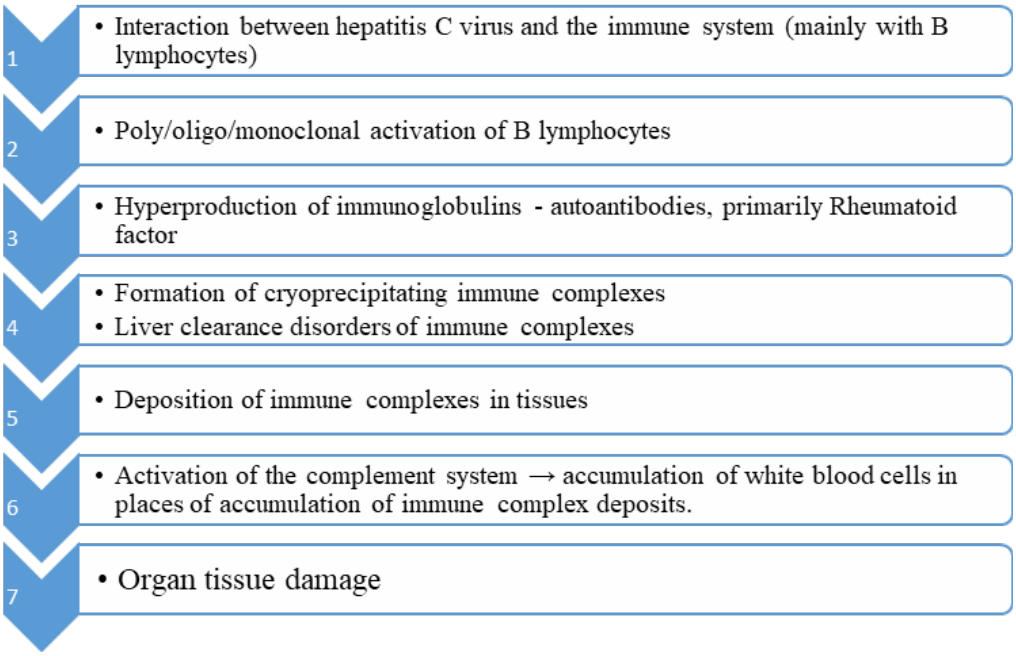


Figure 1 – Pathogenesis of clinical manifestations in mixed cryoglobulinemia

B cell proliferation and HCV infection

A significant mechanism in the pathogenesis of cryoglobulinemia and cryoglobulinemic vasculitis is the proliferation of B cells [48,49,50]. The progression from basic serological modification (cryoglobulinemia) to clinical manifestations (cryoglobulinemic vasculitis) and finally to obvious malignant B lymphoproliferation (such as non-Hodgkin lymphoma) is accompanied by a multi-stage mechanism [51,52]. The discovery of the empathy of the hepatitis C virus envelope to a transmembrane protein, CD81, provided a foundation for understanding the lymphoproliferation-induced mechanisms of HCV [53,54]. CD81 forms a multiprotein complex with CD21 and CD19 on the surface of B cells. This multiprotein complex controls the polyclonal development of B cells when triggered by hepatitis C virus envelope binding. Furthermore, by adding an antigen to the B cell receptor (BCR) on the cell surface, B cells are activated, causing in polyclonal expansion [53;55].

While in vitro researches have indicated that specific anti-HCV antibodies are capable of stimulating BCR in B cells, it appears that HCV envelope protein activation of CD81 provokes naive B cell proliferation independently of the stimulation of BCR. In the production of lymphoproliferative disorders, CD81-mediated activation of naive (CD27-positive) B cells with subsequent differentiation to autoantibody-producing memory cells could make a contribution. Furthermore, chronic antigenic stimulation could cause the overexpression (favoring some clones) of B cells and support immune dysregulation mechanisms that give rise to the development of mixed cryoglobulinemia and finally to malignant transformation that is occasionally found in patients with chronic hepatitis C virus infection [55;56; 57; 58 ;59].

B cell transformation

Hepatitis C virus infection can lead to B cell transformation in addition to the stimulation of B cell expansion and the decrease of the B cell activation threshold [55;56; 57; 58 ;59]. HCV infection patients have clonal populations of B cells that are primarily memory B lymphocytes generating IgM, expressing modestly hypermutated immunoglobulin genes [55;56; 57; 58 ;59].In both HCV-positive non-Hodgkin lymphoma and cryoglobulinemic vasculitis, several of the same immunoglobulin idiotypes and restricted gene sequence rearrangements are observed, indicating a common pathophysiology. Furthermore, novel research on the pathogenesis of lymphomas associated with hepatitis C virus have shown evidence that this virus could have mutagenic potential. In the immunoglobulin heavy chain gene and other locations, B cells exposed to HCV in vitro had up to a tenfold increase in mutations. In addition, relative to

HCV negative lymphomas, increased mutations are seen in HCV-associated lymphomas [49]. Between genetic mutations, the most frequent chromosomal rearrangement in lymphoid cancers, mainly follicular lymphoma, a subtype of non-Hodgkin lymphoma, is the translocation [14;18] of the anti-apoptotic BCL2gene that encodes apoptosis regulator BCL2. Patients with chronic hepatitis C virus infection in 35% of cases have proof in their peripheral mononuclear cells of a widespread chromosomal rearrangement t [14;18] translocation [50].

This HCV-dependent translocation of genes blocks apoptosis of B cells, resulting in oligoclonal monotypic lymphoproliferation. The significant 'missing link' to our understanding of lymphomagenesis in the environment of chronic hepatitis C virus infection could be mutations in other oncogenes, such as MYC, and regulators of apoptosis [60].

Autoantibody production

B cells are induced to develop a variety of autoantibodies by chronic stimulation by hepatitis C virus infection [61]. This extensive production of autoantibodies promotes the creation of a variety of HCV infection-related immune manifestations that are variably assembled in what is commonly called 'HCV syndrome' [62, 63 ,64]. In addition to the characteristic image of cryoglobulinemic vasculitis, HCV syndrome could be included clinical symptoms such as autoimmune thyroiditis, sicca syndrome (dryness of the exocrine glands, especially the eyes and mouth), thrombocytopenia, hemolytic anemia, autoimmune diabetes, and pulmonary fibrosis [65 ;53; 66; 57; 54].

In patients that have chronic hepatitis C virus infection, populations of clonal B cells are found in the liver and peripheral blood. Curiously, clonally restricted B cells show biased use of the heavy1-69 and variable 3-20 immunoglobulin gene segments of the rheumatoid factor coding variable, as do B cells isolated from the lymph nodes of patients with non-Hodgkin lymphoma related with HCV [49 ;58; 50].

In patients with HCV-related mixed cryoglobulinemia, at many organs, including the portal tracts of the liver, spleen, and bone marrow, can find lymphoid infiltrates with cells expressing oligoclonal or monoclonal IgM with rheumatoid factor involvement. Mixed cryoglobulinemia thus tends to be a crosslink between conventional autoimmune disorders and hematological (i.e. B cell lymphoma) neoplasia [66; 67 ;68; 69 ;70 ;71; 72]. Continuous stimulation of B cells thought viral antigens and increased expression of lymphomagenesis-related genes, especially activation-induced cytidine deaminase, which is critical for somatic hypermutation, leads to polyclonal and later monoclonal expansion of B cells [73]. Finally, these interactions cause a lymphoproliferative disease that can ultimately develop into non-Hodgkin lymphoma of B cells. Indeed, a significant correlation between HCV infection and large B cell lymphoma, marginal zone lymphoma and lymphoplasmacytic lymphoma has been identified among other hematologic malignancies [74].

In short, lymphoproliferation of HCV-induced B cells and the development of autoantibodies are possibly the direct result of the transformation of infected B cells, but also an indirect mechanism resulting from chronic antigenic stimulation of a small pool of autoreactive B cells.

Immune complex formation

Deposition of immune complexes in small blood vessels and subsequent endothelial damage are responsible for the clinical signs of cryoglobulinemic vasculitis. In HCV-associated mixed cryoglobulinemia, a permanent clone of B cells induced by chronic HCV infection sustains the appearance of immune complexes produced by circulating HCV particles, anti-HCV polyclonal IgG and monoclonal IgM with rheumatoid factor involvement.

Because of clonically limited IgM, these cryoprecipitable immune complexes are known to avoid the erythrocyte transport system. The existence of IgM in cryoprecipitable immune complexes enables them to persuade activation and consumption of complements, but not to integrate complement fragments, including complement C3b (a complementary component that promotes the binding of immune complexes to erythrocyte complement receptor 1 (CR1))[61].

In addition to escaping the erythrocyte transport system, these immune complexes stay free to circulate in the blood, since hepatic and splenic macrophages are unable to process the immune complexes due to HCV-induced defects in lysosomal enzyme biogenesis. Furthermore, in circulating monocytes, this defect was clearly seen[74]. Excitingly, electron microscopy studies of renal tissue samples found monocytes containing engulfed cryoglobulins; however, the precise function of these cells is indistinct [75].A phagocyte influx into the glomerulus is present in cryoglobulinaemic nephritis. Phagocytes try to extract accumulated

cryoglobulins; however, they are unable to process phagocytic cryoglobulins, and cryoglobulin trapping is likely to represent ineffective clearance of cryoglobulin [75]. This mechanism is likely to perpetuate glomerular injury, as seen in a research using a mouse model of cryoglobulinaemic membrane proliferative glomerulonephritis, where macrophage ablation provided defense against expansion of the mesangial matrix and collection of collagen (nephritis markers) deprived of affecting the removal of cryoglobulin (Guo et al., 2011). In place of cleaning cryoglobulins from the glomeruli, this experimental model indicates that macrophage recruitment into the glomeruli plays a crucial role in the development of kidney damage; macrophage influx, vessel infiltration and diapedesis are linked to amplification of injury after immune complex deposition [76].

Altered lysosomal enzymes of monocytes (probably associated with hepatitis C virus infection), comprising extracellular release of procathepsin D and/or release of danger-associated molecular patterns (DAMPs) from injured resident cells, could decrease the inherent role of macrophages via immunoglobulin crystallizable fragment (Fc) gamma receptor to clear immune complexes. increase of the mesangial matrix and proliferation of glomerular cells may be maintained by extracellular activation of procathepsin D released or by proinflammatory cytokines released from macrophages triggered by DAMP [74,76].

Clonally limited IgM shares clear affinity for the constituents of the glomerular matrix, counting fibronectin, as well as the classical immune complex deposition pathway, opening the likehood for a 'in situ' binding mechanism of immune complexes to kidney components [77]. Consequently, the pathogenetic function of cryoglobulins in the induction of vasculitis is linked both to the enrolment of vessel leukocytes and to the deposition of immune complexes, to the activation of the complementary system and to microvascular damages [62,78].

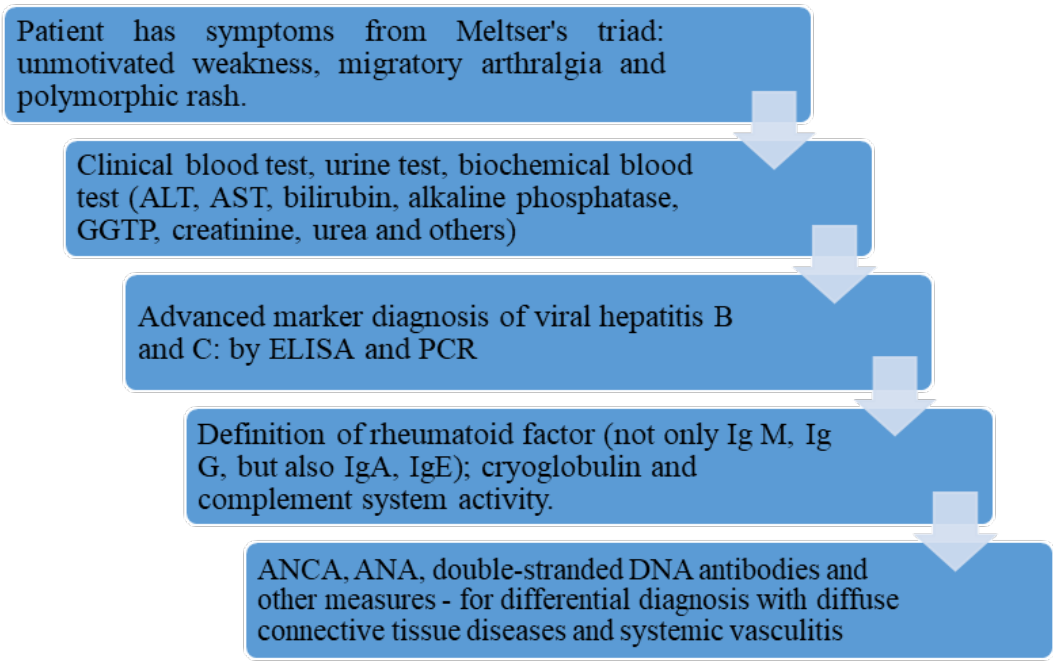


Figure 2 – Diagnostic algorithm of patients with mixed cryoglobulinemia

a. Non-HCV-related cryoglobulinemia

The major factors are other infectious disorders, B cell malignancies and autoimmune diseases in 10-20 percent of mixed cryoglobulinemia cases that are not related with chronic HCV infection [80]. Specially, it was proposed to link cryoglobulinemia with chronic HBV infection [81]. Nevertheless, only about 2% of cryoglobulinemic vasculitis cases tend to be caused by hepatitis B virus infection [66].

Cryoglobulinemic vasculitis sometimes can be related with HIV infection, particularly in cases of hepatitis C virus coinfection [82]. Mixed cryoglobulinemia associated with non-HCV is

primarily caused by viruses, bacterial pathogens or parasites. Circulating serum cryoglobulins can be present in patients who have active SLE and rheumatoid arthritis; mixed cryoglobulinemia has been seen in ~10% of patients with SLE or rheumatoid arthritis, but these patients generally do not have the same clinical manifestation as patients with SLE or rheumatoid arthritis who have cryoglobulinemic vasculitis[83].

Type II cryoglobulinemia may be present in around 5-20 percent of patients who have primary Sjögren syndrome [84]. One of the main predictive factors in primary Sjögren's syndrome is currently considered to be type II mixed cryoglobulinemia as it has been correlated with extraglandular involvement, appearing of systemic vasculitis, B cell lymphoma and reduced survival[84].

b. HCV-related non-cryoglobulinemic vasculitis

Few studies have addressed systemic vasculitis caused by HCV without evidence of cryoglobulinemia in the literature, most of which are HCV-related polyarthritis nodosa (PAN).

PAN is a medium sized necrotizing vasculitis classically associated with HBV but can be observed to a lesser degree in patients with HCV infection. In certain ways, HCV-related PAN patients vary from those connected to cryoglobulinemic vasculitis. Clinically, life-threatening vasculitis, severe multifocal sensorimotor mononeuropathy as opposed to distal mild sensory polyneuropathy, malignant hypertension, cerebral angiitis, ischemic abdominal pain, microaneurysms of the kidneys and liver, but lesser rates of arthralgia, purpura, and chronic hepatitis activity have been reported to differentiate this type from cryoglobulinemic vasculitis.

Higher acute phase reactants such as ESR and CRP and more recorded renal insufficiency are shown to occur. Histopathologically HCV associated PAN affects medium-sized arteries to a greater extent with necrotizing vasculitis rather than immune complex disease indicating cell-mediated inflammation, whereas mononuclear cell infiltration is more generally recorded in cryoglobulinemic vasculitis in perivascular areas [85,86].

In the case of cryoglobulinemic vasculitis, a national-level mass campaign is to be carried out and where prioritization is to be valued, it was suggested that cases of cryoglobulinemic vasculitis and HCV-related PAN must be among the most important patients with hepatitis C virus infection in whom viral clearance is warranted, as stated in a latest research[87].

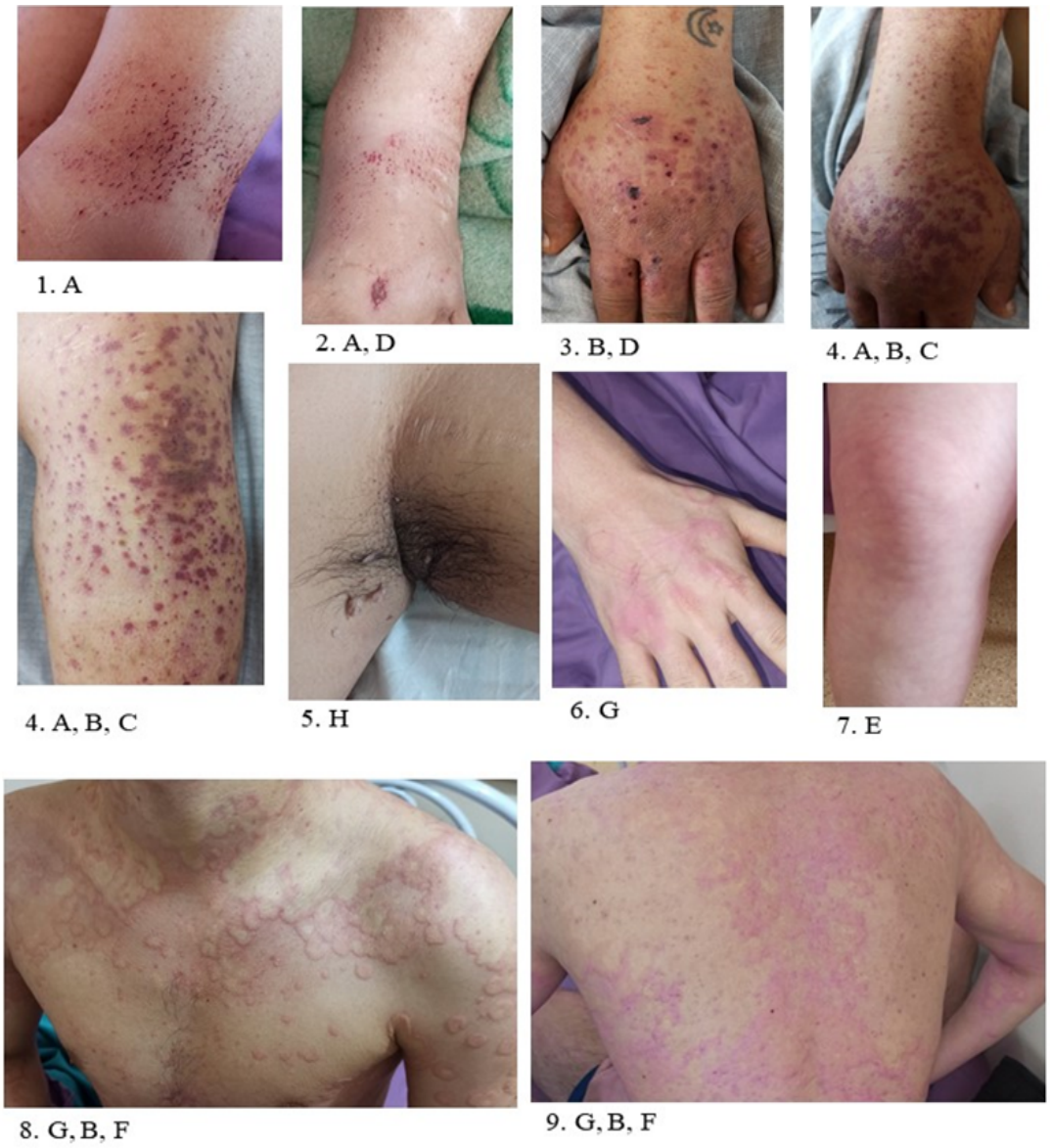
HCV-related cryoglobulinemic vasculitis manifestation

Cryoglobulinemia is an autoimmune manifestation most commonly identified among patients with hepatitis C virus infection. Purpura, arthralgia, fatigue, myalgia, polyneuropathy, glomerulonephritis, ophthalmopathy, and intestinal ischemia are the major clinical symptoms [88,18]. A large variety of clinical characteristics are present in patients with cryoglobulinemia and are discussed as follows:

1. Cutaneous manifestations

It is the most usual manifestation of the disease, commonly in the form of palpable purpura and less frequently maculopapular rash, mostly affecting to a lesser degree the lower limbs, the lower trunk, and the upper limbs. Typically, these purpuric lesions are transient and irregular, but leaving hyperpigmented areas will coalesce and recover.

The phenomena of Raynaud, acral cyanosis and livedo reticularis, usually seen in Type I cryoglobulinemia and seldom seen in mixed cryoglobulinemia, are other less common skin lesions. Skin ulcers usually originate on the lower extremities, particularly in the malleoli, are a more serious severe type, which can complicate confluent purpura eruptions and cause secondary infection and gangrene in certain patients [89, 90].



Skin manifestations of vasculitis: A) Petechiae. B) Macula. C.) Purpura. D) Ulcer. E) Livedo reticularis. F) Urticaria. G) Erythema. H) Papillomatosis

2. Musculoskeletal manifestations

The second most frequent manifestation (60-90 percent of cases) typically involve arthralgia in the form of intermittent monooligoarthralgia that mostly affects large joints, mainly the ankles and this type, along with rheumatoid artheritis such as polyarthritis that affects small joints, which are the two most common hepatitis C virus joint manifestations. In HCV-related Cryoglobulinemic vasculitis, myalgia is also commonly stated, whereas arthritis and myositis are rarer manifestations of the disease [40].

3. Neurological manifestations

In up to 50 percent of cases, HCV mediated Cryoglobulinemic Vasculitis predominantly affects the peripheral nervous system and usually affects sensory nerves rather than motor nerves. The mixed form, however, was also noted. Distribution encompasses, to a lesser degree, polyneuropathy and mononeuritis multiplex. Patients complain of paresthesia, tingling and lower limb numbness that appears to worsen throughout the night [91].

Cryoglobulinemic Vasculitis could affect the central nervous system (CNS) less frequently,

typically in the form of cerebral vasculitis, which may present with ischemic stroke, TIA or cognitive dysfunction and may occur with high-intensity MRI lesions of white matter [92].

4. Renal manifestations

This happens in around 20-30 percent of patients and, even though treated, brings a poor prognosis. They have a high rate of deficiencies and relapses in care. Mild proteinuria and isolated hematuria are generally present, but nephrotic and nephritic syndromes and chronic renal insufficiency have also been identified to a smaller extent [93].

In comparison to MPGN, the frequently observed histopathological pattern is membranoproliferative glomerulonephritis (MPGN) with immune complex deposition in glomeruli and IgM staining, which can also be seen in HCV without cryoglobulinemia, where staining is of the form IgG.

Excitingly, in renal biopsies of patients who have negative serum anti-HCV antibodies and PCR, several authors find hepatitis C virus antigens denoting the potential intake of the antigen and its antibody in the immune complex [34]. Mesangioproliferative and focal proliferative glomerulonephritis in up to 20 percent of renal involvement are other forms of glomerulonephritis identified in mixed cryoglobulinemia associated with HCV [94,95].

5. Sicca symptoms

As previously mentioned, HCV is a sialotropic virus with a clinical image of dry mouth and dry eyes, close to that seen in primary Sjogren's syndrome, which has a similar histopathological image, namely focal lymphocytic infiltration, but with two major variations. With the absence of glandular canal injury, infiltrates are primarily perivascular rather than pericanalicular, and also predominantly with CD8+ ve rather than CD4+ve. A point of distinction may be anti SSA and anti SSB antibodies as well. They appear to be more optimistic in patients with primary Sjogren's syndrome [96].

6. Pulmonary manifestations

In accordance with Bronchoalveolar Lavage findings, subclinical alveolitis was identified in mixed cryoglobulinemia that may progress to clinically obvious interstitial lung disease in unusual cases.

Pulmonary function tests may show evidence of minor airway disease and gas exchange dysfunction, with symptoms ranging from dyspnea to pleurisy and cough. Mixed cryoglobulinemias less frequently observed in Bronchiolitis Obliterans Organizing Pneumonia (BOOP), pulmonary hemorrhage, and pulmonary vasculitis [97].

7. Endocrine disorders

In comparison with the general population, autoimmune thyroiditis, hypothyroidism and papillary thyroid carcinoma are more prevalent in mixed cryoglobulinemia patients. Type 2 diabetes mellitus, with and without mixed cryoglobulinemia, was also statistically related to HCV more than the general population [98,99].

8. Gastrointestinal and hepatic manifestations

Hepatomegaly, abnormal liver function tests or abnormal liver biopsy, splenomegaly, lymphadenopathy and abdominal pain have been defined in up to 90 percent, 30%, 20 percent and 20 percent of cases respectively.

Nearly 3/4 of the population, liver involvement happens with almost a threefold rise in advanced liver fibrosis and steatosis, as well as a substantial association with cirrhosis after age, gender and length of infection adjustment [100].

9. Cardiovascular manifestations

Mixed cryoglobulinemia has been documented for ischemic heart disease with coronary vasculitis, valvular heart disease with mitral valve damage and incompetence, pericarditis, cardiomyopathy, in particular hypertrophic form, and congestive heart failure [101].

10. Female reproductive dysfunctions

It should be remembered that generalized vascular disease triggers reproductive function disorders in hepatitis B virus and hepatitis C virus infections. With the successive development of hormonal homeostasis dysfunction, immune complex vasculitis produces degenerative changes in the hypothalamic pituitary area [88].

Conclusion

Systemic vasculitis, which is observed in HCV infection, underlies most extrahepatic manifestations with the involvement of many organs and tissues in the pathological process,

which complicates the timely diagnosis and treatment of chronic hepatitis. A variety of systemic extrahepatic pathology, which often outstrips the clinical picture of hepatitis itself, masquerading as another disease, and for many years prevails over a moderate and mild process in the liver, means that a specialist of any profile can meet with chronic HCV infection and its outcomes.

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RECOMBINANT CYTOKINES IN THE TREATMENT OF PNEUMONIA. CLINICAL EXPERIENCE

Antimicrobial chemotherapy is a keystone of the treatment of pneumonia. Prescription of antibacterial drugs does not always ensure the success of treatment due to the secondary immune deficiency developing in the process of the disease and the rapid growthof acquired antibiotic resistance.

The article presents experience and clinical and immunological effectiveness of the use of recombinant interleukin-2 (rIL-2) in the treatment and prevention of pneumonia in order to reduce the risk of pneumonia in cerebral strokes and severe exogenous poisoning.

In our study, we analyzed two clinical cases with of pneumonia

In patients with severe forms of pneumonia using complex therapy with recombinant interleukin-2, the time to achieve clinical and laboratory remission is reduced, the manifestations of respiratory failure and intoxication syndrome are stopped

Thus, accumulated clinical experience the administration of the recombinant drug interleukin-2 in combination with antimicrobial drugs in basic therapy showed positive effectiveness, validity and expediency, in order to improve the clinical course, normalize immunological parameters, as well as for the rapid and complete treatment of the inflammatory process in patients of different ages with severe pneumonia.

Key words: pneumonia, interleukin-2 (IL-2), immunity.

Introduction

Respiratory pathology covers all countries of the world, leads to long-term disability, to a decrease in the quality of life, which indicates the great social and economic significance of this pathology. Pneumonia remains one of the most common respiratory diseases in the structure of respiratory diseases and mortality from these diseases. One of the most urgent problems in pulmonology is the treatment of pneumonia. The characteristic of nosocomial pneumonia are:

The proportion of severe and prolonged diseases in the elderly, young and middle-aged without concurrent pathology is increased.

Higher pulmonary complication frequency [1, 2, 3].

Various disorders of immunological reactivity are revealed during clinical and immunological examination of patients with pneumonia of varying severity. The imbalance of cytokines, the development of a systemic inflammatory response and changes in the systems of cellular and humoral immunity are characteristic of the complicated form of community- and hospital-acquired pneumonia that develops in presence of systemic bacterial invasion. The period of transition of microbial aggression to the stage of the beginning of stabilization of the inflammation process is characterized by a decrease in the absolute number of lymphocytes and functional activity of cells with the CD3 + CD4 + phenotype in severe forms of community-acquired pneumonia with leukopenic syndrome [1, 4, 5].

Antimicrobial chemotherapy is a keystone of the treatment of pneumonia. Prescription of antibacterial drugs does not always ensure the success of treatment due to the secondary immune deficiency developing in the process of the disease and the rapid growth of acquired antibiotic resistance [6]. These facts show that the treatment regimes for pneumonia are necessary with the aim of activating the organism's protective and adaptive reactions and also significantly restricting the selection of microorganism resistant strains.

Inclusion in the system of complicated therapy for the treatment of serious forms of pneumonia and their complications of cytokine imbalance and incomplete phagocytosis will be pathogenetically justified. The quick and full resolution of

inflammatory syndromes and lung tissue damage are facilitated using recombinant cytokines that are known as recombinant interleukine-2. Recombinant interleukin-2 has been used in clinical practise for the treatment of pyo-inflammatory, infectious and oncological diseases since 1995.

Pharmacodynamic effects of IL-2 are associated with activation of clonal proliferation of T-lymphocytes, with the stimulation of cell differentiation of cytotoxic T lymphocytes, with the stimulation of clonal proliferation of b-lymphocytes, with increased synthesis of immunoglobulins by plasma cells of all classes, an increase in the functional activity of mononuclear phagocytes, a decrease in the level of spontaneous apoptosis of T-helper cells, increasing the synthesis of specific immunoglobulin isotypes of the majority of plasma cells. [7].

The experience of using recombinant interleukin-2 in complex therapy in pulmonology and phthisiology began in 1995 [8,9], it was prescribed to patients with severe community-acquired and hospital-acquired pneumonia of various etiologies, in the postoperative period and in wound sepsis, including in elderly patients [12], atypical pneumonia of chlamydia and mycoplasma etiology [13, 14].

In the literature, there is information about the use of recombinant interleukin-2 in the prevention of pneumonia, acute poisoning [2, 3] and cerebral strokes [15], and also showed good preventive results [2,3,15].

Clinical studies of the effectiveness of recombinant interleukin-2 were carried out in medical centers in Moscow [2, 3], St. Petersburg [10, 16], Saratov [4], Znamensk, Astrakhan region [5], Blagoveshchensk [13], etc.

The aim of the study was to evaluate the effectiveness of the use of recombinant interleukin-2 in the complex therapy of pneumonia of various etiology.

Results and discussion

The after effects of a clinical report assessing the utilization of recombinant interleukin-2 for the treatment of serious acute pneumonia were gotten at S.M. Kirov Military State Academy in St. Petersburg [17]. They proved the efficacy of use of intravenous infusion of 0.25 mg of recombinant interleukin-2 for the treatment of pneumonia developed in wound sepsis. The course of treatment of patients included 2-4 daily intravenous infusions of recombinant interleukin-2 at dose 0.125-0.25 mg. Surgical cleaning of primary and secondary metastatic seats of infection is a necessary condition for starting the treatment with recombin int interleukin-2

On days first third of the treatment with recombinant interleukin-2 there were a decline in manifestations of intoxication, of internal body temperature and shortness of breath. It was noticed a positive dynamic of indications of respiratory distress syndrome (by X-ray) on third to fifth day of treatment.

In addition, a positive dynamics of laboratory parameters was observed: a decrease in the white blood cells index of intoxication, an increase in the absolute number of lymphocytes in the peripheral blood along with clinical improvement of the condition of patients. On average, the duration of antibiotic therapy decreased by 7 days, the recovery process was accelerated by 14 days, and the mortality rate decreased by 28% when using recombinant interleukin-2 (Table 1) [11, 18].

Table 2 – Laboratory results Clinical efficacy of Roncoleukin® in the treatment of acute pneumonia developed in wound sepsis

Indicators	The value of indicators by groups	
	Treatment with recombinant interleukin-2 (n = 47)	Treatment without recombinant interleukin-2 (n = 30)
Duration of antibiotic therapy	Reduction by 7 days compared to control	
General mortality, %	8.55	36.78*
Recovery, day	15.05 ± 2.85	29.2 9± *5.27**

*p<0,05

Conclusion

1. In patients with severe forms of pneumonia using complex therapy with recombinant interleukin-2, the time to achieve clinical and laboratory remission is reduced, the manifestations of respiratory failure and intoxication syndrome are stopped, the duration of the febrile period is reduced, there is a clear positive X-ray and laboratory improvement in most patients.

2. The immunological results showed that the normalization of inflammatory changes in the clinical and biochemical analysis of blood and the restoration of previously reduced parameters of the cellular link of immunity correlates with the clinical effects of immunocorrection.

3. Clinical experience with the use of recombinant interleukin-2 has proven the effectiveness of intravenous, subcutaneous and inhalation administration of the drug in patients of different age groups.

4. When the drug is administered in the phase of stabilization of infiltration, the effects of immunotherapy with recombinant interleukin-2 are most pronounced.

5. The accumulated clinical experience the administration of the recombinant drug interleukin-2 in combination with antimicrobial drugs in basic therapy showed positive effectiveness, validity and expediency, in order to improve the clinical course, normalize immunological parameters, as well as for the rapid and complete treatment of the inflammatory process in patients of different ages with severe pneumonia.

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Section 3
Cardiology

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THE RELATIONSHIP BETWEEN ABO BLOOD GROUP AND ATRIAL FIBRILLATION

Atrial fibrillation is the most common type of cardiac arrhythmia associated with substantial mortality and morbidity, largely due to thromboembolism, particularly stroke. AF shares strong association with cardiovascular diseases like hypertension, ischemic heart disease, congestive heart failure, valvular heart disease. Although almost all risks of AF have been overlooked but correlation between ABO blood group and AF in general has not been investigated. Hence, we decided to study and identify the link between ABO blood group and AF.

To fully assess effects of ABO blood group on AF and investigate the interaction between blood groups and sex on the prevalence of atrial fibrillation.

This is a retrospective descriptive cross-sectional study. The data originates from database of "Scientific Research Institute of Cardiology and Internal Diseases" Almaty city, Kazakhstan during 2019. AF was confirmed using an electrocardiograph. IBM SPSS version 22 was used to conduct the statistical analyses.

There were 475 patients with atrial fibrillation included in this study. A total of 279 patients (58.7%) were male, and 196 patients (41.3%) were female. The distribution of ABO blood group in the patients was as follows: 165 patients had blood group A (34.7%), 112 patients had blood group B (23.6%), 52 patients had blood group AB (10.9%) and 146 patients had blood group O (30.7%). After comparison of O blood group with non O blood groups there was no significant difference in number of O and A blood groups (P = 0.282), but other non O blood groups had significant differences in number [B (P = 0.035), AB (P = 0,000)].

Our results establish that non-O blood groups act as an independent risk factor for AF compared with individuals having O type blood.

Key words: Atrial fibrillation, ABO blood group, comorbidities.

Introduction

The most common form of cardiac arrhythmia is atrial fibrillation (AF) (1). Patients are at raised risk for death, heart failure, hospitalization, and thromboembolic occurrences (2–4). In the United States, it affects between 2.7 and 6.1 million people (5). AF is highly age-related and affecting 4% of people over the age of 60 and 8% over the age of 80. Approximately 25% of people over the age of 40 will experience AF at some point in their lives (6). In addition to age, there are many types of cardiac and medical conditions that are also closely linked to AF such as: hypertension, coronary artery disease, heart failure, obesity, valvular heart disease, diabetes mellitus, thyrotoxicosis, and sleep apnea syndrome (7). Therefore, AF has a strong association with cardiovascular diseases.

The ability of human ABO blood type to influence von Willebrand factor (VWF) and factor VIII (FVIII) plasma levels has been shown to be a risk factor for cardiovascular disorders (8,9). Blood group O can protect against non-valvular atrial fibrillation related to peripheral cardioembolic complications, which could be due to lower circulating of the von Willebrand factor levels(10). Beyond immunity, the ABO blood groups are involved in physiological and pathological processes (11). Nonetheless, no

previous correlation between ABO blood group and cardiac arrhythmias has been identified or published in the literature. Except one article to figure out the possible link between ABO blood group and isolated AF (12).

To fully evaluate ABO blood group and other possible risk factors for AF and types of AF, we conducted a cross-sectional study and included hypertension, CHF, IHD, diabetes mellitus (DM) and history of CVA in the comorbidities. We also investigated the interaction between ABO blood group and sex on the prevalence of AF. Based on a study in 2014 which included 369 healthy Kazakh donors, blood group O is the most common blood group, followed by A, B, and AB (13).

Justification of the choice of articles and goals and objectives

Aim

To assess the link between ABO blood group and atrial fibrillation

Objectives

- To compare non-O blood groups with O type blood in atrial fibrillation.
- To assess the most common association comorbidities for atrial fibrillation.
- To assess the evidence of ABO blood group and sex impact on the prevalence of atrial fibrillation.

Scientific research methodology

This was a year-long retrospective descriptive cross-sectional study. A consecutive nonrandom sampling technique was used to pool all patients with AF who admitted in «Scientific Research Institute of Cardiology and Internal Diseases» Almaty city, Kazakhstan. A total of 475 patients (279 males and 196 females) were selected. Median age of patients was 65 years and IQR between 58-70. All were diagnosed with AF by the cardiologist, and AF was confirmed using an electrocardiogram (ECG). Patients were given a comprehensive physical examination with a detailed clinical history collection. IBM SPSS version 22 was used to conduct the statistical analyses. Normality of variables was tested by Kolmogorov-Smirnov test. Abnormally-distributed data is presented as median (interquartile range), and analyzed using Mann–Whitney U test. Dichotomous variables were analyzed with Pearson's chi-squared test, and expressed as percentages. Multivariate logistic regression analysis was performed using a forced entry method of base-line clinical characteristics to examine the associations of the non-O and O blood groups with risks AF, as well as to examine those of any type of the ABO blood group. The P-value cutoff point of 0.05 was used to assess the degree of significance.

Results

As shown in Table 1, there were 475 patients with atrial fibrillation included in this study. A total of 279 patients (58.7%) were male, and 196 patients (41.3%) were female. The distribution of ABO blood group in the patients was as follows: 165 patients had blood group A (34.7%), 112 patients had blood group B (23.6%), 52 patients had blood group AB (10.9%) and 146 patients had blood group O (30.7%).

Table 1 – General characteristics of study population (n=475)

variables	All cases	%	ABO blood groups								Test of differences	
		A		B		AB		O				
		N	%	N	%	N	%	N	%	X2	P-Value	
Sex												
male	279	58.7%	88	53.3%	71	63.4%	30	57.7%	90	61.6%	3.522	0.318
female	196	41.3%	77	46.7%	41	36.6%	22	42.3%	56	38.4%		
Age median (IQR) years	65 (58 - 70)		65 (59 - 70)		66 (59 - 70)		68 (59 - 73)		64 (57 - 70)		0.000	
Age group												

<39		12	2.5%	5	3.0%	2	1.8%	0	0.0%	5	3.4%	10.797	.546
40-49		33	6.9%	12	7.3%	7	6.3%	5	9.6%	9	6.2%		
50-59		83	17.5%	25	15.2%	20	17.9%	9	17.3%	29	19.9%		
60-69		212	44.6%	78	47.3%	54	48.2%	16	30.8%	64	43.8%		
>=70		135	28.4%	45	27.3%	29	25.9%	22	42.3%	39	26.7%		
Rh_Factor													
Negative		43	9.1%	21	12.7%	7	6.3%	3	5.8%	12	8.2%	4.579	0.205
Positive		432	90.9%	144	87.3%	105	93.8%	49	94.2%	134	91.8%		
Comorbidities													
HTN	no	60	12.6%	19	11.5%	16	14.3%	6	11.5%	19	13.0%	0.540	0.910
	yes	415	87.4%	146	88.5%	96	85.7%	46	88.5%	127	87.0%		
CHF	no	204	42.9%	70	42.4%	48	42.9%	20	38.5%	66	45.2%	0.750	0.861
	yes	271	57.1%	95	57.6%	64	57.1%	32	61.5%	80	54.8%		
IHD	no	157	33.1%	56	33.9%	35	31.3%	14	26.9%	52	35.6%	1.540	0.673
	yes	318	66.9%	109	66.1%	77	68.8%	38	73.1%	94	64.4%		
DM2	no	363	76.4%	127	77.0%	83	74.1%	42	80.8%	111	76.0%	0.919	0.821
	yes	112	23.6%	38	23.0%	29	25.9%	10	19.2%	35	24.0%		
History of CVA	no	424	89.3%	148	89.7%	105	93.8%	46	88.5%	125	85.6%	4.446	0.217
	yes	51	10.7%	17	10.3%	7	6.3%	6	11.5%	21	14.4%		
Obesity	no	286	60.2%	96	58.2%	73	65.2%	31	59.6%	86	58.9%	1.549	0.671
	yes	189	39.8%	69	41.8%	39	34.8%	21	40.4%	60	41.1%		
TTx	no	469	98.7%	164	99.4%	110	98.2%	51	98.1%	144	98.6%	1.011	.799[a,b]
	yes	6	1.3%	1	.6%	2	1.8%	1	1.9%	2	1.4%		
RVHD	no	463	97.5%	160	97.0%	109	97.3%	51	98.1%	143	97.9%	0.389	.942[a]
	yes	12	2.5%	5	3.0%	3	2.7%	1	1.9%	3	2.1%		
Smoking	no	421	88.6%	143	86.7%	98	87.5%	44	84.6%	136	93.2%	4.566	0.206
	yes	54	11.4%	22	13.3%	14	12.5%	8	15.4%	10	6.8%		
Types of AF													
paroxysmal		179	37.7%	71	43.0%	50	44.6%	16	30.8%	42	28.8%	15.735	.073
persistent		118	24.8%	31	18.8%	24	21.4%	14	26.9%	49	33.6%		
long standing persistent		76	16.0%	27	16.4%	17	15.2%	11	21.2%	21	14.4%		
permanent		102	21.5%	36	21.8%	21	18.8%	11	21.2%	34	23.3%		
Total		475	100.0%	165	34.7%	112	23.6%	52	10.9%	146	30.7		

After comparison of O blood group with non-O blood groups there was no significant difference in number of O and A blood groups (P = 0.282), but other non-O blood groups had significant differences in number [B (P = 0.035), AB (P = 0,000)] (Table 2).

Table 2 – Comparison of O and non-O blood groups (n=475)

Comparison of O and non-O blood group				Test of difference		
Blood groups		Number	%	P -Value		
A		165	34.7%	0.282		
B		112	23.6%	0.35		
AB		52	10.9%	0,000		
O		146	30.7%			
Total		475	100.0%			
Estimation of blood groups						
Blood groups		B	Std. Error	Wald	DF	Sig.
A	Intercept	.122	.114	1.159	1	.282
B	Intercept	-.265	.126	4.454	1	.035
AB	Intercept	-1.032	.161	40.865	1	.000
a. The reference category is: O.						

Types of atrial fibrillation distributed as follows: 179 patients had paroxysmal AF (37.7%), 118 patients had persistent AF (24.8%), 102 patients had permanent AF (21.5%) and 76 patients had long standing persistent AF (16.0%). Differences in sex, age groups, Rh factor, comorbidities such as hypertension, congestive heart failure, ischemic heart diseases, diabetes mellitus, history of CVA, obesity, thyrotoxicosis, rheumatic heart disease and smoking between patients with different ABO blood groups were not significant. The most common associated comorbidities for atrial fibrillation were hypertension 415 (87.4%), IHD 318 (66.9%) and CHF 271 (57.1%), DM 112 (23.6%) and a history of CVA 51 (10.7). Paroxysmal atrial fibrillation was the most common type of AF which accounted in 179 (37.7%) patients.

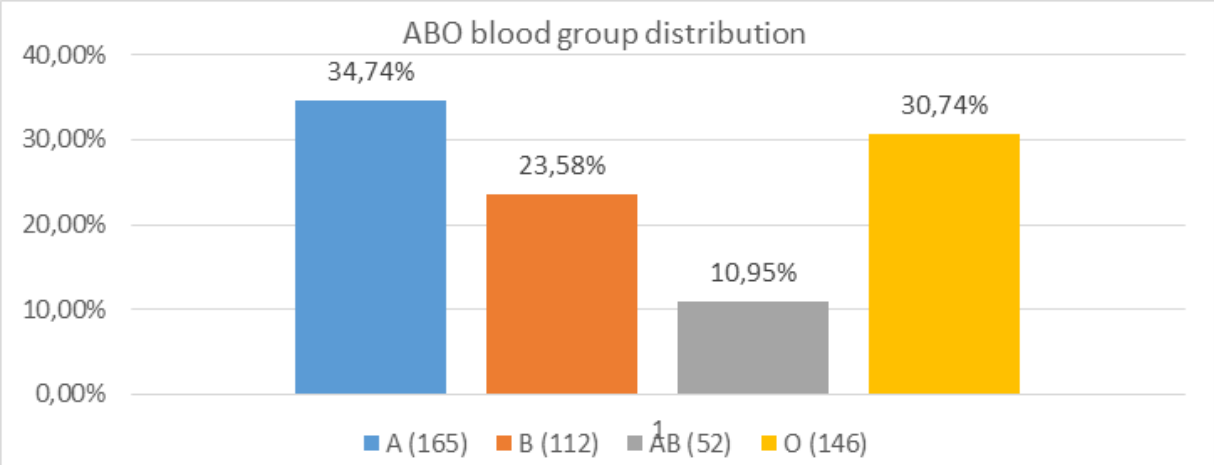

Figure 1– Distribution of ABO blood group in patients with atrial fibrillation

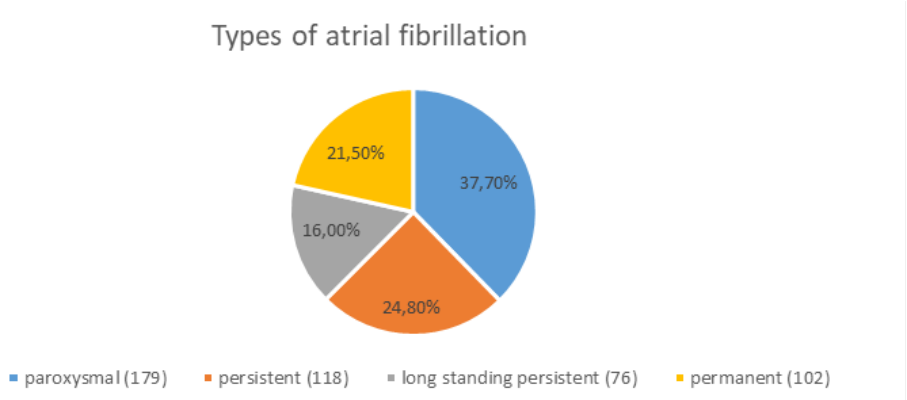

Figure 2 – The distribution of types of atrial fibrillation

In this cross-sectional study, we found that patients with non-O blood groups were at significantly increased risk for atrial fibrillation over that in patients with blood group O. However, the risk has not been statistically estimated although roughly suggested from the results. The relationship between non-O blood groups and risk of myocardial infarction and venous thromboembolism reported by many studies (14). The blood group O is the most common type in Kazakhstan (13)genotyping employs a different strategy and is aimed directly at genes that determine the surface proteins. ABO blood group genotyping by real-time PCR has several crucial advantages over other PCR-based techniques, such as high rapidity and reliability of analysis. The purpose of this study was to examine nucleotide substitutions differences by blood types using a PCR-based method on Kazakh blood donors.Methods. The study was approved by the Ethics Committee of the National Center for Biotechnology. Venous blood samples from 369 healthy Kazakh blood donors, whose blood types had been determined by serological methods, were collected after obtaining informed consent. The phenotypes of the samples included blood group A (n = 99, however, non-O blood groups (mostly A type) show strong association with atrial fibrillation according to the results of our study. Many studies demonstrated that the immune system (inflammatory process) plays an important role in the production of systolic and diastolic hypertension (15). This is what raises the red flag when considering a possible connection and clarification between blood group and AF. Generally, patients with non-O blood groups have higher tendency to develop atrial fibrillation. There was no evidence between ABO blood group interaction and sex on the prevalence of atrial fibrillation. Paroxysmal atrial fibrillation was the most common types of AF which accounts 179 (37.7%).

Conclusion

Results from the study of relationship between ABO blood group and AF show that non-O blood groups, especially A group, have a significant correlation with the risk of developing AF when compared to people with O blood group. Differences in data by sex, age groups, Rh factor, concomitant diseases, such as arterial hypertension, congestive heart failure, coronary heart disease, diabetes mellitus, history of cardiovascular disease, obesity, thyrotoxicosis, rheumatic heart disease, and smoking among the patients with various ABO blood groups were not significant. The most frequent comorbidities of atrial fibrillation were arterial hypertension 415 (87.4%), IHD 318 (66.9%) and 271 CHF (57.1%), DM 112 (23.6%) and a history of CVA 51 (10.7%).

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PREVALENCE OF ACS IN AVICENNA BALKHI TEACHING HOSPITAL IN AFGHANISTAN

Background: One third of global deaths are caused by CVD, and the most common is IHD. Approximately 80% of IHD which is caused by atherosclerosis, with the remainder caused by non-atherosclerotic causes such as VHD, radiation, vasculitis, and other.

Aim: To study the prevalence of ACS in Avicenna Balkhi Teaching Hospital.

Methods: This is a retrospective cross sectional study, we collected data of 180 ACS patients from 01.01.2019 till 01.06.2019 in Avicenna Balkhi Teaching Hospital; data was evaluated on clinical traits, treatment, and outcome in ACS patients.

Results: 180 patients of ACS admitted during the first six months of 2019. From the aforementioned ACS%, 62.7% (113) were STEMI and 37.2% (67) were NSTEMI/UA, with a male to female ratio was 2.64:1. 66.7% of patients had an age of 60 – 79 years. The mean time of patients' admission in CCU was15.5h and was higher in NSTEMI/UA than STEMI (18.3 h vs 11.8 h) respectively. Treatment of all ACS patients such as STEMI, NSTEMI, UA was the same in 90% and received antiplatelet, statins, anticoagulants, anxiolytics. 30,4% of STEMI patients received thrombolytic therapy with streptokinase (which is available in Afghanistan), just 10% from 30.4% we saw the effective role of streptokinase. The most common comorbidity diseases include; Hypertension 45.6%, DM 22.2%, Smoking 27.8%, Heart failure 21.7%, COPD 5.6%.

Conclusion: Most of the ACS patients were STEMI, which was more male than female. More than 50% of patients had an age of 60-79 years old, the mean time of admission in the CCU room was more than 10, and the most common comorbidities were HTN, smoking, DM and heart failure. Increasing public awareness of heart disease, expanding professional medical staff capacity, and outfitting the cath lab and cardiac surgery ward. Finally, this study will serve as a resource for future research.

Key words: ACS, IHD, STEMI.

Introduction

Cardiovascular disease is responsible for 33.3% of deaths around the world [1]. There are lots of cardiovascular diseases but ischemic heart disease is the most common one[2]. In approximately 80% of IHD, the cause is atherosclerosis (ACD) [3]. In most cases(70%) multiple risk factors are responsible for IHD ,and in 4.5% have no risk factors [4].Besides modifiable risk factors in past several decades age of population is getting rise [5,6] and united nation predict that number of individuals over 65 years from one in 11 in 2019 may increase to one in six in 2050[7]. Sleeplessness, mood and affect disorders, social problems contribute IHD in new population [8, 9]. Cost either for treatment, primary and secondary prevention regarding IHD will rise from 863million USD to 1 trillion USD in 2030 [10]. In developing countries, the frequency of non-ST elevation ACS is two to three times higher than that of ST elevation myocardial infarction (STEMI) based on hospitalization rates [14, 15]. Incidence of IHD in overall, and ACS in specific, rises with age, though it occurs 7–10 years earlier in men than in women on average. Men are much more likely than women under the age of 60 to develop ACS, but women account for the majority of patients over 75years.In Europe, three-fifths of all CVD deaths occur in people over 75, and one-fifth of all CVD deaths occur in people under 65. CVD affects the lives of more men (0.9 million) than women (0.5 million) before they reach 75; but, owing to the larger number of overall premature deaths in men, CVD claims the lives of both sexes before they reach 75 [16]. In comparison to those between the ages of 35 and 64, the overall incidence of CHD is double for men and triple for women between the ages of 65 and 95. The most serious effects of CHD, such as myocardial infarction and sudden death, are uncommon in premenopausal women. Following

menopause, the incidence and severity of coronary heart disease (CHD) increases dramatically.

Unfortunately, in Afghanistan we have not performed any standard research regarding compiling data especially in cardiology field yet. Between 2009 and 2014 Kabul NATO role 3 hospital provided medical services to NATO coalition military forces whom were engaged in Afghanistan as well as Afghan national security forces and non-Afghan civilian from Jun 16 th and October 1th 2012 [11], during this time 52 patients were assessed that most of them were non Afghan citizens.34.2% were suffered from acute coronary syndrome and 76.9% of these ACS were civilians, 30.8% diagnosed cardiomyopathy [12]. Among four patients with STEMI, three of them had fatal complications such as death, acute heart failure, and failed of thrombolysis [13]. The aim of this study is to reveal prevalence of ACS in Avicenna Balkhi Teaching Hospital during 2019, and correction of other comorbidities in outcome of ACS, and will offer some recommendations for early detection of ACS.

Justification of the choice of articles and goals and objectives

Aim: To determine the prevalence of ACS in Avicenna Balkhi Teaching Hospital.

Objectives:

– To specify the prevalence of ACS according to age.

– To defining the role of other comorbidities in outcome of ACS.

– To clarify the prevalence of ACS in different gender category.

Scientific research methodology

This is a descriptive cross sectional retrospective study of all registered patients presenting with ACS from 01.01.2019 till 01.06.2019 in the emergency room (ER) were included in the study. Detailed history, physical examination, and necessary investigations were done in all patients. These data were arranged by IBM SPSS 22 and excel to compare variables. Independent T test for analysis of grouping variables with scale variables, one sample T test for comparison of scale variable with scale variable from literatues,chi squire test for inferential statistic of categorical data and one way ANOVA for correlation of dependent and independent variables. Included patients were; Patients who visited ER due medical problems and completed lab exams after that they diagnosed ACS and patients should have the diagnostic criteria of ACS as given below;

Diagnosis of MI was made if there is: Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:(a) Ischemic symptoms; (b) Development of pathologic Q waves on the ECG;(c) ECG changes indicative of ischemia (ST segment elevation or depression) ,[14].

Unstable Angina (UA) was defined as angina pectoris (or equivalent type of ischemic discomfort) with at least one of three features:(1) occurring at rest (or minimal exertion) and usually lasting >20 min (if not interrupted by nitroglycerin administration); (2) being severe and described as frank pain, and of new onset (i.e., within 1 month; and (3) occurring with a crescendo pattern (i.e., more severe, prolonged, or frequent than previously).(4) Patients with above features without elevation in cardiac markers were categorized as UA) [15].

Clinical and lab findings which were analyzed include; age,gender,HTN, DM, smoking, BMI, family history of CHD, ECG finding, echocardiography findings, cardiac biomarkers, complications, and treatment .Considering of atypical presentations like dyspnea, nausea/vomiting, indigestion, fatigue, sweating, and arm or shoulder pain in the absence of chest pain (15).

Unfortunately, absence of equipped cardiology centers, fully experienced physicians in cardiology fields especially in interventional and cardiac surgery increased mortality rate due to ACS in north zone of Afghanistan (Avicenna Balkhi Teaching Hospital).

Result

Total number of acute coronary syndrome patients were 180 patients, from aforementioned ACS % 62.77% (113) of all registered patients were STEMI, and 37.2%(67) NSTEMI or UA, male female ratio (2.64:1).Mean of age in this study was 66.43±13.38 years. 8.4% of male and 16.3% of female had age of under 39 years,13.7% of male and 18.4% of female had age between 40 -59 years,69.5% of male and 59.2% of female had age between 60 -79 years , and finally 8.4% of male and 6.1% of female had age over 80 years. (P V = 0.329). Mean time to admission in CCU was15.5h and was higher in NSTEMI/UA than STEMI (18.3 h vs 11.8 h). Atypical presentations of IHD were common in NSTEMI/UA.Treatment of all ACS patients such as STEMI ,NSTEMI,UA are the same in 90% and received antiplatelet, statins, anticoagulants, ACEI/ARB,Beta-Blocker,anxiolytics.30,4% of STEMI patients received thrombolytic therapy with streptokinase

(which is available in Afghanistan),just in 10% from 30.4% we saw the effective role of streptokinase. The mean time for door to needle was 2h and 23min. Number male ACS patients who had heart failure 21.4% and female was 22.4%.(PV =0.876) (table – 2, Figure – 4). 67.9% of male and 61.2% of female had normal BMI, 5.3% of male and 6.1% of female were in pre-obesity stage ,16.8% of male and 16.3% of female were in obesity stage – 1 , 6.1% of male and 8.2% of female had obesity – 2 , 3.8% of male and 8.2% of female had obesity – 3 (PV =0.761).Table -3, Figure -5). In this study diabetes mellitus seen in 23.7% of male and 18.4% of female .(PV =0.447), and HTN was seen in 38.9% of male and 63.3% of female.(PV=0.004).Percentage of COPD as comorbidity disease in ACS was 5.3% in male and 6.1% in female .(PV = 0.839).finally hyperlipidemia as a risk factor seen in 35.1% of male and 26.5% of female,PV(0.275).(Table -4,Figure – 6) . 27.8% of ACS patients were either current smoker or smoker in the past. (Table -7).

Table – a: General characteristics of study population

General characteristic of study population		Sex				Test of difference	
	Male		Female				
	Number	%	Number	%	χ2	PV	
Age Group	< 39 y	11	8.4%	8	16.3%	3.436	0.329
	40 - 59 y	18	13.7%	9	18.4%		
	60 -79 y	91	69.5%	29	59.2%		
	>80 y	11	8.4%	3	6.1%		
BMI Group	Normal	89	67.9%	30	61.2%	1.86	0.761
	Pre-Obese	7	5.3%	3	6.1%		
	Obesity -1	22	16.8%	8	16.3%		
	Obesity - 2	8	6.1%	4	8.2%		
	Obesity - 3	5	3.8%	4	8.2%		
HF	No	103	78.6%	38	77.6%	0.24	0.876
	Yes	28	21.4%	11	22.4%		
DM	No	100	76.3%	40	81.6%	0.579	0.447
	Yes	31	23.7%	9	18.4%		
COPD	No	124	94.7%	46	93.9%	0.041	0.839
	Yes	7	5.3%	3	6.1%		
HTN	.No	80	61.1%	18	36.7%	8.514	0.004
	Yes	51	38.9%	31	63.3%		
Hyperlipidemia	.No	85	64.9%	36	73.5%	1.193	0.275
	Yes	46	35.1%	13	26.5%		

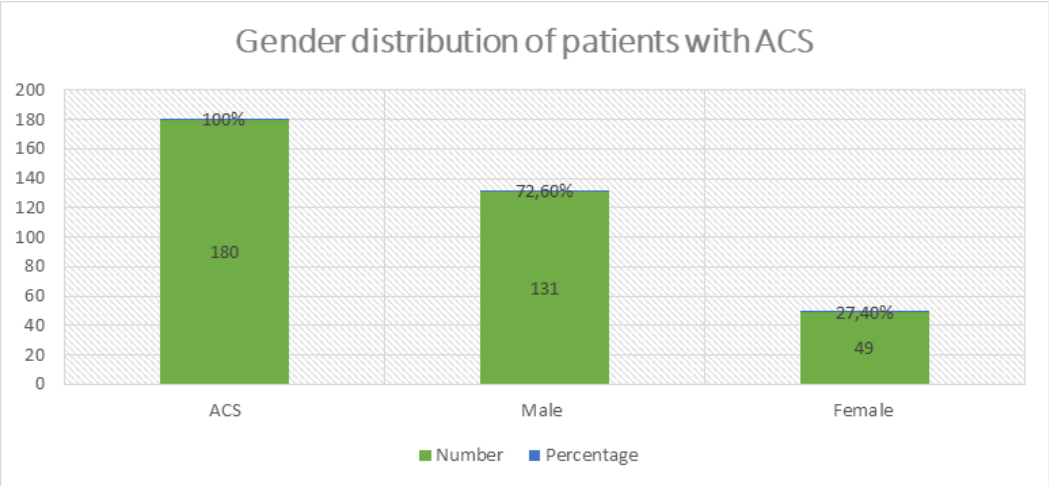


Figure 1 – Relation of Gender with ACS

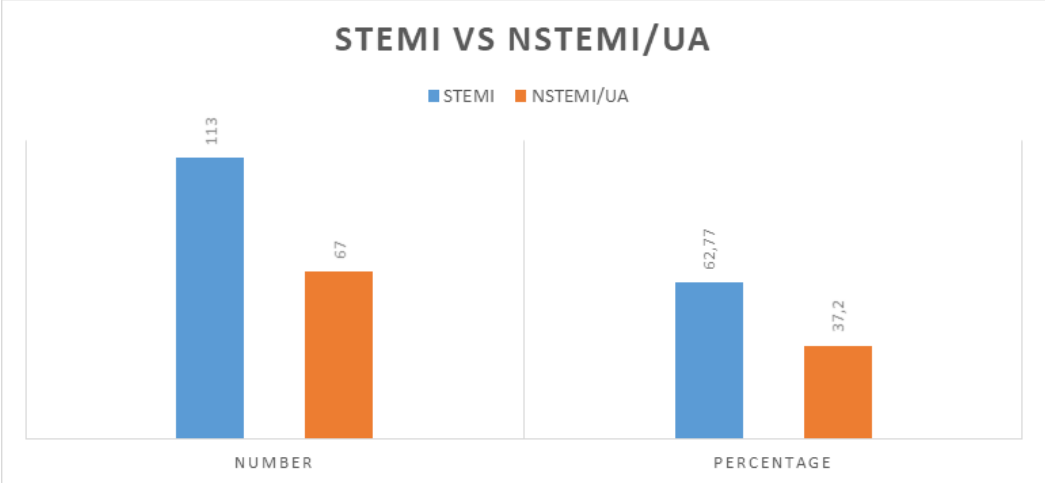


Figure 2 – Types of ACS (STEMI &NSTEMI/UA)

Table 1 – Age category and sex

		Sex				Test of difference	
	Male		Female				
	Number	%	Number	%	χ2	PV	
Age Category	Under 39y	11	8.4%	8	16.3%	3.436	0.329
	40 - 59 y	18	13.7%	9	18.4%		
	60 - 79 y	91	69.5%	29	59.2%		
	Over 80 y	11	8.4%	3	6.1%		

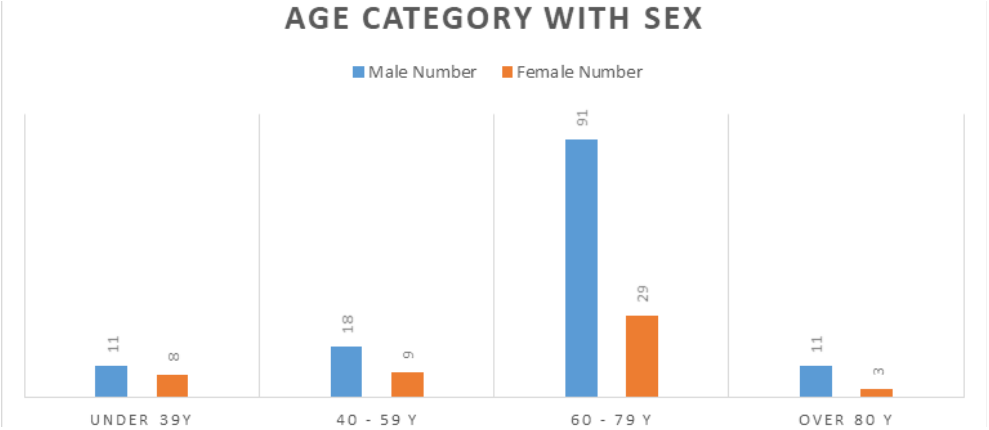


Figure 3 – Age category with sex

Table 2 – Heart failure in ACS patients according to sex

		Sex				Test of difference	
	Male		Female		χ2	PV	
	Number	%	Number	%	0.024 77.60% 22.40%	0.876	
HF	No	103	78.60%	38			
	Yes	28	21.40%	11			

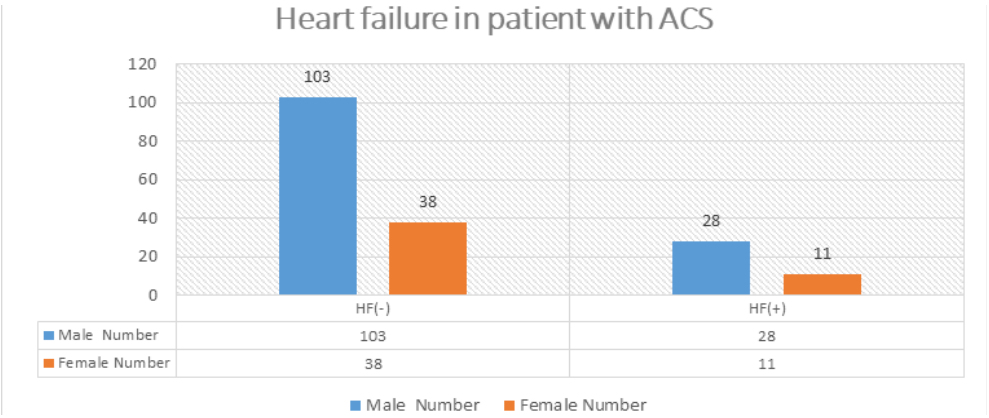


Figure 4 – Heart failure in ACS patients

Table 3 – BMI in ACS patients

		Sex				Test of difference	
	Male		Female				
	Number	%	Number	%	χ2	PV	
BMI Category	Normal	89	67.9%	30	61.2%	1.86	0.761
	Pre-Obese	7	5.3%	3	6.1%		
	Obesity -1	22	16.8%	8	16.3%		
	Obesity - 2	8	6.1%	4	8.2%		
	Obesity - 3	5	3.8%	4	8.2%		

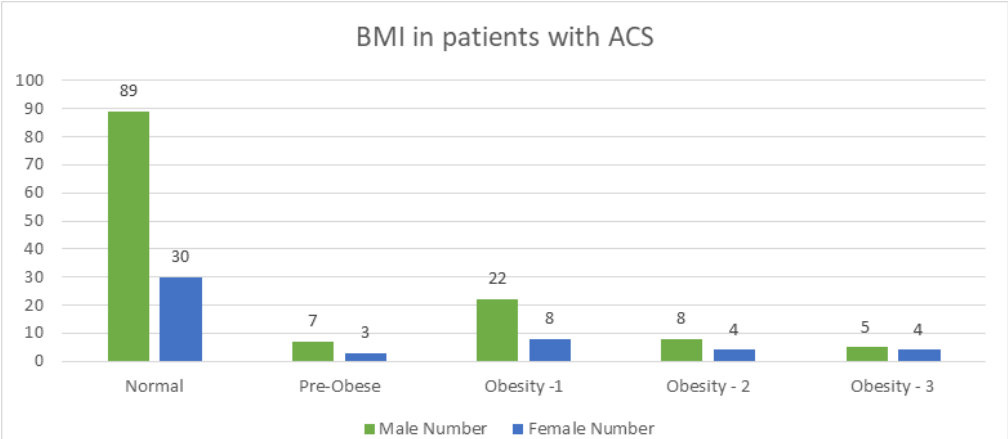


Figure 5 – BMI in ACS patients

Table 4 – DM, COPD, HTN and hyperlipidemia as comorbidity diseases in ACS

		Sex				Test of difference	
	Male		Female				
	Number	%	Number	%	χ2	PV	
DM	No	100	76.3%	40	81.6%	0.579	0.447
	Yes	31	23.7%	9	18.4%		
COPD	No	124	94.7%	46	93.9%	0.041	0.839
	Yes	7	5.3%	3	6.1%		
HTN	No	80	61.1%	18	36.7%	8.514	0.004
	Yes	51	38.9%	31	63.3%		
Hyperlipidemia	No	85	64.9%	36	73.5%	1.193	0.275
	Yes	46	35.1%	13	26.5%		

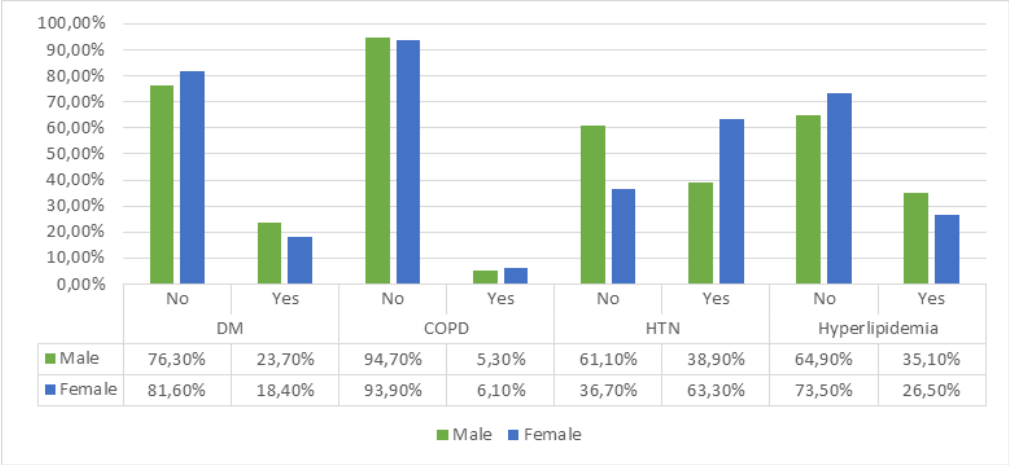


Figure 6 – DM, COPD, HTN and hyperlipidemia as comorbidity diseases in ACS

Table 5 – Smoking in ACS patients

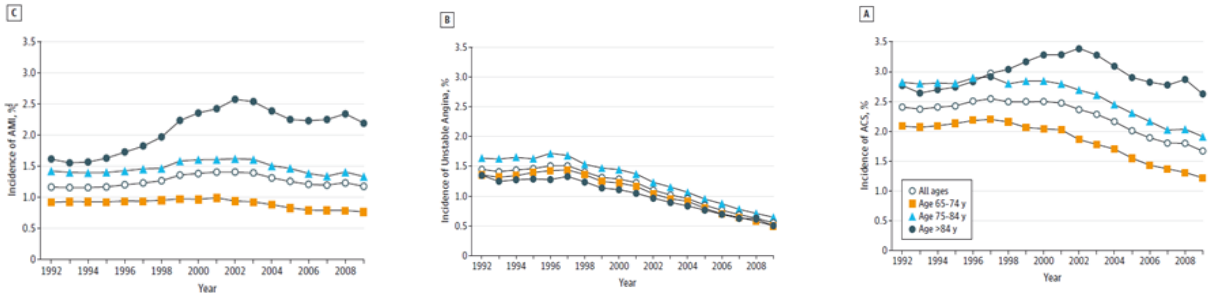
Smoking in ACS patients										
F		Levene's Test		t-test for Equality of Means						
		Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference		
								Lower	Upper	
Smoking	Equal variances assumed	1.575	.211	.600	178	.550	.045	.075	-.104	.194
	Equal variances not assumed			.613	89.972	.542	.045	.074	-.101	.192

Discussion

This is the first study of ACS prevalence in North zone of Afghanistan that will be published in a foreign journal. Similar studies were performed in some Asian countries; during this study, we found some significant differences, and some similarities with other studies.

In our study of STEMI was 62.77%, while in a study that was done by Farhin Iqbal et al in north west of India showed 72.4% [16], we can introduce some reasons that why prevalence of STEMI is lower than north west of India; Patients' and their relatives' perception and knowledge of heart disease is very low. Therefore, most patients do not go to the doctor or hospital in the early stages of the disease. Afghanistan is a war-torn country and most of Afghanistan's population live below the poverty line and is unable to make a living on a daily basis. The exorbitant costs of treating heart disease cannot be paid in any way. Why the prevalence of ACS is low? low of misperception of patients regarding heart diseases, inattention to diseases, Inability to perform examinations before the disease, Inability to continue treatment due to economic problems, lack of equipped heart centers in Afghanistan and lack of professional staff in the heart disease department, also in Afghanistan we do not have any computer base registration system, all of registration is hand writing base. In a study by Shukri M. Al-Saif et al showed that 77% of ACS patients were male [17], in our study 72.8% of patients were male ,according to some wrong accepted traditions, even in some literate families when some of female member of family become sick they ignore their sicknesses, and other relatives ignore too, even they don't want to be admitted in hospital.In this study the incidence of HTN as a risk factor for AMI is 55% [17] ,whereas in our collected data prevalence of HTN is 45.6%,we face with lots of patients that come to hospital for some other problems, when responsible physicians check their blood pressure, show high and patients even have no any sensible signs and symptoms to accept that have high blood pressure, even if they are known patients of HTN either emergency ,urgency or malignant HTN , they don't visit regularly their responsible physicians. In another study named "Temporal trends in the prevalence and outcomes of geriatric patients with acute myocardial infarction in Japan–A report from the Miyagi AMI Registry Study" by Koichi Sato,et al in Japan examined total of 6596 AMI from 2005 to 2016 , male –female ratio was 4.141;2.455, they divided them in age sub groups; ag[70–79y (n = 3,485), 80–89y (n = 2,601), and _90 years (n = 510)] [15]. Same as our finding in Avicenna Balkhi Teaching Hospital. In another study under name of "prevalence of Acute Coronary Syndrome in the General Medicare Population, 1992 to 2009" was performed by Gautam R, et al show that there are some fluctuations in the aspect of age of patients during 1992 to 2009., the proportion of patients aged 65 to 74 years decreased from 56% to 50%, while the proportion older than 84 years increased from11%to 15%. However, the proportions of women (60% to 58%) and white patients (88%to 87%) remained relatively constant. The annual unadjusted prevalence of ACS was about 2.4%to 2.5%until 2002 and then steadily declined to about 1.7% in 2009. (Figure, A). The incidence of unstable angina steadily declined (from 1.5% in 1997 to 0.6%in 2009; Figure, B), but that of AMI

remained constant, about 1.2%to 1.4%, throughout the study period (Figure,C). This trend was similar for all age, sex, and race groups except patients older than 84 years, in whom the ACS incidence Initially increased, from2.8%in 1992 to 3.4%in 2002, and then declined to 2.6% by 2009 % [16].



Best diagnostic and therapeutic procedure of ACS is angiography and angioplasty; as previously mentioned in Afghanistan this facilities are impossible in most governmental and private hospitals, except in one or two private hospitals in capital of Afghanistan Kabul.

Study limitations

Certain limitations of this study are; first this is a single center base study of ACS, and may differ from other centers in other cities of Afghanistan even may differ from other centers in Balkh province. Second, all of patients' documents are not saved and registered in computer data base so there are lots of problem in documents of patients .Third, in Avicenna Balkhi Teaching Hospital we don't have any equipped ward of cardiology with professional physicians, even though this hospital is training center for new generation of physicians in different fields. Forth, patients and their relatives in most of the cases do not give full information about their illnesses, some time they leave CCU room without permission of responsible physician. Fifth, until now in Afghanistan, there is no any formal academic publications to encourage medical staffs to research regarding different subject, and finally we have not seen yet, that governmental officials support medical staffs in research fields.

Conclusion

These data represent the first reported study on spectrum of ACS in North zone of Afghanistan and this is the first study will published in foreign journal, we tried our best to collect data significantly acceptable. The majority of ACS patients had STEMI, which was more common in men than in women. More than half of the patients were between the ages of 60 and 79, most of the patients admitted in the CCU room ten hours after onset of symptoms, and the most prevalent comorbidities were HTN, smoking, diabetes, and heart failure. Citizens' economic troubles, a lack of awareness about cardiac diseases, and patients' refusal to follow doctors' advice can all lead to a poor prognosis. Our recommendations are; Raising people's awareness of heart diseases, increasing the capacity of professional medical staffs, equipped the cath –lab and cardiac surgery ward.

1 – Most of ACS cases were in 60-79 years old (male 69.5%, female 59.2%, P value =0.333).

2 – Male – female ratio was 2.64:1.

3 – 21.40% of male, and 22.40% of female had heart failure, (P value = 0.87), most of the patients had normal BMI (male 67.9% , female 61.2%, P value = 0.76), 23.7% of male and 18.4% of female involved with diabetes mellitus, (P value = 0.44), 38.9% of male 63.3% of female had high blood pressure, (P value =0.004), and 35.1% of male and 26.5% of female had hyperlipidemia, (P value = 0.27).

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Section 4
Otorhinolaryngology

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PREVALENCE OF NASAL POLYPS IN CHRONIC RHINOSINUSITIS PATIENTS UNDERGOING FUNCTIONAL ENDOSCOPIC SINUS SURGERY

Chronic Rhinosinusitis (CRS) is a common disease that affects a large percentage of the population, Nasal obstruction, nasal discharge, headache and the decline in quality of life are all symptoms that have social and economic consequences. CRS with nasal polyps is a common problem, it is a subgroup of CRS in which polyps in the middle meatus can be seen. It has a high social impact because of its chronic disease burden. Due to a large number of people with medically refractory rhinosinusitis, it is now widely accepted to use functional endoscopic sinus surgery (FESS) and the number of FESS procedures that are performed has increased. The study aimed to assess nasal polyps in chronic rhinosinusitis patients who underwent FESS. A retrospective study was conducted among patients aged between 18 and 86 years. The clinical records of patients who underwent functional endoscopic sinus surgery over the two years (2019-2020) were carefully reviewed and pertinent information was extracted from the database. Overall, 1671 patients underwent FESS, 1197 of them were for CRS. We found 165 (13.78%) patients with nasal polyps and 1032 (86.21%) of them were without nasal polyps. The study group's mean age was 38.87 ± 14.74 years. The mean age of patients for CRS with nasal polyps and without nasal polyps was 50.53 ± 16.13 and 37 ± 13.61 years respectively, which was statically significant ($\chi 2 = 216.303$; $p < 0.001$). Most of the patients with nasal polyps (43%) were aged between 41-60 years. In the subgroup of CRS with nasal polyp females and males were 79 (47.88%) and 86 (52.12%) respectively. In our study, both CRS with nasal polyps and without nasal polyps showed significant age differences. In CRS with nasal polyp, males were more affected than females. More research is needed to assess demographic variables and outcomes of nasal polyps after FESS.

Key words: Chronic rhinosinusitis, FESS, Nasal polyp.

Introduction

Chronic rhinosinusitis (CRS) is a common disease that affects approximately 7%-30% of the population [1]. Nasal blockage, rhinorrhea, facial pain, headache, hyposmia, and a decline in the patient's standard of life are all symptoms that have social and economic consequences [2]. The link between functional endoscopic sinus surgery (FESS), sinusitis-related symptoms, and overall quality of life is still being researched [3]. CRS is one of the most common medical conditions in the United States of America, affecting about 12% of adults each year. Overall healthcare expenses are high, ranging from $6.9 billion to $9.9 billion per year in 2014. Between 2006 and 2010, acute rhinosinusitis (ARS) and CRS accounted for more primary care visits with antibiotic prescriptions than any other condition [4].

CRS with nasal polyps (CRSwNP) is a subgroup of CRS in which polyps in the middle meatus can be seen. The exact cause of nasal polyp is unknown but maybe multifactorial. Polyps are linked to respiratory illnesses such as asthma and cystic fibrosis, as well as primary ciliary dyskinesia and aspirin sensitivity [5]. The drainage facilitation and elimination of the tissue obstructing the osteo-metal complex is known as functional endoscopic sinus surgery, and it is done while preserving the usual non-obstructing anatomy and mucous membrane [6].

FESS is commonly conducted in the United States due to a significant number of individuals with medically refractory rhinosinusitis, more than 500,000 procedures performed each year [7]. It is now widely accepted to use FESS [8], and the number of FESS procedures that are carried out has increased [9]. One of the more common procedures for treating chronic sinus diseases is functional endoscopic sinus surgery [10]. When traditional treatments fail to alleviate symptoms, FESS can be used. For these patients, FESS is an effective treatment modality and has been reported to provide both immediate and long-term symptom reduction and improve the quality of life in 85% of patients [7,11]. It is unknown how common nasal polyps are in the general population of patients receiving FESS.

Aim of the study: To assess the prevalence of nasal polyps in chronic rhinosinusitis patients who underwent functional endoscopic sinus surgery.

Material and methods

Study design

This retrospective study was conducted among patients aged 18-86 years.

Data source

The clinical records of patients who underwent functional endoscopic sinus surgery were closely checked, and relevant data were collected from the Almaty Otolaryngology hospital database (MedElement). Every step of the study regarding human subjects during the study period was carried out in compliance with the institutional study committee's ethical guidelines. Due to the type of the study, informed consent was not required.

Patient selection

Patients who underwent FESS at Almaty # 5 hospital's adult department between January 1, 2019, and December 31, 2020, were identified. During these two years, 1197 CRS patients underwent sinus surgery. Patients who had chronic rhinosinusitis at the time of admission were included. Patients under the age of 18, mucoceles and cysts of the sinuses, as well as those who were candidates for FESS other than CRS (sinus tumors, choanal atresia), were excluded. Patients with chronic rhinosinusitis who underwent sinus surgery were divided into two groups based on their clinical manifestations [12].

1. Group 1: CRsNP; chronic rhinosinusitis without polyp
2. Group 2: CRSwNP; chronic rhinosinusitis with nasal polyp

Clinical examination and investigations

A detailed history, complete clinical examination, and diagnostic endoscopy were done. After an appropriate course of medical treatment for persistent rhinosinusitis and nasal polyposis, surgery was performed. All patients selected for surgery underwent a diagnostic endoscopic examination in the outpatient department for the nose, nasopharynx, with and without nasal decongestant. A preoperative CT scan was asked in all cases to identify the skeletal anatomy and the extent of the disease. Before surgery, the anatomic structures are typically examined in the coronal, axial, and sagittal planes. FESS was conducted in all cases by a single surgeon and an assistant or assistants, effectively following Stammberger's (ant-post) method used; The procedure involved uncinectomy, middle meatal antrostomy, anterior ethmoidectomy, and perforation of the ground lamella of the middle turbinate, as well as posterior ethmoidectomy, sphenoidectomy, and clearance of the frontal recess, depending on the extent of the disease. All cases were placed under general anesthesia and had oral intubation.

Statistical analysis

Study data were entered in a Microsoft Excel sheet. Data were analyzed using the statistical package for social sciences (SPSS) 24. Study data related to demographics, history, outcome, surgeon, type of surgeries for related problems were analyzed. After exclusion criteria, data were categorized into two groups for endoscopic sinus procedures. All of the qualitative data was summed up using numbers and percentages. The Pearson Chi-square test ($\chi 2$) was used to analyze the variations in proportions. Significant was defined as a P-value less than 0.05, and Non-Significant was defined as a P-value greater than 0.05 (P-value > 0.05).

Result

Overall, 1671 patients underwent FESS, 1197 of them were for CRS. In this study, FESS for treatment of CRS was divided into two groups; CRSsNP and CRSwNP. 1032 (86.21%) patients were with CRS without nasal polyp and 165 (13.78%) had Nasal polyp. The overall mean age was 38.87±14.74 years. The mean age of groups was 37±13.61 and 50.53±16.13 years, respectively, which was statically significant ($\chi 2$=216.303; p<0.001).

Female and male were 561 (46.86%) and 636 (53.13%), respectively (table 1), but this was not statistically significant (p-value =0.799; $\chi 2$=0.078).

The average days of hospital stay in group1 were 5.82±1.88 and, for group 2, that was 5.14±1.86. Hospital stay days were statistically significant between the groups ($\chi 2$=43.9133; p-value=0.002).

Table 1 – Patients' general characteristics according to the type of chronic rhinosinusitis

N=1197 Group1 (CRSsNP) N=1032(86.21%)		Groups χ^2 Group2 (CRSwNP) N=165(13.78%)		Total p-value	Test of differences	
Age (Mean±SD)		37±13.61	50.53±16.13		216.303	<0.001
Sex N, (%)	Female	482(40.26)	79(6.59)	561(46.86)	0.078	0.779
	Male	550(45.94)	86(7.18)	636(53.13)		
Hospital stay days (mean±SD)		5.82±1.88	5.14±1.86		43.9133	0.002

In the chronic rhinosinusitis group without nasal polyps, the majority of patients (66.66%) were between the ages of 18 and 40 (table 2), but in the nasal polyps group, the majority of patients (43%) were between the ages of 41 and 60. Between the groups, age was statistically significant ($\chi 2$= 129.38 p-value < 0.001).

Table 2 – Age categories of CRS without Polyp and CRS with polyp

N=1197 18-40		Age categories in years			Test of differences	
		41-60	>60	χ^2	p-value	
Groups	CRSsNP ,n (%)	688(66.66%)	270(26.16%)	74(7.17%)	129.38	<0.001
	CRSwNP ,n(%)	43(26%)	71(43%)	51(30.9%)		
Total (CRS)		731(61.1%)	341(28.48%)	125(10.44%)		

In the CRSsNP group, the most common surgery was maxillary antrostomy combined with ethmoidectomy (42.92%). In the CRSwNP group, the most common surgery was ethmoidectomy (73.73%). Among the groups according to the type of surgery (table 3), there was a highly significant association (χ^2=828.43; P < 0.001).

Table 3 – Type of sinus surgeries underwent for chronic rhinosinusitis

N=1197 M		The type of sinus operation										Total	Test of differences
		E	F	S	ME	MF	MEF	MES	EFS	Whole sinuses			
Groups	CRS sNP, n (%)	280 (27.1)	8 (0.77)	11 (1)	10 (0.96)	443 (42.92)	6 (0.5)	24 (2.3)	79 (6.59)	2 (0.19)	169 (16.37)	1032 (100)	χ^2=828.43 P<0.001
	CRS wNP, n (%)	0 (0)	121 (73.73)	0 (0)	0 (0)	13 (7.87)	6 (3.63)	4 (2.42)	5 (3)	4 (2.42)	12 (7.27)	165 (100)	
Total(CRS), n %		280 (23.3)	129 (10.7)	11 (0.91)	10 (0.83)	456 (38)	12 (1)	28 (2.33)	84 (7.01)	6 (0.5)	181 (15.12)	1197 (100)	

M=maxillary antrostomy; E= ethmoidectomy; F= frontal sinusotomy; S= sphenoidectomy; ME= middle antrostomy with ethmoidectomy; MF= middle antrostomy with frontal sinusotomy; MEF= middle antrostomy and ethmoidectomy with frontal sinusotomy; MES= middle antrostomy and ethmoidectomy with sphenoidectomy; EFS= ethmoidectomy and frontal sinusotomy with sphenoidectomy.

Discussion

Patients were aged between 18 to 86 years. The overall study group age was 38.87±14.74 years. CRS without nasal polyp was 1032 (86.21%) patients with a mean age of 37±13.61 and 165 (13.78%) patients with nasal polyp with a mean age of 50.53±16.13 years. In a study by Nair et al., (n= 90) patients aged group 16–71 years, with a mean age of 34.8 years CRS without nasal polyp included 38 patients with an average age of 31.2 years and a 9:10 male-to-female ratio. In CRS with nasal polyps, 52 patients were included, with a mean age of 37.5 years and a male-to-female ratio of 9:17 has been reported [13].

Females and males were 56 (46.86%) and 636 (53.13%) respectively. According to our findings, 165 (13.78%) of all patients with CRS had nasal polyps (CRSwNP). Nasal polyps affect 4 percent of the population, 7–15 percent of asthmatics, and up to 36–60 percent of Samter's triad patients [14]. Nasal polyps are typical presentations in CRS patients and are thought to be linked to more serious types of disease with poor post-treatment outcomes. In the EPOS (European Position Paper on Rhinosinusitis and Nasal Polyps), a nasal polyp is classified as a subgroup of CRS [15]. Stevens et al. observed that 25% –30% of patients with chronic rhinosinusitis had CRSwNP [16].

In patients with chronic rhinosinusitis with nasal polyp, females and males were 79 (47.88%) and 86 (52.12%), respectively. Stevens and colleagues discovered in 2015 that females with CRSwNP had more severe disease than males undergoing sinus surgery at a tertiary care center [17]. Males were more than females affected, but no known genetic or environmental factors have been identified as being strongly linked to the development of this condition. Males were found to be more likely than females to have CRSwNP, according to Fokkens et al. [17]. Stevens and colleagues discovered in 2015 that females with CRSwNP had more severe disease than males undergoing sinus surgery at a tertiary care center [18].

The mean age for patients with CRwNP was 50.53±16.13 years. According to Fokkens et al., CRSwNP is a middle-aged problem, with an average age of diagnosis of 40–60 years [18]. Presumptive nasal polyps in patients younger than 20 or older than 80 years pose concerns about other medical conditions. [16]. According to Juan et al., finding; (n=288) patients with chronic rhinosinusitis, there were 177 men and 111 women among the participants, ages ranged from 22 to 83 years, with an average age of 52±14 years [19]. Polyps were found in the majority of patients aged 40–60 years old, with a very small number in children and a very small number in those over 80 years old, according to Larsen and Tos. Males were more likely than females to have polyps in the 20-year-old classes, with a mean male: female ratio of 2.23. In the 40–50-year age group, the male: female ratio peaked at 2.9, and in the 80–89-year age group, it peaked at 6.0 [20].

The retrospective nature of this study had limitations, such as unrecorded confounding factors such as major and minor factors of CRS, revision surgery, and individual anatomical variations. Further research is needed to better understand the functional endoscopic sinus surgery outcome in chronic rhinosinusitis.

Conclusion

In our study, both groups showed a significant age difference between chronic rhinosinusitis without polyps and with nasal polyps. In chronic rhinosinusitis with nasal polyp, males were more affected than females. According to a study of the literature, there was a wide variety of demographic data. More research is needed to assess demographic variables and outcomes following functional endoscopic sinus surgery.

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ASSESSMENT OF PATIENT BENEFIT FROM SEPTOPLASTY WITH TURBINOPLASTY

Patients' benefits and quality of life are profoundly influencing how health services are delivered. In recent years, there has been a trend in emphasis toward subjective outcome measures. Although the effects of septoplasty are not entirely comparable, various scales have been considered to support more studies based on assessing results following functional nasal surgery. Glasgow Benefit Inventory (GBI) is a standardized patient benefit measure developed specifically for otolaryngological treatments. The aim of this study is the use of GBI to assess the impact of undergoing septoplasty with turbinoplasty on patients' quality of life after one year. This study was conducted as a retrospective observational study. Patients over eighteen years of age who obtained septoplasty concurrent with turbinoplasty for the treatment of nasal blockage at the Almaty, City Hospital No. 5, were included. GBI questionnaire (-100 to +100) was used to measure the outcomes one year after surgery. A total of 309 patients who meet the eligibility criteria volunteered to participate, 112 females (36.2%) and 197 males (63.8%). The mean age was 26 years (SD = 13, range 18-76 years). A total of 87.1% of the patients reported improvement in their quality of life. Better outcomes in the perception of quality of life were observed in the younger population; these findings are consistent with current international existing literature.

Key words: septoplasty, turbinoplasty, retrospective studies, nasal blockage, quality of life, Glasgow benefit inventory.

Introduction

One of the most common clinical indications for referral to otolaryngology is nasal blockage (NB) and it is characterized as a sense of distress arising from the perception of inadequate airflow through the nose or increased air resistance [1] [2]. While NB can be caused by a variety of conditions, deviated nasal septum (DNS) and protruding turbinate constitute two major reasons. NB caused by DNS together with associated medical conditions like headache, facial pressure, or nasal discharge, has a negatively impact on patients' quality of life (QOL) [3]. Septoplasty as the third most frequent ear/nose/throat (ENT) operation is commonly performed with turbinate reduction procedures (turbinoplasty) for the treatment of nasal blockage caused by deviated nasal septum [4]. Compensatory concha bullosa or inferior turbinate hypertrophy as structural airway barriers in the nose found in 40% of patients with high septal deviation [5]. Since hypertrophy and/or hyperplasia of the conchal bone, nasal mucosa, or cavernous body may induce enlargement of the inferior turbinates, various surgical methods for reducing the size of the turbinates should be considered. Physical examination as well as objective measures (rhinomanometry, acoustic rhinometry, and nasal peak flow) have always been used in the past to assess nasal airway function [6] [7] [8]. These measures do not necessarily match up with patient reports of nasal obstruction. The effectiveness of surgery depends on an accurate preoperative diagnosis. The surgeon benefits greatly from intraoperative imaging with a microscope or endoscope. Mobilization, resection/repositioning, and reconstruction/fixation are the approach's phases of the existing septoplasty process. Since pathologies of the caudal septum are responsible for septal surgery failures, some unique problems in this area, such as vertical caudal septum fractures, the absence of a caudal septum, or anterior convexities of the cartilaginous septum, are being debated [9]. Anterior nasal packing is generally performed on a routine basis after septal and turbinate surgery to prevent postoperative bleeding, septal hematoma, and nasal synechia. Transseptal sutures are also used more often, not only to avoid complications including septal hematoma and bleeding but also to close any unintended septal mucosa tears and provide additional protection for the cartilage fragments preserved in septoplasty [10]. Methodological errors in septal and turbinate surgery procedures, from the incision of anesthetic agent to the nasal packing, will lead to complications. Infections affecting either the

mid-facial region or the whole body may arise as early and late complications in the postoperative phase. Harm to the septal soft and hard tissues and a huge reduction of turbinate may also cause postoperative and late complications [11].

Patients' interests and quality of life are profoundly influencing how health services are delivered. In recent years, there has been a trend in emphasis toward subjective outcome measures. Although the effects of septoplasty are not entirely comparable, various measures have been considered to support more studies based on assessing results following functional nasal surgery. GBI (Glasgow Benefit Inventory) is a standardized patient benefit measure developed specifically for otolaryngological treatments [12]. The GBI has previously been used to evaluate patient perceptions of rhinoplasty/ septorhinoplasty benefit [13] [14]. To date, we are only able to find a few reports that looked at the effect of nasal septal surgery on patient quality of life in Almaty, Kazakhstan. In addition, the key benefits of parallel turbinoplasty remain unclear. In the existing context, this retrospective study enables us to increase the knowledge on the use of the GBI scale for the assessment of nasal symptoms following septoplasty with turbinoplasty.

Aim

The aim of this study is the use of GBI to assess the impact of undergoing septoplasty with turbinoplasty on patients' quality of life after one year period.

Objectives

To determine is there significant difference between the subjective progress in patients receiving septoplasty concurrent with turbinoplasty surgery regarding their gender.

To understand, which age group received the most benefit from the septoplasty combined with turbinoplasty.

Materials and methods

This study was conducted as a retrospective observational study. Clinical records, as well as the contact information of patients who underwent septoplasty concurrent with turbinoplasty at the City Hospital No.5 in Almaty during the period of Jan 1, 2020, and Mar 30, 2020, were provided. Only patients over eighteen years of age who obtained surgery due to nasal blockage (unilateral or bilateral) were included; patients who presented other causes of nasal obstruction such as nasal polyposis and sinusitis and endured endoscopic sinus surgery, nasal polypectomy, and rhinoplasty along with nasal septal surgery, were excluded from the study.

In addition, patients with a history of nasal trauma (since the surgery), pregnant women, patients with ongoing cancer therapy, and patients suffering from cognitive problems were also excluded from the study.

Outcomes Measures

A total of 309 patients who met the eligibility criteria for inclusion, volunteered to participate in the study. One year after the surgery, an electronic format of GBI questionnaire was prepared in the google form and was sent to the participants to assess their quality of life. The GBI is a post-intervention questionnaire and has been shown to be sensitive to changes caused by otorhinolaryngological procedures. It is an 18-item questionnaire that can be separated into three different sections: twelve questions measure changes to the overall benefit and the two other subscales each consist of three questions that evaluate changes to social support and physical wellbeing. The GBI score goes from -100 (maximum negative benefit), 0 (no benefit), to +100 (positive benefit).

Statistical Analysis

Using SPSS Statistic software, the statistical analysis was done. Based on absolute and relative frequencies for qualitative variables, a descriptive study of the variables was performed, as well as measures of central tendency and dispersion for quantitative variables. Statistical analyses were carried out with Chi-square testing, and averages were compared using the Mann-Whitney U test and the Kruskal-Wallis test. Differences were considered significant when there was a 95% confidence interval.

Result

Data collected from 309 respondents, 112 females (36.2%) and 197 males (63.8%). The mean age was 26 years (standard deviation (SD)=13, range 18-76 years). There was no statistically significant difference between the mean ages of males (26.56 ± 13.1) and females (23.68 ± 12.1) ($p = 0.057 > 0.05$).

The median Total GBI score was 36.11 (interquartile range: 22.22 to 50.00), and in the General benefit subscale it was 37.5 (16.66 to 58.33), for Physical health it was 33.33 (16.67 to 50) and in Social support, it was

33.33 (16.67 to 66.67). A total of 87.1% of the patients reported improvement based on their Total GBI score. Improvement in subscales results is shown in Table 1.

Further, scores have been checked at men's and women's separately (figure 1). The median Total GBI score for females was 27.78 (19.44 to 47.22), with subscale scores of 29.16 (16.66 to 41.667) for general advantage, 16.67 (16.67 to 50) for physical benefit, and 16.67 (0 to 50) for social benefit.

Table 1 – Subjective Quality of Life (GBI).

Variable	Median	IQR[c]	n (%)
General benefit[a]	37.5	(16.67; 58.33)	
Improvement in general benefit[b]			270 (87.4%)
Social support[a]	33.33	(16.67; 66.67)	
Improvement in social support[b]			236 (76.4%)
Physical health[a]	33.33	(16.67; 50)	
Improvement in physical health[b]			246 (79.6%)
Total GBI	36.11	(22.22; 50)	
Improvement in total GBI[b]			269 (87.1%)

[a]GBI subscales.

[b]Corresponds to the number of subjects and percentage of the population with improvement by respective subscale.

[c]IQR: Interquartile range corresponding to interval formed from percentile 25 to 75.

The male's scores were 25 (16.67 to 47.22), 29.16 (16.66 to 41.66), 33.33 (16.67 to 50), and 33.33 (16.67 to 50), respectively. There was no statistically significant difference between the males and females in Total advantage ($p = 0.809 > 0.05$, two-tailed), general benefit ($p = 0.967 > 0.05$, two-tailed), physical benefit ($p = 0.922 > 0.05$, two-tailed), or social benefit ($p = 0.589 > 0.05$, two-tailed), according to the Mann-Whitney U test.

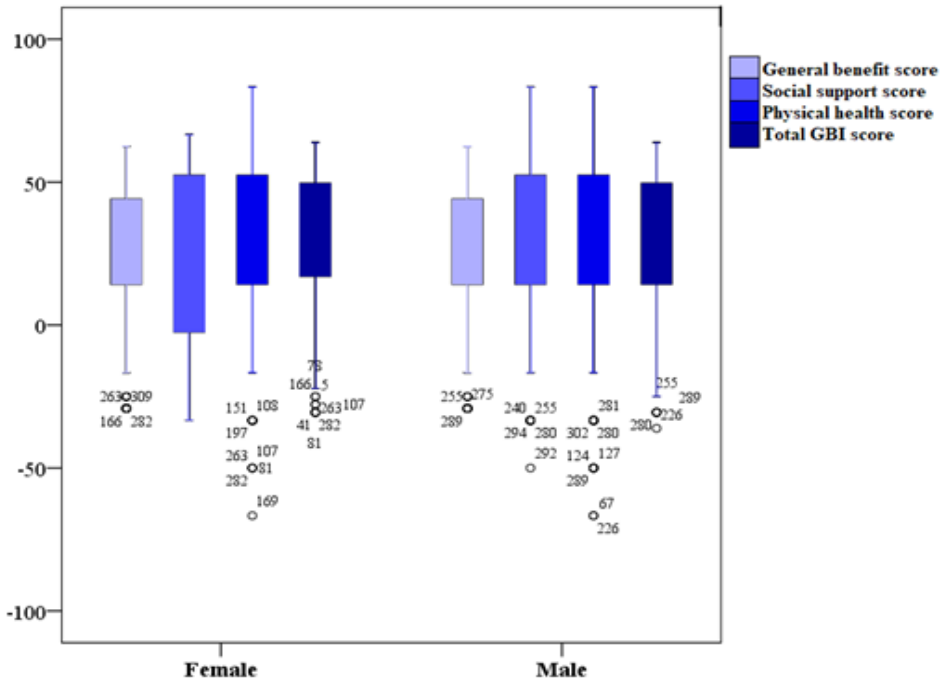

Figure 1 – Box plots show scales' scores between females and males

There was a statistically significant difference between the scales' scores regarding age groups ($p < 0.001$), according to Kruskal-Wallis H test (Figure 2). The age group 18-40 years was found to benefit the most from the surgery.

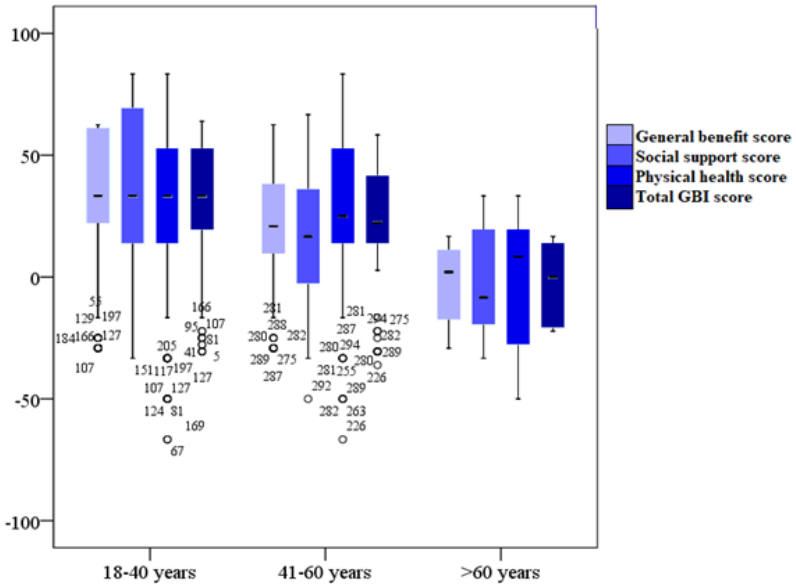

Figure 2 – Box plots show scales' scores between age groups

Discussion

The evaluation of the quality of life following certain surgical interventions, rather than objective measures that evaluate only one physical parameter, has become increasingly prevalent in recent years as part of research outcomes. In this regard, in the present study, we attempted to assess the overall improvement in quality of life after one year of septoplasty concurrent with turbinoplasty. Our assessment is based on the improvement of the initial complaints related to the quality of life since the nasal surgery.

It is essential to mention that there is still a lack of reports on the issue of assessing the quality of life. However, according to data reported by Valsamidis et al., the mean and SD of the Total GBI was 19.86±9.27, and the mean and SD of the General benefit subscale was 22.49±12.86, Physical health was 20.83±22.24, and Social support was 5.2±11.43 [15]. An indirect comparison with our study's medians differs markedly. The median Total GBI score in our sample was 36.11, representing a high increase in patients' quality of life. In our sample, the average age of patients undergoing surgery was 26 years, relatively lower to 31.5 years in Valsamidis et al. study. The increased progress in patients' status in our research may indicate that septoplasty concurrent with turbinoplasty is more beneficial to younger patients. The young patients' nasal obstruction may be more anatomically dependent, so surgery may be more effective in this population, and dynamic causes may be more relevant in older patients.

In our research, 261 (87.1%) patients reported a subjective improvement in the quality of life based on their Total GBI score. This markedly positive result represents overall progress in health status that is attributable to the septoplasty concomitant with turbinoplasty procedures. This is consistent with research previously reported in the literature by Corredor-Rojas et al. in 2020 in Colombia [16].

It is important to acknowledge the study's limitations. The findings of our research are based on a cross-sectional survey conducted via questionnaire. The findings are based on the experiences of patients who underwent surgery one year prior to the study date. Patients' memory of symptoms fades with time, which may have influenced the results of the observed outcomes. The implicit biases of retrospective studies, such as memory bias with specific questions in the GBI questionnaire are recognized. However, Robinson et al. found that the number of years after surgery has little impact on the average score [12].

Conclusion

This is one of the few studies in Almaty using validated subjective scales such as the GBI questionnaire to assess the change in patients' quality of life following septoplasty with turbinoplasty. This data provides a detailed interpretation of nasal obstructive symptoms and their effect on quality-of-life perception. Good outcomes in the perception of quality of life were observed in our study. Younger patients with nasal obstruction and septal deviation were found to get the most from the surgery; these findings are consistent with current international existing reports.

Since non-anatomical causes of nasal symptoms like allergic rhinitis may be confounding variables in the relationship between surgical treatment and improvement perception, a new approach measuring allergic rhinitis in patients receiving septoplasty with turbinoplasty is needed. Additionally, it is recommended that patients be evaluated both before and after surgery in order to more precisely assess clinical progress.

Abbreviations

NB: Nasal blockage; DNS: Deviated Nasal Septum; GBI: Glasgow Benefit Inventory; SD: Standard Deviation; IQR: Interquartile range

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Section 5
Molecular genetics

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ESTIMATION AND ASSESSMENT OF CYTOGENETIC CHANGES IN BONE MARROW CELLS OF LABORATORY ANIMALS RECEIVED A GENE-MODIFIED PRODUCT

Current trends in the change in the structure of morbidity indicate an increase in the relative importance of

genetically determined diseases. The results of biological monitoring of human populations have shown that at present there is not only an increase in hereditary pathology, but also an increase in the frequency of diseases with a genetic component. The aim was to study cytogenetic changes in the cells of the bone marrow of laboratory animals that received and did not receive GMO soy. It is found in white mongrel rats treated with GMO soybean detected

cytogenetic changes in their red om bone ohm brain e lead partially m the inhibition and proliferation of bone marrow cells. Of all be analyzed metaphases among them revealed altered karyotypes – polyploidy (5.6%) and aneuploidy (5.6%). In the remaining groups (group 2 and 3), no such changes were observed. In the group of animals that did not receive soy with and without GMO, all bone marrow samples had only metaphase plates with a normal karyotype, and the cells did not contain genomic abnormalities.

Key words: genetically modified soybeans, cytogenetic changes, bone marrow, polyploidy, aneuploidy, experiment.

Introduction

Genetically modified (GM) organisms are plant or animal organisms, the genotype of which has been changed in a way that is not natural for nature, using methods of genetic engineering to give the body new properties: resistance to herbicides, pests, diseases and salinity, to the action of high and low temperatures, increase calories; to solve the problems of cleaning the environment from organic pollution and heavy metals; to ensure the synthesis of certain compounds in the plant organism and the use of plants for the production of these compounds [1, 2, 3, 4].

Genetic changes are made for scientific or economic purposesand distinguished by a purposeful change in the genotype of an organism, in contrast to the random, characteristic of a natural mutation process. The main trait inherent in most GMO plants is herbicide and pest resistance. Cultivation of GM-soybeans does not have a single positive moment [5, 6, 7].

The most serious risks associated with products of genetic engineering are combined into 2 main groups: food and Ecological [8, 9].

Food – weakening of the immune system; the occurrence of allergic reactions; the development of pathologies associated with the accumulation of pesticides in the human body, introduced by the used GMO products,

Ecological – the loss of the diversity of the gene pool of wild relatives of cultivated plants due to their cross-pollination with related GM plants; contamination of water resources by the use of pesticides; depletion and disturbance of natural soil fertility associated with the suppression of GM plants by toxins, the vital activity of soil invertebrates and microflora; acceleration of the second plant

growth to a much greater extent than in traditional agricultural RMS households Affiliations cultures. In general, the above studies indicate the insufficient substantiation of the safety of GMO plant products for humans and the environment.

Current trends in the change in the structure of morbidity indicate an increase in the relative importance of genetically determined diseases [9, 10].

Many authors believe that now important is to solve the urgent problems and correlating the rate of changes in the environment with the ability to adapt human populations, in addition it is necessary to assess the extent to which, in the biosphere changes that affect the rate of mutation [6, 11, 12].

The results of biological monitoring of human populations have shown that at present there is not only an increase in hereditary pathology, but also an increase in the frequency of diseases with a genetic component. The danger of induced mutagenesis is that newly emerging mutations have a negative impact on the fitness of the population and on the health of the population.

In this regard, new research in this direction is relevant and in demand at the present time.

The aim of the study was to learn the evaluation cytogenetic changes in bone marrow cells in laboratory animals, treated and not treated with GMO-product in a comparative aspect.

Materials and methods

To perform the planned research used 30 white outbred rats weighing bodies 150-180 g of both sexes, contained in a standardized vivarium conditions-with relative humidity 50-60%, temperature vivarium 22 0 C, light conditions (12 h aces darkness and light). The maintenance of laboratory animals, feeding and caring for them, selection of animals, cleaning and disinfection of the vivarium premises were carried out in accordance with the approved recommendations [13]. All laboratory animals were obtained from the same nursery and were of the same age. All laboratory animals were quarantined for 21 days prior to the start of experimental studies.

When working with experimental animals, all ethical principles of working with laboratory animals and the rules of biological safety were strictly observed [13].

When conducting cytogenetic studies, all operations when working with growth media and preparations were performed under sterile conditions using a laminar box. Buffers were prepared with double-distilled water, filtered through membrane filters (0.22 um «Millipor», Germany) and autoclaved at 1.2 bar for 30 minutes. Before use, glassware is pre-sterilized at 1600C for 120 minutes. Equipment, fixtures, utensils made of polymeric materials were exposed to ultraviolet light for 30 minutes.

Bone marrow cells were isolated according to a standard technique from the femur bones of animals sacrificed using a device for euthanasia.

Direct method. Red bone marrow was washed out of the femur with a nutrient medium with 0.04% colchicine into a centrifuge tube and incubated for 2-2.5 hours in a thermostat at 37 ° C. Then it was further incubated with a hypotonic solution of KS L for 40 minutes in a thermostat at 37 0 C. After hypotonization, it is treated three times with a fixative in the proportion of one part of glacial acetic acid and three parts of 960-1000 ethyl alcohol. The resulting precipitate was applied to a previously cleaned defatted glass slide and stained with Giemsa dye.

Method according to Ford. After the end of the drug administration, all the animals were injected intraperitoneally with 0.5 ml of a 0.1% colchicine solution, after 2 hours the animals were killed in strict accordance with the ethical principles of working with laboratory animals. Red bone marrow flushed from a femur hypotonic solution COP L and incubated for 40 minutes in an oven at 37 0 C. After hypotension, they were treated three times with a fixative in the proportion of one part of glacial acetic acid and three parts of 960-1000 ethyl alcohol. The resulting precipitate was applied to a previously cleaned defatted glass slide and stained with Giemsa dye.

Statistical processing was carried out by the generally accepted methods of variation statistics.

All laboratory animals were divided into the following groups:

1 – group – white outbred rats (n = 12), receiving GMO soy with food for 30 days at 0.02-0.03 grams per one laboratory animal;

Group 2 – white outbred rats (n = 12), who received a standard diet and conventional soy.;

Group 3 – white outbred rats (n = 6), who received a standard diet without GMO soy and conventional soy.

ОБОСНОВАНИЕ ДОЗЫ и сроков воздействия. Ссылка.

As a GMO product in experiments used to I grown overseas and imported into our country only to perform scientific research of their work (see Pic. 1).

Picture 1 – Appearance of GMO soybeans

Using the method of polymerase chain reaction (PCR), the presence of the 35 S + FMV promoter in the studied GMO- soy was revealed, which proves that the studied soy is a GMO-product. [15].

Cytogenetic changes in rat bone marrow cells were studied using the following methods: Direct method. Red bone marrow was washed out of the femur with a nutrient medium with 0.04% colchicine into a centrifuge tube and incubated for 2-2.5 hours in a thermostat at 37 ° C. Then it was further incubated with a hypotonic solution of KS L for 40 minutes in a thermostat at 37 0 C. After hypotonization, it is treated three times with a fixative in the proportion of one part of glacial acetic acid and three parts of 960-1000 ethyl alcohol. The resulting precipitate was applied to a previously cleaned defatted glass slide and stained with Giemsa dye.

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Statistical processing was carried out by the generally accepted methods of variation statistics.

Research results and discussion

For the analysis, cells of the red bone marrow were used, in which elements of the mitotic apparatus were detected. Metaphase plates – this cells in which chromosomes are in the metaphase mitotic (somatic cell division stage). The number of chromosomes in rats is normally 42 (diploid set).

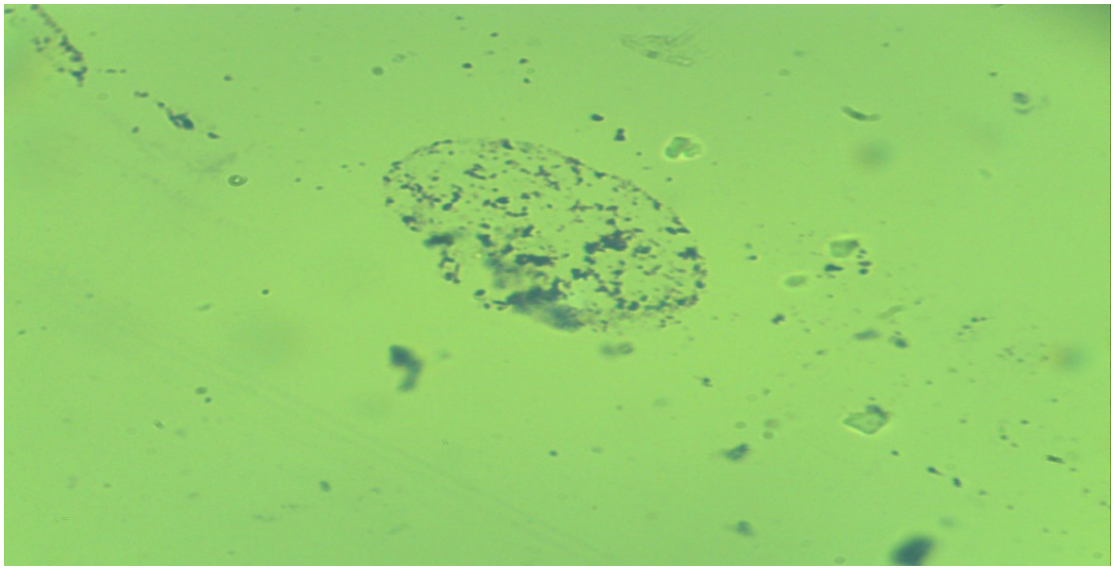
Analysis revealed that – the low mitotic activity of bone marrow cells in 1 – group (treated with GMO -soy) only at part in the bone marrow samples detected metaphase plate (tab.1).

Table 1 – Indicators of cytogenetic changes in bone marrow cells of laboratory animals treated with a GMO product (soy)

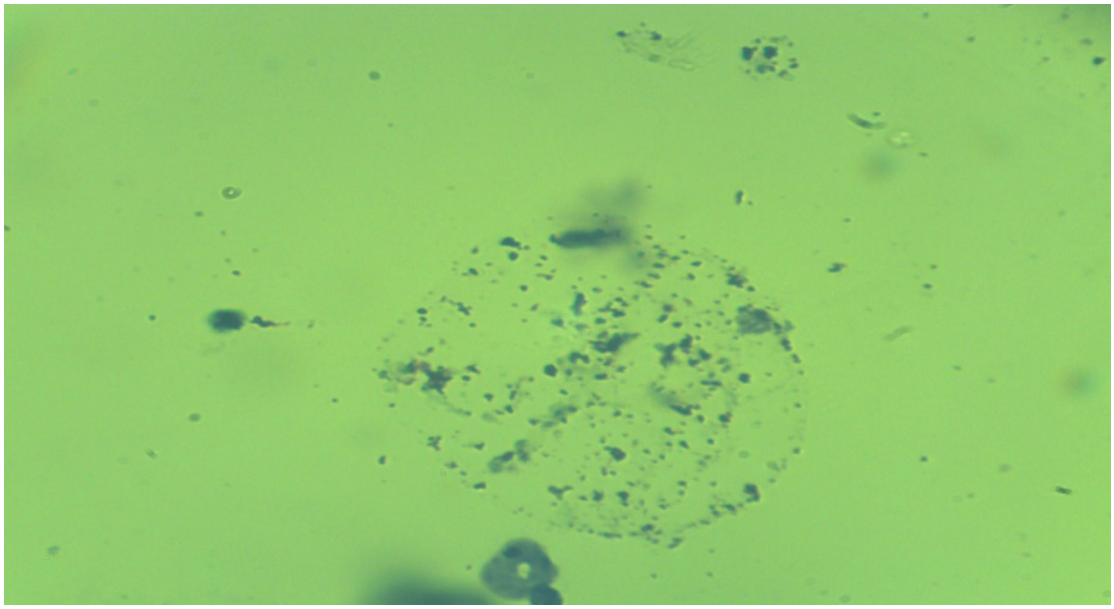
Group	Types of aberrations		
	Polyploidy	Aneuploidy	Structural changes in chromosomes
1 – group	5,6%	5,6%	Dispersion, Pulverization, Delayed mitosis in prophase
2 – group	Lack of	Lack of	Pulverization of chromosomes, K-mitosis
3 – group	Lack of	Lack of	Lack of

Of all the metaphases to be analyzed in laboratory animals of the 1st group, in 11.2% cases, polyploid (the cell contains a set of chromosomes more by a multiple than normal; 5.6%) and aneuploid (cells contain the number of chromosomes less or more than a multiple haploid set; 5.6%) karyotypes.

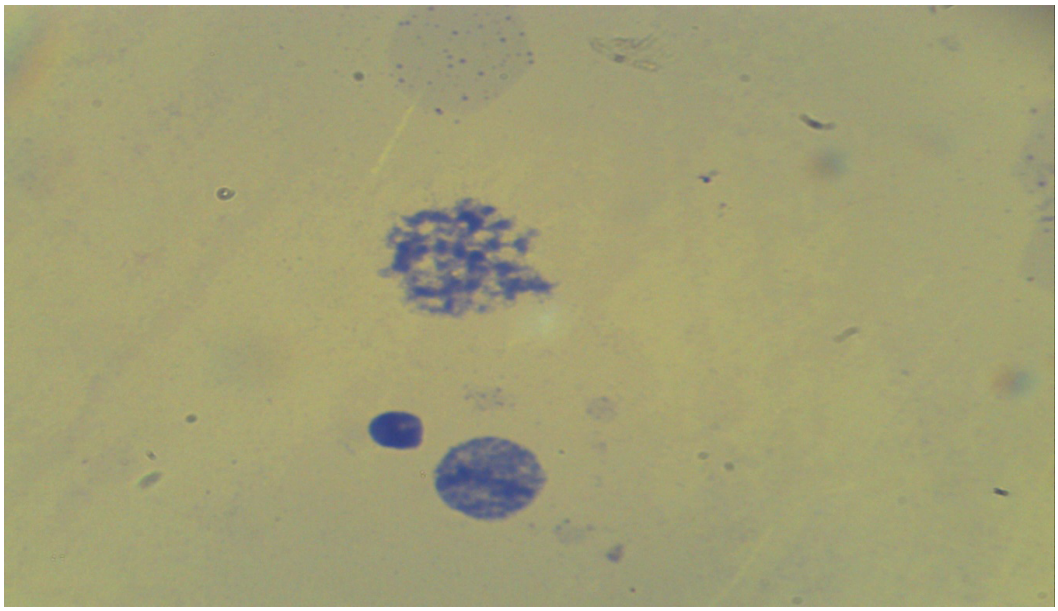
In other bone marrow samples from rats of this experimental group, metaphase plates were absent, but there were blast cells (cells at the stage preceding mitosis) and cells with mitotic pathology: chromosome pulverization (Pic. 2 and Pic. 3), impaired chromosome spiralization and despiralization (Pic. 4), premature spiralization of chromosomes (Pic. 5), delayed mitosis at the prophase stage. The rest of the metaphase plates contained a normal (42 chromosomes) karyotype.



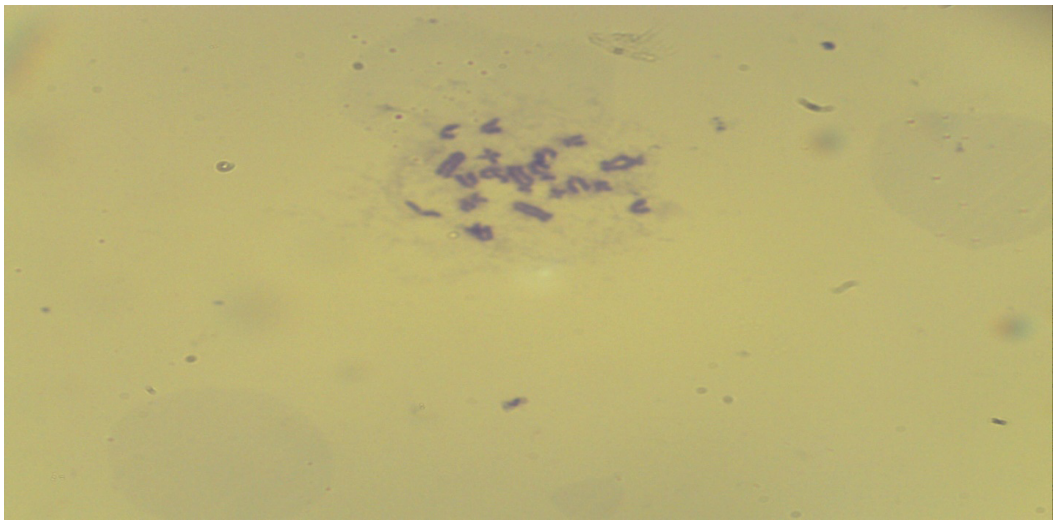
Picture 2 – Bone marrow cells of laboratory animals treated with GM-soy (group 1). Pulverization of chromosomes (approx. X 10, vol. X 100)



Picture 3 – Bone marrow cells of laboratory animals treated with GM-soy (group 1). Pulverization of chromosomes (approx. X 10, vol. X 100)



Picture 4 – Bone marrow cells of laboratory animals treated with GM-soy (group 1). Violation of spiralization and despiralization of chromosomes (approx. X 10, Ob. X 100)

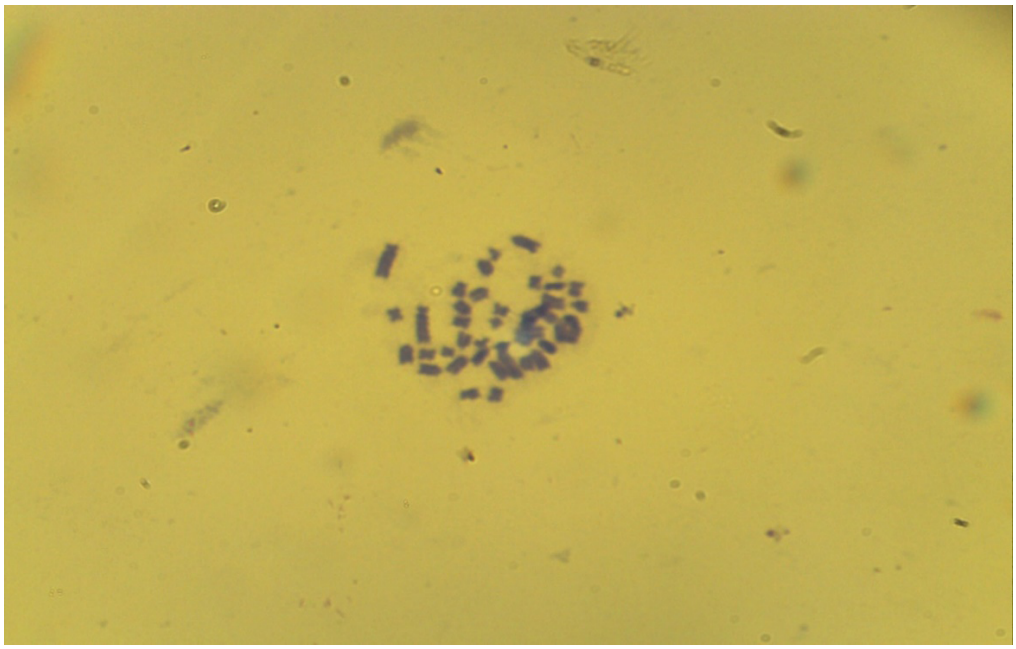


Picture 5 – Bone marrow cells of laboratory animals treated with GM-soy (group 1). Premature spiralization of chromosomes (Approx. X 10, Ob. x 100)

Experimental studies on laboratory animals proved that the used GM product (soy) led to cytogenetic changes in the cells of highly proliferating tissues, such as the red bone marrow of white outbred rats.

There is a partial inhibition of the proliferation of bone marrow cells due to the cytotoxic action, which can lead to cytopenia.

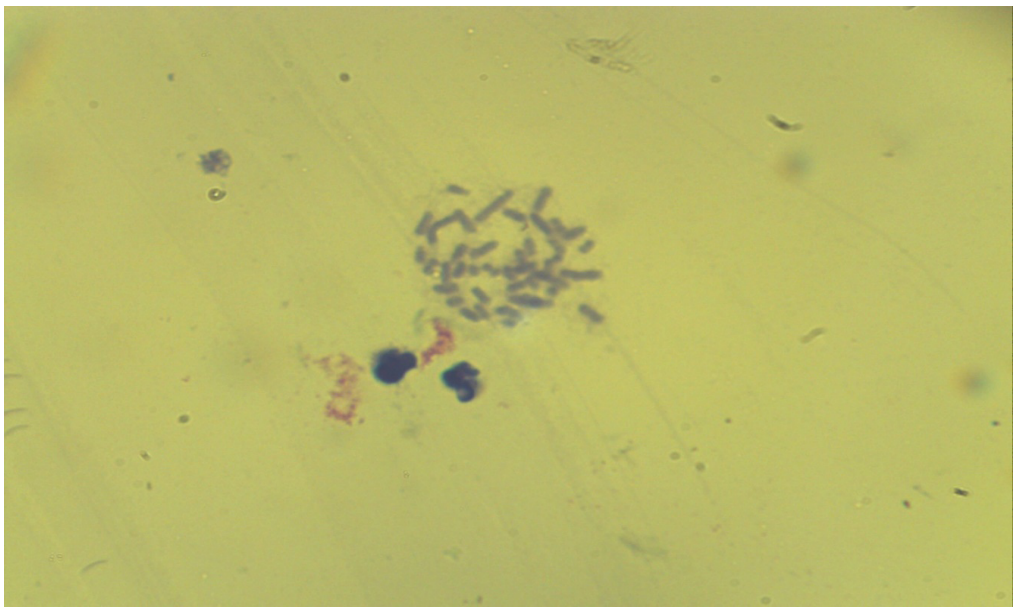
In group 2, polyploid (polyploidy) and aneuploid (aneuploidy) karyotypes were not detected in only 50% of laboratory animals. The number of metaphase plates found in the bone marrow was the same with the animals of group 1. In all analyzed metaphases, the karyotype was not changed (Pic. 6).



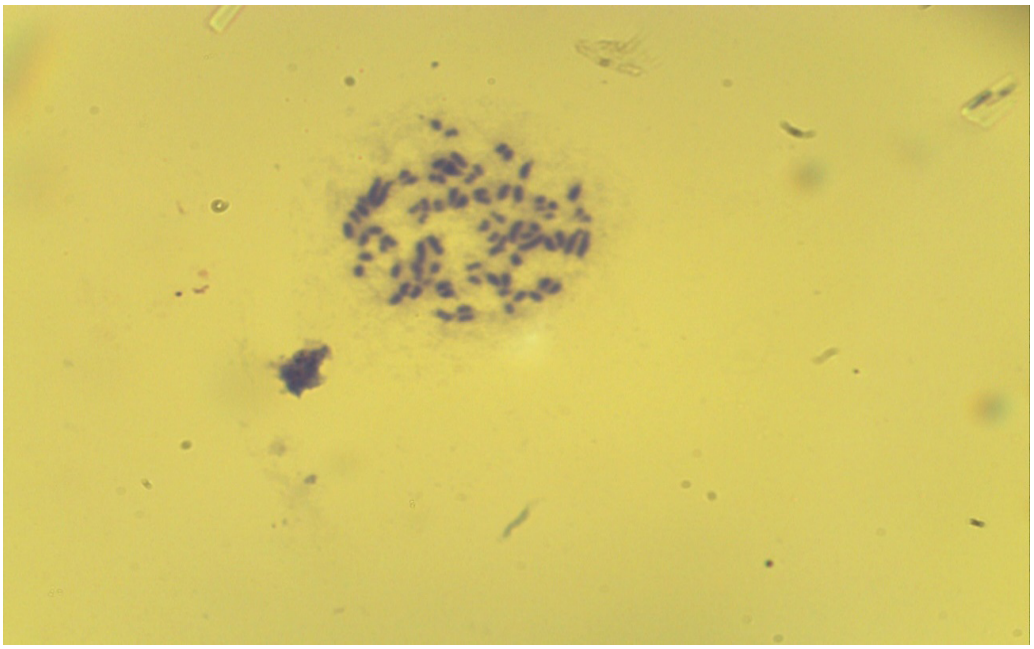
Picture 6 – Bone marrow cells of laboratory animals that received soy without GM (group 2). Normal karyotype (approx. X 10, vol. X 100)

It was found that the cells did not contain genomic abnormalities, all metaphases had a normal karyotype (42 chromosomes). In the remaining (50%) bone marrow samples, cells with mitotic pathology (chromosome pulverization, K-mitosis) were present, as well as in the bone marrow cells of group 1 outbred white rats.

In group 3 (control group), all bone marrow samples contained only metaphase plates with a normal karyotype (Pic. 7 – early metaphase; Pic. 7 – late metaphase).



Picture 7 – Bone marrow cells of laboratory animals that received a standard diet (group 3 – control). Normal karyotype, early metaphase. (Approx. X 10, Ob. x 100)



Picture 8 – Bone marrow cells of laboratory animals fed a standard diet (group 3 – control).
Normal karyotype, late metaphase (approx. X 10, vol. X 100)
The mitotic activity of rat bone marrow cells was higher than in the experimental groups (groups 1 and 2).

Conclusions

1. As a result, in the group of white mongrel rats treated with GM soybean detected cytogenetic changes in their red om bone ohm brain e lead partially m the inhibition and proliferation of bone marrow cells by the cytotoxic action, which may lead to cytopenias.

2. Of all be analyzed metaphases in laboratory animals Group 1 at 11, 2 % cases were identified altered karyotypes – polyploidy (5.6%) and aneuploidy (5.6%). In the remaining groups (group 2 and 3), no such changes were observed.

3. Bone marrow samples from 1-group rats contained blast cells and cells with mitotic pathology: chromosome pulverization, chromosome spiralization and despiralization disorders, premature chromosome spiralization, mitosis delay at the prophase stage.

4. In the group of laboratory animals as feed given to w without GM (group 2) was found to decrease the proliferation of bone marrow cells (at 50%), the rest in the bone marrow were present metaphase plate in all metaphases analyzed (36) the karyotype was not changed. The cells did not contain genomic abnormalities; all metaphases had a normal karyotype (42 chromosomes).

5. In the group of animals that did not receive soy with and without GM (3 – groups a control group), all bone marrow samples contained only metaphase plates with normal karyotype, and the cells did not contain genomic abnormalities.

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