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The beautiful thing about learning is nobody can take it away from you—B. B. King

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SOME FEATURES OF THE MOVEMENT OF NON-NEWTONIAN OILS INTO THE WELL, TAKING INTO ACCOUNT THE SPHERICAL-RADIAL FLOW CHARACTER ACCORDING TO THE LINEAR LAW OF FILTRATION

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ABSTRACT

When studying the behavior of a fluid in a reservoir, taking into account anomalous properties, a necessary condition is to determine the lower limit of applicability of Darcy's law for very small values of the Reynolds number. At the same time, it should be noted that these properties arise upon contact with a porous medium and explained by the fact that at very low filtration rates, along with viscous resistance forces, there are these characteristics that do not depend on the filtration rate and are associated with the physical and chemical dependencies of filtering liquids with the porous medium material. Accounting for these forces leads to the non-linear character of the filtration law.

It is known that the filtration process is described using models. Basically, three types of oil flow models have been defined in the reservoir. If we assume that all fluid particles move in a porous medium in such a way that their filtration velocities are not parallel to the same plane, then such a movement is called spherical-radial. One can give such an example of a spherical radial flow in various cases of filtration. Let us assume that a hydrodynamically imperfect well barely penetrates the impermeable horizontal top of a homogeneous formation of a very large thickness; corresponds to the spherical-radial model.

Keywords: spherical-radial model, contour and bottom hole pressure, volume flow, cross-sectional area, non-Newtonian fluids, oils, anomalous fluids.

Introduction

The analysis shows that during the development of many fields in Azerbaijan, Russia (Tatarstan, Bashkiria), Romania, Kazakhstan, facts that can be explained by the appearance of non-Newtonian anomalous properties of liquids in a porous medium are known. The features of the movement of such anomalous oils are mainly associated with the content of high-molecular components in them: resins, asphaltenes, paraffin, an increase in the proportion of clay particles in the reservoir, etc.

In the world, the price of hydrocarbons is constantly growing. In this regard, interest in such deposits is increasing.

In recent years, various stimulation methods have been used to increase oil recovery in reservoirs. Methods of influencing natural deposits in order to increase oil and gas condensate recovery have led to a significant expansion of the range of substances injected into productive horizons and reservoirs. Note that many of these substances do not have the properties of Newtonian fluids, and

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therefore the study of the features of the filtration of non-Newtonian fluids is of particular importance and is relevant.

The aim of the study is to study the issue of non-Newtonian fluid filtration in a spherical-radial model.

The scientific novelty lies in the study of the influence of a non-Newtonian fluid on the main indicators of filtration.

In this paper, non-linear laws of filtration are considered, provided that the filtering liquid has non-Newtonian properties.

It is known that for a non-Newtonian fluid, the main parameter characterizing its motion is the dynamic coefficient of viscosity. This coefficient is proportional in Newton's law. The relationship between the shear stresses, and the velocity gradient is in this case a straight line passing through the origin.

Fluids that do not obey the law of friction are called anomalous or non-Newtonian. Basically, according to literature analysis, non-Newtonian fluids can be divided into three groups:

1. non-Newtonian fluids, for which shear stress depends only on the velocity gradient (stationary rheological oils)

$$\tau = f\left(\frac{dv}{dy}\right) \tag{1}$$

2. non-Newtonian fluids, for which the relationship between shear stress and velocity gradient depends on the time of stress action (non-stationary rheological oils)

$$\tau = f\left(\frac{dv}{dy}; t\right) \tag{2}$$

Where t - time of stress, sec.

3. viscoelastic oils, i.e. a medium that has the properties of both a solid and a liquid, as well as the tendency of its physical properties and shape to partially recover after stress relief.

Among non-Newtonian fluids of the first class, three classes can be distinguished:

a) viscoplastic fluids, for which the equation has the form

$$\tau = \mu\frac{dv}{dy} + \tau_0 \tag{3}$$

b) pseudoplastic fluids, for which the equation takes the form

$$\tau = k\left(\frac{dv}{dy}\right)^n \tag{4}$$

c) dilatant fluids are described by a power equation, but with $n \succ 1$.

Models of dilatant liquids describe well the properties of suspensions with a high solids content.

Problem statement

The main studies are based on the laws of hydro-mechanics and are solved by mathematical methods.

Where k and n are constant coefficients for a given fluid. This model is used, in particular, to describe the motion of solutions and polymer compositions.

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In porous media, consisting of many micro-capillaries of various diameters, as the pressure drop decreases, the capillaries gradually “plug”; at first, the flow stops in the smallest pores, and as the pressure decreases, this process is observed in large capillaries.

Note that in this case, anomalous properties of reservoir systems arise. The literature [1–5] provides numerous properties of a liquid, such as viscosity, porosity, ultimate shear stress, pressure etc. at low flow rates and low permeability of a porous medium. This is also typical for heterogeneous layers. Note that in the area of low permeability, the appearance of anomalous properties of oil is most likely.

It is known, that the determination of the filtration of liquids and gases is not only of theoretical interest, but also of wide practical importance, because without knowledge of the law of filtration in the rock, especially near the bottom of the well, it is impossible to calculate the possible flow rates of oil and gas, their change over time under various operating conditions wells, and it is also impossible to determine the parameters of the horizon, reservoir, such as permeability, porosity, etc. These parameters, in particular, are determined according to the data of studies of production wells producing hydrocarbons.

Basically, three types of reservoir models are considered. One of these models is spherical-radial. If all fluid particles move in a porous medium so that their filtration rates are not parallel to the same plane, then such movement is called spatial or three-dimensional, since three coordinates are required to determine the position of a hydrocarbon particle in space. Note that if during spatial motion all trajectories are rectilinear and converge radially at one point, then this motion is called three-dimensional radial or spherical-radial.

In this case, due to the spatial symmetry relative to the center of the well, the value of the filtration rate and pressure at an arbitrary point in the flow will be a function of the distance between this point and the center, the well.

Since the magnitude of the filtration rate and pressure are functions of only one variable, a complete study of spherical radial flow can be performed mathematically. Note that an example of a spherical radial flow is a hydrodynamically imperfect well that has barely penetrated an impermeable horizontal top of the layer. In this case, the inflow of hydrocarbons in the immediate vicinity to the bottom of the well will comply with the laws of three-dimensional radial motion.

The problem of fluid inflow to a well that is imperfect in terms of the degree of opening of the reservoir in a reservoir of finite thickness was studied by M. Masket [6]. I.A. Charniy proposed a method for determining the flow rate of a well that is imperfect in terms of the degree of opening. In this case, the well area is conditionally divided into two zones. The first zone is located between the feed loop and a radius equal to or greater than the formation thickness. in this zone, the motion can be considered plane-radial. The second zone is located between the borehole wall and the cylindrical surface, where the movement is spatial, that is, spherical-radial, taken as radial-spherical.

This paper proposes a method for studying the movement of a fluid in a given zone, taking into account the anomalous properties of the fluid (oil).

It is known that in a spherical-radial flow for non-Newtonian, viscous-plastic fluids, the velocity can be written

$$v = \frac{k}{\mu}\left(\frac{dP}{dr} - G\right) \tag{5}$$

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where v - is the filtration rate of the anomalous, viscous-plastic liquid, m/sec; k - permeability coefficient, m^2; μ - dynamic viscosity, Pa*sec; $\frac{dP}{dr}$ - pressure gradient, Pa/m; G - limit value of the pressure gradient, Pa/m.

Let's take the cross-sectional area $S = 2\pi r^2$. Multiplying the right and left parts of this expression by the cross-sectional area:

$$Sv = \frac{k}{\mu} 2\pi r^2 \left(\frac{dP}{dr} - G \right) \quad (6)$$

We have

$$Q = \frac{k}{\mu} 2\pi r^2 \left(\frac{dP}{dr} - G \right) \quad (7)$$

Let's solve the equation in the given range

$$\frac{Q\mu}{2\pi k} \frac{1}{r^2} + G = \frac{dP}{dr} \quad (8)$$

We accept the boundary conditions

$$r = R_w \qquad P = P_w$$
$$r = R_c \qquad P = P_c$$

Then we obtain,

$$\frac{Q\mu}{2\pi k} \left(\frac{1}{R_w} - \frac{1}{R_c} \right) + G\left(P_c - P_w\right) = P_c - P_w \quad (9)$$

As a first approximation $P_c = P_w$. Then, with respect to the volumetric flow, we have

$$Q = \frac{2\pi k}{\mu} \frac{\left(P_c - P_w\right) - G\left(R_c - R_w\right)}{\left(\frac{1}{R_w} - \frac{1}{R_c} \right)} \quad (10)$$

where P_c - pressure on the well contour; P_w - bottom hole pressure; R_c - pressure on the well contour; R_w - well radius.

If we accept that $G = 0$, then we have an equation for the inflow in a spherically radial flow [3, 4]. If we assume that $P_c - P_w = G\left(R_c - R_w\right)$, then in this case the volume flow is equal to zero. In [7-14], it is proposed $R_w = 1,5h$, where h is the thickness or height of the reservoir.

This equation makes it possible to determine the volumetric flow rate of a liquid, taking into account the spherical-radial model for viscous-plastic liquids.

The solution of the problem

The experiments were carried out in laboratory conditions. As can be seen from the figure, the applied model in a particular case affects the filtering process. Figure 1 shows the dependence of the flow rate on the value of the limiting pressure gradient. Obviously, with an increase in the latter, the volumetric flow rate decreases significantly, while it should be noted that this graph is a dependence for small volumes, in well conditions, which is of great importance.

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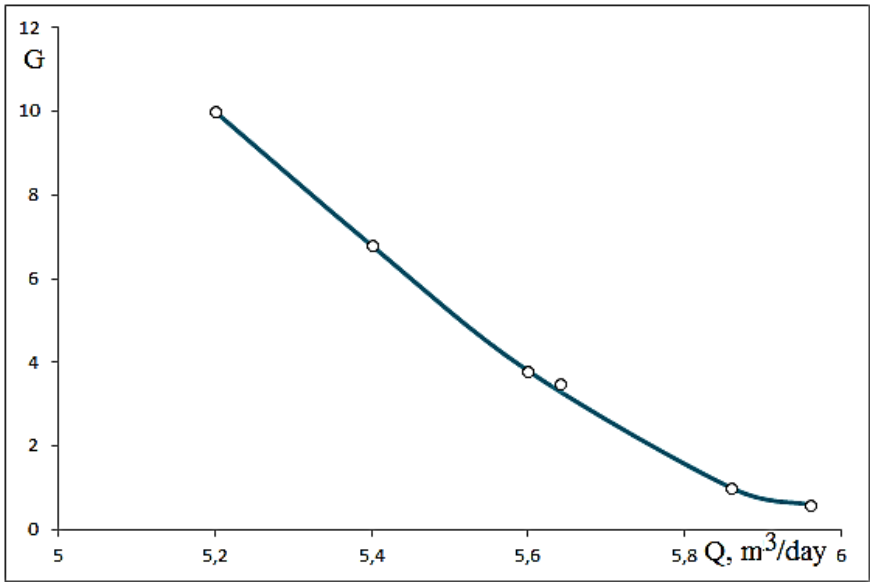

Figure 1. Dependence of liquid consumption Q on G.

Results discussion

The study shows that, taking into account the imperfection of the well, a three-dimensional spherical-radial flow movement is more realistic in practice. Many researchers have pointed to this process. This issue is considered in more detail in [4, 5, 6, 7] for conventional oils.

This paper discusses the issue of non-Newtonian fluid filtration in a spherical-radial model, which is closer to the fields of Russia (Tatarstan, Bashkiria), Romania, Azerbaijan, etc. Given the above, in the development and operation process, it is necessary to take into account these issues.

Conclusion

1. A technique that considers changes in the model at the bottom of the well is proposed.
2. A procedure for determining the volumetric flow rate, taking into account the use of a spherical-radial model for a viscous-plastic fluid has been obtained.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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ELECTRO-CLINICAL PATTERN OF EPILEPSY IN A CHILD WITH SCN8A EPILEPTIC ENCEPHALOPATHY (CUTE SYNDROME): CASE REPORT OF DRUG-RESISTENT EPILEPSY

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ABSTRACT

Having into consideration the expansion research of the epilepsy in children, this study tries to investigate the electro – clinical pattern of the epilepsy in children with SCN8A Epileptic Encephalopathy (Cute syndrome). It is known that there exists a different epilepticus etiology due to the genetic, structural, metabolic, infectious and immune reasons, yet although plenty of research has been made in this regard, in most cases the cause of the epilepsy is unknown, thus leading to a lack of consensus regarding the cause of the epilepsy among the scholars and researches.

Thus, this paper will give a contribution to the existing research, by elaborating a case report of a drug – resistant epilepsy in a 7-year-old child for recurrent afebrile unprovoked seizures, since the age of 16 months. In addition, genetic and clinical features, as well as effectiveness of sodium channel blockers were assessed in the patient confirmed with SCN8A mutation, while to identify the pathogenic epileptic gene next generation sequencing (NGS) was performed. Further, to analyze the electroencephalographic characteristics, electroencephalogram (EEG) was performed initially and during follow-ups.

Finally, the findings suggest that she suffered from focal, febrile to tonic-clonic seizures, treated with various AEDs, making a drug-resistant epilepsy diagnosis. Even though the result cannot be conclusive, we hypothesize that the represented EEG pattern together with the epilepsy and seizure type, ID, and behavioral disorders, may help to characterize the phenotype of Cute syndrome.

Keywords: epilepsy; drug-resistant epilepsy; SCN8A.

Introduction

Epilepsy is known as one of the most common neurological disorder in pediatric population, affecting 1% to 3% of children, defined as any disorder in which spontaneous recurrence of unprovoked seizures is the main symptom. It has also been informed about the etiology of epilepsy which can be different, including structural, genetic, infectious, metabolic and immune causes, yet in most of the cases the cause of epilepsy is unknown. Although there has been made a recent introduction of new antiepileptic drugs (AEDs), about one-third of epilepsy patients have drug resistant (refractory) epilepsy, affecting about 30% of children with epilepsy. In addition, refractory epilepsy, which is the most severe form of epilepsy, according to International league against epilepsy (ILAE), is defined as failure to control seizures when using two or more appropriately chosen and tolerated antiepileptic drugs (as monotherapy or in combination) during an appropriate period of time. Severe and refractory epilepsies in children affect their cognitive

function, leading to worsening of the prognosis, serious psychosocial consequences, difficulties in care and quality of life, anxiety in the family, as well as an increase in the risk of death, including unexpected death in epilepsy (SUDEP).

Recently, extensive genetic research and technology development and the advance development in next-generation sequencing (NGS) has shown that a large proportion of unexplained epilepsies have a genetic basis. The published mutations are all missense except for one splice site mutation resulting in an in-frame deletion. Most mutations arise de novo.

Having into consideration such facts, SCN8A-related epilepsy and/or neurodevelopmental disorders are autosomal dominant epileptic encephalopathies caused by de novo missense mutations in the gene that is part of the voltage gated sodium channels (VGSCs) gene family. VGSC, encoded by the gene SCN8A, plays important role in controlling neuronal excitability and, initiation and propagation of action potentials. SCN8A mutations cause dramatic increase in persistent sodium current and incomplete channel inactivation. De novo SCN8A mutation, was firstly reported in a patient with an infantile epileptic encephalopathy who died of SUDEP. Studies suggest that clinical presentation of SCN8A-related epilepsy and/or neurodevelopmental disorders include variable phenotypes. Thus, indicating that genetic testing of SCN8A should be considered in children with unclassified severe epilepsy.

Epilepsy phenotypes of SCN8A mutations include developmental and epileptic encephalopathy (DEE) associated with severe developmental delays and usually drug resistant epilepsy with multiple seizure types; mild-to-moderate DEE, or intermediate epilepsy with partially treatable epilepsy; self-limited familial infantile epilepsy (SeLFIE, also known as benign familial infantile epilepsy or BFIE) with normal cognition and medically treatable seizures; neurodevelopmental delays with generalized epilepsy (NDDwGE); and neurodevelopmental disorder without epilepsy (NDDwoE) with mild-to-moderate intellectual disability (though it can be severe in ~10% of affected individuals).

SCN8A encephalopathy is characterized by onset of drug-resistant seizures at a mean age of 5 months (range 1 day–18 months). Patients develop multiple seizure types, including generalized tonic–clonic seizures that are present in most patients; tonic, atonic, myoclonic, focal, and absence seizures, febrile seizures and epileptic spasms have also been described. Electroencephalography at the time of seizure onset is normal in approximately 50 % of cases. However, in the following months, most individuals develop electroencephalographic abnormalities, often comprising moderate-to-severe background slowing with focal or multifocal epileptiform discharges. Prior to seizure onset, development is normal for approximately half of patients, and after seizure onset developmental stagnation or regression often results in mild-to-severe intellectual disability. Movement disorders such as ataxia and choreoathetosis are common, and hypotonia, hypertonia, and/or dystonia are present in 50 % of cases. Sudden unexpected death in epilepsy has been reported in approximately 10 % of cases.

Seizures in patients with SCN8A mutations are often refractory to conventional antiepileptic treatment. However, in approximately half of patients, good responses to sodium channel blockers have been described, either as a reduction in seizures or even seizure-free periods, including OXC, CBZ, lamotrigine (LTG), Phenobarbital (PB), topiramate (TPM) and PHT, etc. Reported is worsening of seizures with levetiracetam. Study of 22 patients with SCN8A mutations in who drug-resistant epilepsy started at a median age of 4 months, the most effective antiepileptic drugs reported were OXC, CBZ, PHT, and benzodiazepines. It was reported that EEG findings showed epileptiform abnormalities with a temporo-occipital predominance.

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An already conducted study has reported from 36 patients with SCN8A-related epilepsy and normal intellect (33%) or mild (61%) to moderate ID (6%), having neurological disturbances including ataxia (28%) and hypotonia (19%) as the most prominent features. Interictal electroencephalogram was reported to be normal in 41%. Wang et al. identified seven SCN8A mutations in a Chinese family and six sporadic patients, half of which showed good responses to sodium channel blockers, either as a reduction in seizures frequency or even seizure-free.

In their study, authors Anand et al. reported a family with SCN8A mutation, who had early onset focal epileptic seizures without cognitive or neurological impairment. The seizures were controlled well by mono-therapy, with CBZ and phenytoin (PHT). Additionally, in the report of Parrini et al., patients with the same mutation presented with drug resistant focal epilepsy and mild intellectual disability. This study and previous reports suggest that same mutation in SCN8A can lead to a different phenotype. In addition, it was the authors Trudeau et al. who first reported a frame-shift mutation of SCN8A in a family with mental retardation and ataxia, but without epilepsy. Gardella et al. discovered a SCN8A mutation in 16 affected members of three families with BFIS/ICCA.

Meanwhile, research reported brain magnetic resonance imaging (MRI) to show cerebellar and cerebral atrophy in one and six patients, respectively. In addition, Lyu et al. collected genetic and electro-clinical data from unrelated families carrying novel SCN8A variants associated with chronic progressive or episodic ataxia, and reported variants in SCN8A to be associated with a spectrum of epilepsies and neurodevelopmental disorders including ataxia as a predominant symptom. Moreover, authors Larsen et al. studying seventeen patients with de novo heterozygous mutations of SCN8A, reported multiple refractory seizures including focal, tonic, clonic, myoclonic and absence seizures, and epileptic spasms, as well as motor manifestations including hypotonia, dystonia, hyperreflexia, and ataxia. Furthermore, EEG findings were reported to be moderate to severe background slowing with focal or multifocal epileptiform discharges.

Boerma et al. report patients with SCN8A encephalopathy successfully treated with high doses of PHT, and describe the first study suggesting PHT as a treatment option in patients with SCN8A encephalopathy. CBZ is thought to have a similar working mechanism but with 3 times lower affinity for inactivated sodium channels. Boerma et al. report that high levels of PHT were required before optimal treatment effect was achieved. High serum levels of PHT increase the risk of irreversible adverse effects such as cerebellar atrophy and ataxia, therefore, high doses of PHT could be considered in patients who do not respond adequately to other sodium channel blockers.

Research methodology

Aim: To delineate the onset, electroencephalographic and clinical features of SCN8A-related drug resistant epilepsy (SCN8A developmental and epileptic encephalopathy – Cute syndrome) in order to facilitate early recognition, and eventually early and effective treatment with sodium channel blockers.

Methods: Genetic and electroclinical features, as well as effectiveness of sodium channel blockers were assessed in the patient confirmed with SCN8A mutation. To identify the pathogenic epileptic gene NGS was performed. A detailed clinical history was obtained. To analyze the electroencephalographic characteristics, EEG was performed initially and during follow-ups.

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Case report

We report on a now 7-year-old girl, referred to our department for recurrent afebrile unprovoked seizures, since the age of 18 months. First seizures were noted by the parents since the age of 16 months old. She was born at term by spontaneous vaginal delivery, with average birth weight, of healthy non-consanguineous parents, and with uneventful perinatal and postnatal period. She did not experience traumatic brain injury, or central nervous system infections. There was no medical history of excessive vomiting, abnormal urine or body odor, unconsciousness, feeding abnormality, skin manifestation, trauma, altered sensorium etc. Meanwhile, there was noted history of frequent fever and respiratory tract infections as well as recurrent febrile convulsions. Before the onset of seizures, development was normal for her age. Over time she was found to have progressive regression of achieved milestones, was least responsive to surroundings, leading to intermediate global learning and speech difficulty that improved over time with occupational and speech therapy. In addition, she had difficulty with fine and gross motor skills, and ataxia that improved with physical therapy. During clinical assessment, there was a normal systemic examination and no craniofacial dysmorphic features were noted. Regarding the neurologic and behavioral aspects, the patient had moderate intellectual disability, learning difficulties, and neurobehavioral problems such as attention deficit hyperactivity disorder (ADHD) since toddler age. However, she was able to participate in normal school life with assistance.

Targeted exome sequencing in human genome (WES) with Illumina technology of next generation sequencing (NGS) of clinically significant genes was performed and a pathogenic heterozygous variant, NM_001330260.2(SCN8A): c.2890G>A, missense, was identified at exon 16 of SCN8A gene, c.2890G>A, p. (Gly964Ser). This variant causes exchange of glycine amino acid with serine in position 964. As the parental genetic tests revealed that the parents did not have this missense, the variation was identified as a de novo variant. This variant was categorized as pathogenic by the American College of Medical Genetics and Genomics (ACMG) guideline (PS2, PM2, PM5, PP3) and has not been reported earlier. The variant is absent from control sequences (Genome Aggregation Database (gnomAD) and no alternative plausible variants or known mutations were identified as competing possibilities in this patient. Disease as per OMIM was EIEE type 13, inheritance-autosomal dominant, classification-likely pathogenic.

Table 1. Electroclinical characteristics of epilepsy.

Seizure type	EEG abnormalities	Age	AEDs	Seizure frequency
FCS, MS, FeS	Multifocal discharges	16-18 mo		First seizures/10 times a day
FCS, GTCS	Multifocal bursts	2 yo	VPA	1-2 /day
FCS, MS	Multifocal discharges	3 yo	VPA	1/week
GTCS	Generalized paroxysmal discharges	4 yo	VPA	2-3 /week
FS, EMS	Multifocal bursts with generalized discharges	4 yo	VPA + OXC	Every day in sleep
FS, MS	Multifocal paroxysmal discharges	4 yo	VPA + OXC (ex, dwz)+ LEV	1/week

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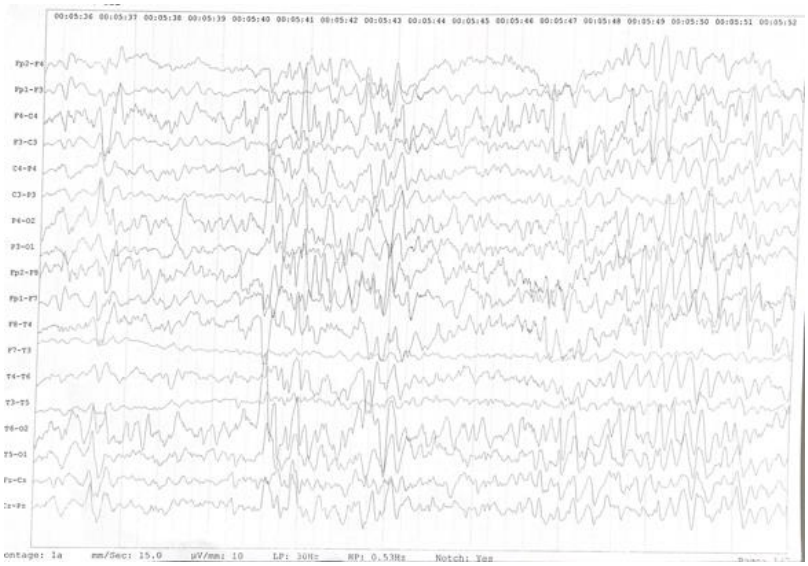
GTCS	Generalised bursts	4.5 yo	VPA + LEV	1/week
FS, MS, FeS	Multifocal bursts	5 yo	VPA + LEV (ex) + CBZ	2-3/day
FS, FeS	Multifocal bursts with generalized discharges	5 yo	VPA + CBZ (ex, dwz) + CLB	1-2/month
FS, MS	Generalised discharges	5.5 yo	VPA + CLB	1/month
FS, EMS	Generalised discharges	5.5 yo	VPA + CLB + TPM	Every day in sleep
FS, MS	Multifocal bursts	6 yo	VPA + CLB + TPM (ex) + LCM	Stabilization
EMS	Multifocal bursts	7 yo	VPA + CLB + LCM	4-5/day in sleep

Abbreviations: Generalized tonic-clonic seizures= GTCS, focal clonic seizures= FCS, FeS= febrile seizures, EMS= eyelid myoclonic seizure, MS= myoclonic seizure, Sodium valproate/valproic acid=VPA, Lacosamide= LCM, Topiramate=TPM, Levetiracetam=LEV, Oxcarbazepine= OXC, Clobazam= CLB, Carbamazepine= CBZ, Drowsiness=dwz, mo= months old, years old=yo, excluded=ex.

Her first seizures were focal clonic seizure by description and myoclonic jerks that occurred at the age of 16 months, with a frequency of around 4-10 seizures a day. The seizure frequency was noted to increase during febrile state. The first sleep interictal EEG showed regular alpha activity, associated with mainly frontal and temporal intermittent multifocal bihemispheric discharges of high voltage spike-and-wave complexes. (*see* picture 1). These seizures were misdiagnosed for extrapyramidal tremor. Therefore, treatment with sodium valproate was started at the age of 2 years old. With AED Initially, there were 1-2 generalized tonic-clonic seizures or focal seizures in a day on average, followed by a partial stabilization in the following year leading to one seizure in a week. Sleep EEG revealed multifocal bursts of spike-and-wave complex discharges. Epilepsy protocol magnetic resonance imaging of the brain was normal.



Picture 1. First interictal sleep EEG showing multifocal bihemispheric discharges of high voltage spike-and-wave complexes.

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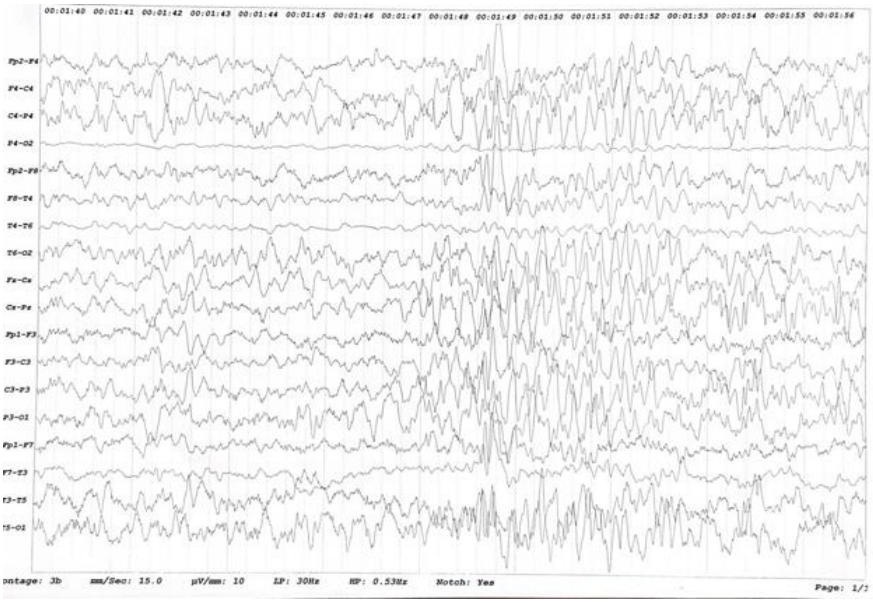
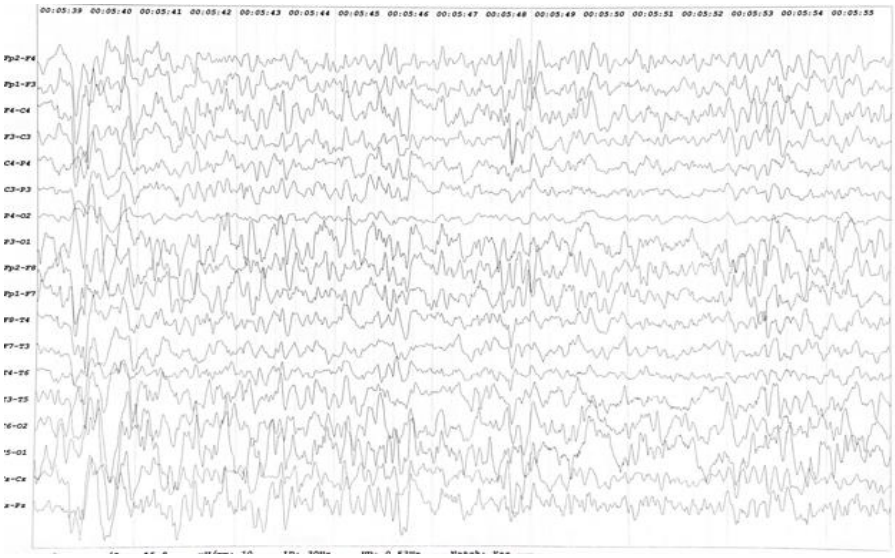
Stabilization of seizures was not achieved, despite GTCS and FCS there were also noted febrile seizures. In addition, the seizures were more frequent, 2-3 times a week. Therefore, a second AED, oxcarbazepine, was added to the treatment. Regarding the adverse effects due to oxcarbazepine, such as dizziness, it was discontinued, and in the treatment was included levetiracetam. During this period the EEG findings in sleep, showed multifocal frontal and temporal bursts of spike-and-waves complexes with generalized discharges (*see* pictures 2). Partial stabilization was achieved with valproic acid in combination with levetiracetam. Sleep EEG showed multifocal, mainly frontal spike-and-wave discharges (*see* picture 3).



Picture 2. Sleep EEG: multifocal bursts of spike-and-waves complexes with generalized discharges



Picture 3. Sleep EEG in stabilization showing multifocal, mainly frontal spike-and-wave discharges.

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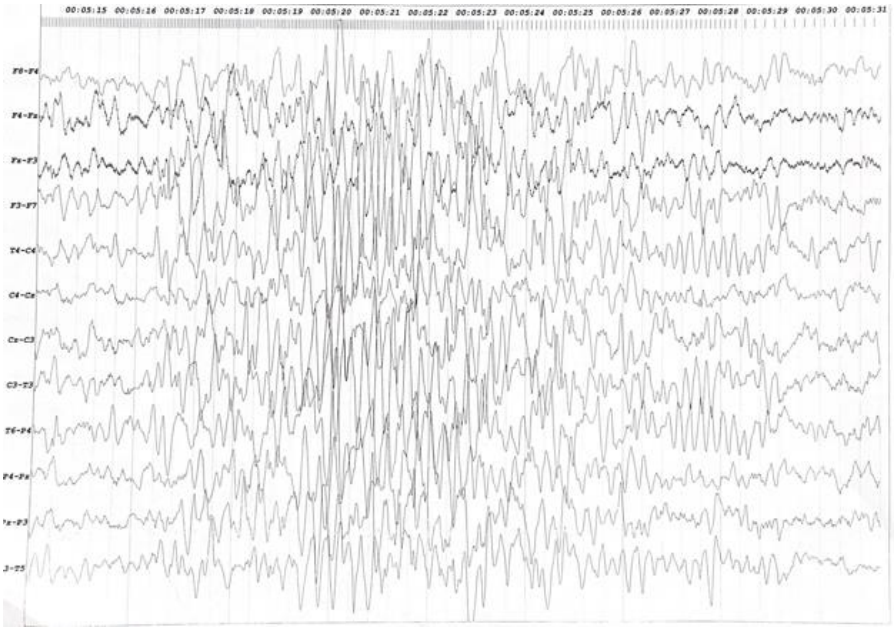
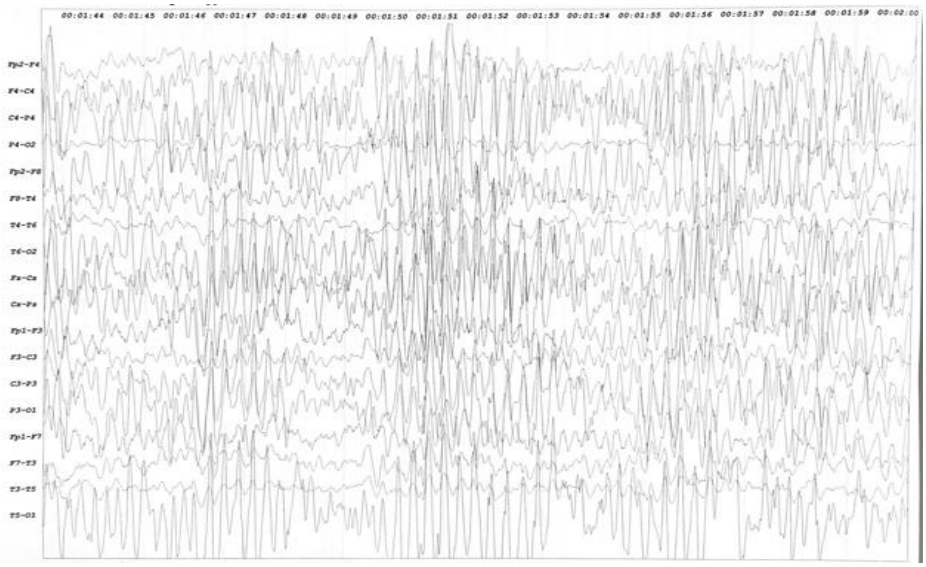
Thereafter followed a period of worsening with GTCS, as well as febrile seizures. The sleep EEG findings showed generalized paroxysmal spike-and-wave discharges (*see* picture 4).



Picture 4. The sleep EEG findings during worsening with generalized paroxysmal spike-and-wave discharges.

Eyelid myoclonic seizures in sleep were also noted. The follow-up sleep EEG findings showed regular brain activity of alpha rhythm with generalized bursts of paroxysmal discharges of spike-and-wave complexes (see picture 5). There followed a period of partial stabilization after commencing clobazam and excluded levetiracetam. The EEG findings showed bifrontal focal spike wave discharges, in stabilization (see picture 6).



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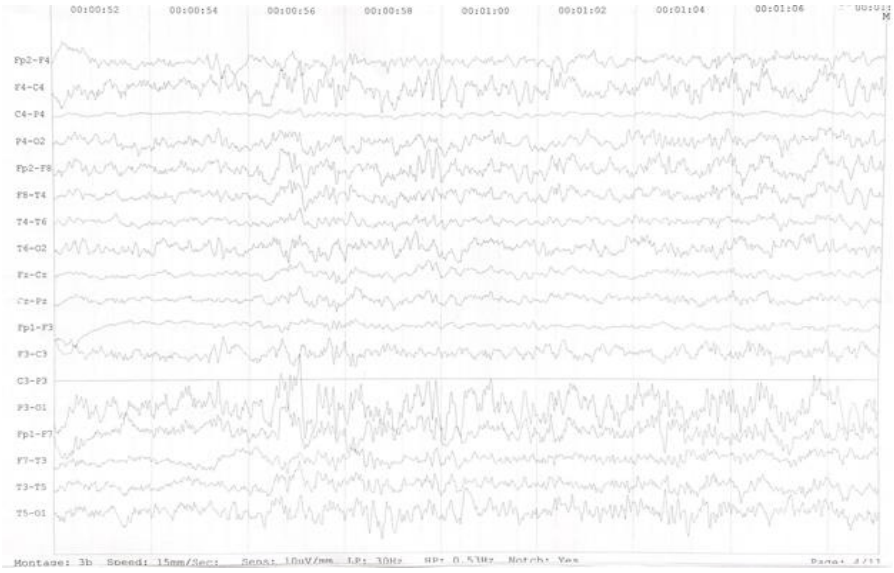
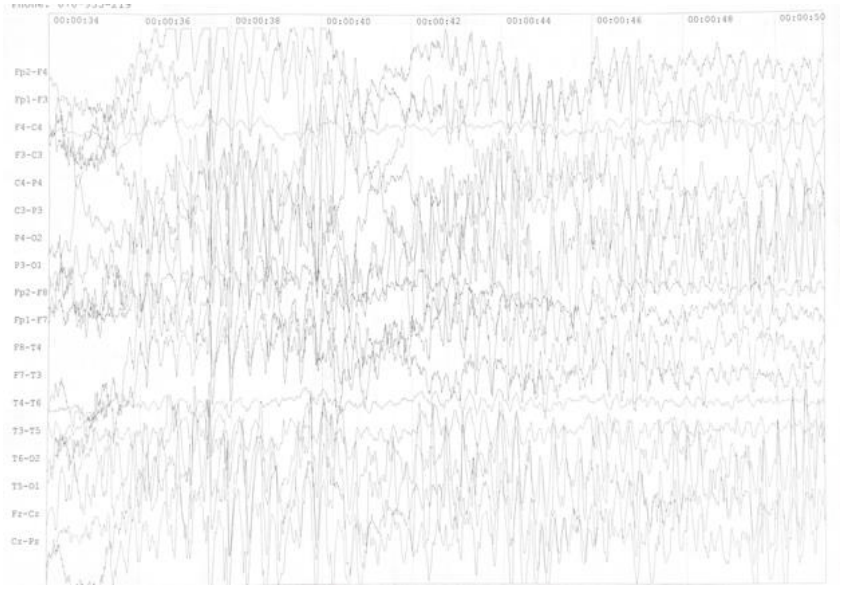
Picture 5. EEG findings generalized bursts of paroxysmal discharges of spike-and-wave complexes.



Picture 6. The EEG findings in stabilization showing bifrontal focal spike wave discharges.

Thereafter, followed a period of frequent everyday focal seizures and eyelid myoclonic seizures in sleep. Topiramate was included in the antiepileptic treatment. There was no improvement on the clinical and EEG findings. The follow-up wakefulness and sleep EEG showed continuous multifocal high voltage discharges of spike-and-wave complexes (*see* picture 7).



Picture 7. Wakefulness and sleep EEG showing continuous multifocal high voltage discharges of spike-and-wave complexes.

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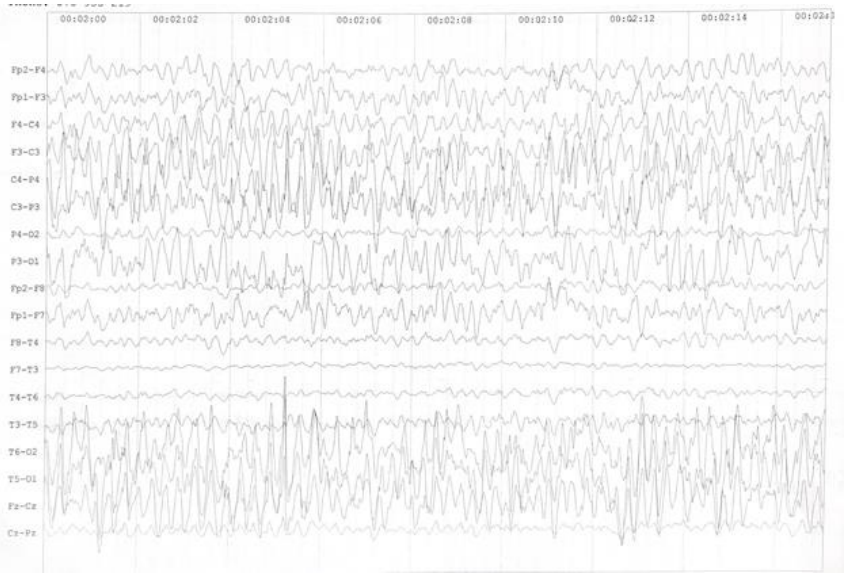
A period of seizure freedom occurred at age 6 to 7, when lacosamide was included in the treatment. During a period of less than a year, the girl had rarely focal seizure, and no generalized tonic-clonic seizures were noted. The sleep EEG findings revealed basic brain activity of regular alpha rhythm with multifocal mainly frontal and temporal bursts of spike-and-waves discharges (*see* picture 8).



Picture 8. The sleep EEG findings: multifocal mainly frontal and temporal bursts of spike-and-waves discharges.

Nowadays, she has mostly short-lasting eyelid myoclonic seizures daily on sleep. Sleep EEG findings showed regular alpha activity with multifocal bilateral paroxysmal discharges of spike-and-waves.

Her seizures proved difficult to control, despite trials of valproic acid in combination with levetiracetam, oxcarbazepine, carbamazepine and topiramate. A trial of lacosamide in combination with valproic acid and clobazam led to a marked reduction in seizure frequency and partial stabilization.

Conclusions and discussion

In many of the studies done in this area it is noted that Cute syndrome is a severe form of epilepsy caused by mutations in SCN8A gene, which is encoding VGSCs that have a crucial role in neuronal excitability.

In addition, it was also discussed that the phenotypic spectrum *SCN8A* mutations varies largely. Most patients can have intractable epilepsy beginning at the first year of life, accompanied by severe developmental delay and intellectual disability (ID), while others have milder phenotype, such as BFIS and ICCA. Furthermore, a few patients with ID or movement disorders without epilepsy have been reported. The epileptic discharges are most prominent in temporal regions, comprised of spike or spike-and-waves.

Literature has suggested that patients with SCN8A encephalopathy respond to the sodium channel blockers such as PHT, valproate, CBZ, lacosomide, LTG, rufinamide and OXC.

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Cranial MRI is not specific in SCN8A encephalopathy; usually it is normal. However, there may be cortical atrophy or corpus callosum abnormality in some cases or progressive cerebral or cerebellar atrophy in follow up imaging. According to several groups of authors the amino acid substitution is severely damaging to the structure of the sodium channel.

Our case had similarities with the previously reported cases. The report illustrated a girl presenting with a drug-resistant, monogenic epilepsy syndrome, epileptic encephalopathy due to SCN8A pathogenic de novo variant found by NGS associated with the Cute syndrome. This variant has never been reported so far in the literature. Clinical features of our patient responded to severe developmental delays and usually drug resistant epilepsy with multiple seizure types. Seizure-free was not achieved by multi-antiepileptic drugs usage. Seizure recurrence increased with age. Seizure type included focal motor seizures, febrile seizures, myoclonic and generalized tonic-clonic seizures. In our patient, movement disorder was present in the form of ataxia. Early EEG features showed focal or multifocal epileptic discharges, that changed over time and the background showed progressive slowing. In our case cortical atrophy was not found in MRI. Partial response has been noted with valproic acid, clobazam and lacosamide. We did not use phenytoin for our case due to its side effects.

The detailed discussion of our case would contribute to early detection and targeted treatment of SCN8A encephalopathy. Even though our result cannot be conclusive, we hypothesize that the represented EEG pattern together with the epilepsy and seizure type, ID, and behavioral disorders, may help to characterize the phenotype of Cute syndrome. Future studies regarding these issues may outline the electroclinical pattern in a larger series of patients with Cute syndrome. This also gives special emphasis on a genetic test in infants with intractable epilepsy, movement disorder and developmental delay.

Authors contributions

All authors had main contribution in literature search, writing and drafting the manuscript. LAA contributed in the diagnosing, treatment, and follow-up of the patient. BA edited the manuscript. All authors approved the final version.

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Conflict of interest

None of the authors have any conflict of interest to disclose.

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Availability of data

The data of the current case report are available from the corresponding author on reasonable request.

Consent

The case report protocol was performed in accordance with the Declaration of Helsinki.

Informed consent

Written informed consent was obtained from the patient's parent to publish this report in accordance with patient consent policy.

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POSTPARTUM PREECLAMPSIA AND BENIGN POSTPARTUM PLEURAL EFFUSION- TIMELY RECOGNITION AND MANAGEMENT OF THE CONDITION WITH CLINICAL CASE

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ABSTRACT

New-onset postpartum preeclampsia (NOPP) is defined as the diagnosis of new-onset postpartum preeclampsia, which develops from ≥48 hours to ≤6 weeks after delivery (these patients did not have hypertension before). This is a little-studied pathology, its exact spread, risk factors and pathophysiologic mechanisms are still not fully known. In this article, the authors present a clinical case, where a 38-year-old woman visited the cardiologist 3 days after the cesarean section with complaints: post-cesarean section headache, slight deterioration of vision, mild respiratory insufficiency, mild peripheral swellings, chest discomfort, arterial hypertension within 140-160/90-95mm/Hg. The patient did not have hypertension in the past. Blood pressure started to rise 48 hours after surgery. Echocardiography revealed bilateral pleural effusion. The patient's condition was evaluated as NOPP, postpartum cardiomyopathy was ruled out, and clinical management was performed in coordination with the doctor gynecologist. Within 3 weeks, the pleural effusion decreased and resolved, it was evaluated as benign postpartum pleural effusion. Hypertension was regulated in 2.5-3 months with labetalol. There is a need to raise awareness about postpartum hypertension, as NOPP can lead to serious complications if symptoms are not properly assessed and left untreated. Thus, postpartum preeclampsia requires timely recognition

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and proper treatment. Future studies should focus on pathophysiology and specific risk factors. A better understanding of pathomechanisms is essential for better postpartum patient care and guideline development, as well as, for reducing maternal morbidity and mortality in the postpartum period. Hypertensive disorders of pregnancy complicate 10 to 20% of pregnancies in the United States. They are responsible for a significant proportion of maternal morbidity and mortality and are a leading cause of readmission to hospital after delivery.1–3 Although most cases are diagnosed in the antenatal period, postpartum preeclampsia de novo or new at birth is increasingly recognized as a major contributor. maternal morbidity and mortality in the postpartum period. Hypertension in the puerperium is most often observed in women with prenatal hypertensive disorders, but can develop de novo in the postpartum period.

Introduction

Postpartum hypertension most commonly occurs in women with antenatal hypertension, but it can develop de novo in the postpartum period. It is unclear whether postpartum preeclampsia is antepartum preeclampsia or a pathology independent of eclampsia. Although definitions vary, the diagnosis of postpartum preeclampsia should be considered between 48 hours and 6 weeks postpartum in women with new-onset hypertension. Postpartum preeclampsia is an understudied disease and guidelines for its diagnosis and management are based on insufficient evidence.

Nevertheless, it is currently recommended, that new-onset postpartum hypertension (including markedly elevated blood pressure in women without a history of hypertension) be termed postpartum preeclampsia after exclusion of other etiologies to facilitate timely recognition and management of the condition. Older maternal age, black race, maternal obesity and cesarean delivery are associated with a higher risk of postpartum preeclampsia.

In most women, late postpartum preeclampsia presents within the first 7-10 days after delivery, most often with neurological symptoms such as headache.

Treatment: use of antihypertensive drugs, magnesium and diuretics. Postpartum preeclampsia may be associated with a higher risk of maternal morbidity than prenatal preeclampsia, although it remains underreported disease.

Future studies should focus on pathophysiology and specific risk factors. A better understanding of pathomechanisms is essential for better postpartum patient care and guideline development, as well as, for reducing maternal morbidity and mortality in the postpartum period [1-7].

Hypertensive disorders of pregnancy complicate 10 to 20% of pregnancies in the United States. They are responsible for a significant proportion of maternal morbidity and mortality and are a leading cause of readmission to hospital after delivery.1–3 Although most cases are diagnosed in the antenatal period, postpartum preeclampsia de novo or new at birth is increasingly recognized as a major contributor. maternal morbidity and mortality in the postpartum period. Hypertension in the puerperium is most often observed in women with prenatal hypertensive disorders, but can develop de novo in the postpartum period. Although definitions vary, the diagnosis of postpartum preeclampsia should be considered in women with new-onset hypertension during the postpartum period. There is a need to improve terminology regarding immediate postpartum preeclampsia (within 48 hours of delivery) and late postpartum preeclampsia, which has traditionally been defined as new-onset preeclampsia between 48 hours and 6 weeks after delivery. Most reports of postpartum preeclampsia are limited to smaller case series, so the overall incidence has not been reliably determined prospectively [8-15].

Few national and international guidelines address the occurrence of postpartum hypertension, and existing guidelines lack clear definitions. The American College of Obstetricians and Gynecologists (ACOG), the Royal College of Obstetricians and Gynecologists (RCOG)/National Institute of Excellence in Health and Care (NICE), and the Society of Obstetricians and Gynecologists of Canada (SOGC) do not specifically define preeclampsia. They do not differentiate between new-onset puerperal preeclampsia and new-onset puerperal hypertension. In our experience, this is a diagnostic issue that frequently arises in the clinical care of this group of women.

Regarding timing, we suggest considering the diagnosis of postpartum preeclampsia in women with new-onset preeclampsia 48 hours postpartum and within 6 weeks postpartum. Although this timing is not clearly defined, this is the terminology used by experts and in existing literature on the subject.8–10 We recognize that the postpartum period is a continuum and may need to be modified as we better understand the pathophysiology. of this state. Traditionally, 48 hours is used as it usually covers immediate postpartum changes and routine hospital management. It is important to note that other causes of postpartum hypertension and seizures at 4 weeks postpartum should be considered. We believe that more research is needed to determine whether new-onset postpartum preeclampsia/eclampsia is distinct from prepartum preeclampsia; However, we recommend highlighting this condition here and in national/international guidelines as it is not sufficiently recognized by service providers [16-21].

Definitions of hypertension and preeclampsia are extrapolated from guidelines on hypertensive disorders in pregnancy with antepartum onset, i.e. 140/90 mmHg possible subtypes of postpartum hypertension. In our clinical experience, women without proteinuria are as likely to have adverse clinical outcomes as women with significant proteinuria. However, given the limited clinical outcome data, we suggest that proteinuria continue to be assessed according to current guidelines until additional studies evaluating outcomes in this population become available. Extrapolating from ACOG guidelines for prenatal diagnosis of preeclampsia and gestational hypertension, we suggest that less attention be paid to the presence of proteinuria in women with new-onset postpartum hypertension.

Preeclampsia is a pregnancy-associated hypertensive disorder and a leading cause of maternal and perinatal morbidity and mortality. Despite its prevalence, clearly classified risk factors and clinical features, the exact pathophysiology of this disease remains unknown. This knowledge gap has hampered the development of targeted therapies and limited treatment options for healthcare providers.

Clinically, preeclampsia is associated with a number of complications for both mother and fetus. It is considered to belong to the spectrum of disorders of hypertension during pregnancy, with gestational hypertension being on the milder end of the spectrum, followed by preeclampsia, chronic hypertension with superimposed preeclampsia, hemolysis, elevated liver enzymes, low platelet counts, and eclampsia on the milder end of the spectrum. form. forms. End of the spectrum. the most extreme [1]. Because preeclampsia is a true systemic disease, it can present in a variety of ways. It is classically defined as maternal hypertension and renal dysfunction, especially characterized by proteinuria [1]. However, recent guidelines mention thrombocytopenia, liver failure, pulmonary edema, and cerebral/visual symptoms as diagnostic features. Other maternal complications include seizures (eclampsia), cerebral hemorrhage, disseminated intravascular coagulation, and liver rupture. Obstetric complications associated with preeclampsia include uteroplacental insufficiency, placental abruption, preterm birth, and

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increased risk of cesarean section [2]. Other fetal complications include fetal distress during labor, intrauterine growth restriction, oligohydramnios, and, in severe cases, fetal death [3]. In addition to obstetric and neonatal consequences, preeclampsia carries a long-term risk of complications, including stroke and hypertension.

As doctors try to better manage this rising tide, a number of risk factors have been identified that reflect the complex nature of preeclampsia. These include diseases such as chronic high blood pressure and other classic cardiovascular risk factors, as well as chronic kidney disease, antiphospholipid syndrome, collagen-related vascular diseases (eg, lupus), and pre-existing diabetes. In addition, factors such as nulliparity, previous diagnosis of preeclampsia, abnormal placentation, multiple pregnancies, and maternal age at both ends of the spectrum (<20 years or >35 years) increase susceptibility. The incidence and severity of preeclampsia is higher in African Americans, likely due to health care disparities as well as higher rates of determinants such as chronic hypertension, obesity, and type 2 diabetes, which are underdiagnosed in the African American community. Finally, there appears to be a genetic component to preeclampsia, as a family history of preeclampsia, hypertension, and type II diabetes (maternal or paternal) also suggests an increased risk [22-25].

Despite the health disparities and significant clinical impact of preeclampsia, childbirth is the only “cure” and even after birth, these mothers and their babies remain at high risk for future cardiovascular and metabolic diseases.

Thus, efforts to promote early detection, better understanding of pregnancy mechanisms, and improved treatment options are essential to improve the treatment outcomes and health of patients with this complex disease. As the field advances, there is growing recognition that there are many subtypes of preeclampsia, and these subtypes may differ in underlying cause, placental transcriptomic landscape, and disease severity. Suggested classifications include early and late onset, with early onset more commonly associated with uterine malposition, impaired uterine perfusion, and fetal growth restriction. On the other hand, late-onset preeclampsia may be associated with excessive growth of the placenta (leading to chorionic villus compression), stress, or aging toward the end of pregnancy. Redman et al. The idea that the placental syncytiotrophoblast layer is sensitive to cellular stress (i.e., oxidative, mitochondrial, and endoplasmic reticulum) during pregnancy, independent of triggering factors, and ultimately the maternal response to These syncytial stress signals determines whether a pregnant woman will develop preeclampsia. Although vascular dysfunction can lead to trophoblastic stress or trophoblastic stress can disrupt the vasculature, many of the risk factors, putative mechanisms, and long-term consequences of preeclampsia are directly related to the maternal and placental vasculature. Therefore, we would like to summarize the main research priorities in the field of preeclampsia and highlight the role of the vascular system in these areas [26-29].

It is generally accepted that placental development is impaired in some pregnancies caused by preeclampsia, resulting in cellular, molecular, immunological and vascular changes, and the role of inappropriate decidualization has also received increasing attention. It is traditionally believed that early preeclampsia is caused by abnormal placentation and superficial invasion of trophoblasts into the uterus, leading to incomplete remodeling of the spiral artery. This can lead to placental hypoxia, an aberrant angiogenic state, endothelial dysfunction, further reduction in placental formation, trophoblastic stress and ultimately the onset of maternal preeclampsia. Although much of the etiology remains unknown, research suggests that impaired decidual

differentiation before pregnancy may contribute to impaired trophoblast invasion and its consequences [31-35].

However, it is a complex syndrome and the exact sequence of pathogenesis is unclear. The prognosis of preeclampsia is imprecise, and it is difficult to determine whether physiological changes are the cause of preeclampsia or whether it is a secondary outcome.

During normal placentation, trophoblasts, divided into cytotrophoblasts and syncytiotrophoblasts, descend from the blastocyst to form extraembryonic cells necessary for the formation of the placenta. Cytotrophoblasts form the inner villous layer of the placenta, closest to the fetal circulation, and syncytiotrophoblasts arise from the fusion of cytotrophoblasts and form the outer villous part in contact with the maternal environment. Together, this arrangement of cells creates a branching structure called chorionic villi. Although chorionic villi are essential for maternal-fetal exchange, the release of syncytiotrophoblastic placental-derived microvilli (STBM) into the maternal circulation is increased in women with preeclampsia and impairs endothelial cell proliferation. In addition, endothelium-dependent vasodilation is also impaired following infusion of placental STBM vesicles into fatty arterioles collected during cesarean section. Electron micrographs after this perfusion confirm severe destruction of the endothelial layer and intracellular organelles, but the underlying smooth muscle remains intact. Therefore, the spread of CTBM in the bloodstream is a mechanism of vascular dysfunction in preeclampsia [36].

These inflammatory, hypotensive, and fetal growth effects were mitigated by nitric oxide (NO) analogue treatment, supporting the theory that vascular dysfunction is a likely etiological factor in preeclampsia. Both TLR4 and TLR9 have suppressive effects on trophoblast migration, suggesting that these receptors are due to placental aberrations. Placental TLR3 is also upregulated in preeclampsia. Viral mimetic treatment in pregnant rats confirmed a more causal relationship and resulted in increased placental TLR3 expression, increased systolic blood pressure, decreased aortic vasodilation, and increased urinary protein excretion, with these effects being limited to pregnant animals. Natural killer cells in the uterus secrete the anti-inflammatory cytokine interleukin 10 (IL-10), which plays an important role in pregnancy. Specific functions of IL-10 include preventing fetal allograft rejection by the maternal immune system, reducing placental endoplasmic reticulum stress, and compensating for antiangiogenic factors. In preeclampsia, there is a decrease in IL-10 immunostaining and an increase in TNFα. In mice, activation of TLR3 and deletion of Il10 alone resulted in preeclampsia phenotypes, and together these manipulations resulted in more severe disease. Exogenous administration of recombinant IL-10 restored impaired endothelium-dependent vasodilatory responses in these mice and may have useful therapeutic potential given the limited treatment options available.

Maternal T cells have many subtypes and a wide range of immunological functions during pregnancy. Group differentiation (CD) 4+ promotes fetal acceptance and consists of regulatory and helper subsets, whereas CD8+ T cells control trophoblast invasion. Adequate levels of T-cell subtypes prevent overactive immune system and fetal-damaging or autoimmune attacks. Regulatory T cells (Tregs) control the defense of T helper cells (Th cells) and are thought to be unbalanced in preeclampsia. In particular, patients with preeclampsia exhibit suppressed Treg cell numbers with increased circulating and decidual activity of the proinflammatory Th1 and Th17 subgroups. Treg cell depletion in mice results in increased uterine artery vasoconstriction and endothelin-1 production, suggesting that altered vasoreactivity in preeclampsia may be related to Treg cell depletion.

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Preeclampsia is characterized by an imbalance of pro- and antiangiogenic factors, which directly affects endothelial function. VEGFA stimulates angiogenesis, vascular permeability and cell migration by binding to its tyrosine kinase receptors VEGFR1 and VEGFR2. Binding of VEGFA to VEGFR2 results in stronger signaling than VEGFR1 through activation of the phospholipase C gamma (PLCγ)/protein kinase C (PKC)/MAPK pathway, which is involved in endothelial cell proliferation. During placental villous development, VEGFA is present in trophoblasts and perivascular cells to support vascular development (i.e., vasculogenesis) as well as vascular dilation by endothelial sprouting (i.e., vasculogenesis). During pregnancy, VEGF induces greater activation of endothelial nitric oxide synthase (eNOS), and NO production occurs primarily through VEGFR2-mediated PI3K/AKT signaling (105,106). PlGF, its proangiogenic counterpart, binds to VEGFR1, increasing the likelihood of VEGF binding to VEGFR-2. The interaction of PlGF with VEGFR1 also promotes other critical events such as: B. Transphosphorylation of VEGFR2, thereby increasing the downstream signaling cascade. Like VEGF, the action of PlGF facilitates the growth and migration of endothelial and trophoblast cells. In a healthy pregnancy, PlGF levels increase until week 32 and then decrease. However, with preeclampsia, there is a significant decrease in venous levels already at 13–16 weeks, which occurs before the appearance of other clinical symptoms. Not only does this have adverse cardiovascular consequences during pregnancy, but these vascular diseases and adverse cardiac remodeling may persist for many years after pregnancy. This suggests that mothers' obvious symptoms often disappear after childbirth.

Platelet activation, aggregation and blood clotting (coagulation) are interrelated processes. In short, platelets have adhesive properties and, when bound to damaged endothelium, release substances such as thromboxane that promote aggregation. Platelet aggregation stimulates platelet plug formation and thrombin-mediated fibrin clot formation. A recent systemic review and meta-analysis suggests that patients with preeclampsia have a higher mean platelet volume (indicating platelet activation) and a higher likelihood of adhesion and aggregation. In this article, Jacobsen et al reported conflicting results regarding aggregation, and additional studies showed no difference or decreased aggregation, but these specific studies did not assess adherence. A study examining platelet adhesion showed decreased immunohistochemical expression of platelet endothelial cell adhesion molecule 1 and increased intercellular adhesion molecule 1 in the human placenta of individuals with preeclampsia, which is believed to play a role in trophoblastic invasion and vascular dysfunction. Consistent with the idea that syncytiotrophoblast stress is the final common factor leading to the maternal elements of preeclampsia and the importance of platelet function in this syndrome, syncytiotrophoblast-derived extracellular vesicles (SDEVs) have been shown to activate platelets ex vivo. SDEVs derived from preeclamptic placentas cause greater platelet activation than in normal pregnancies, but aspirin treatment prevents platelet aggregation.

During pregnancy, there is a natural decrease in platelet counts, partly due to sequestration of blood cells in the interstitial space [37], an increase in plasma volume, and increased aggregation of thromboxane A2. Thrombocytopenia, beyond the normal decrease in platelet count caused by pregnancy, is common in preeclampsia and may be particularly associated with a decrease in platelet count and activation of blood clotting. Together, these hemostatic effects increase the risk of bleeding and microthrombi in mothers with preeclampsia.

The generation of reactive oxygen species as a result of placental hypoxia, immune activation, and other cellular damage has numerous consequences, including damage to mitochondrial DNA (mtDNA). The DNA repair capabilities of mitochondria are less extensive than those of nuclear DNA, which increases the likelihood of cell death with mtDNA mutations as a result of apoptosis

or necrosis. This results in the release of DNA into the maternal bloodstream, which is considered a damage-associated molecular pattern (DAMP) and is recognized by pattern recognition receptors such as TLR9. TLR9 is a proinflammatory component of the innate immune system activated by hypomethylated CpG dinucleotides widely expressed in mtDNA and bacteria. Although surface receptors are also present, DNA recognition by TLR9 occurs preferentially on endolysosomes because the acidic environment allows TLR9 to bind negative DNA more easily. Thus, DNA enters the cell via endocytosis and, upon TLR9 binding, triggers a cascade of subsequent proinflammatory events, including IFN, NFκB, and AP-1 signaling.

This hypothesis is supported by the fact that preeclamptic plasma contains higher amounts of serum mtDNA and that TLR9 activity increases with the onset of preeclamptic symptoms. linking the TLR9 inflammatory response to other aspects of preeclampsia, including angiogenesis and trophoblast function. In this study, VEGFA levels were reduced in human placenta, but TLR9 and sFLT-1 were increased in preeclamptic samples (83). Applying these results to a mouse model, the TLR9 agonist induced traditional features of preeclampsia and also recapitulated the downregulation of VEGFA and upregulation of sFLT-1 observed in human tissues. SiRNA knockdown of TLR9 in human trophoblast cells facilitates migration and invasion, highlighting the importance of TLR9 also in the early stages of placentation. Dendritic cells from women with preeclampsia appear to be hypersensitive to immune stimulating agents, suggesting a possible cause of over-recruitment of TLR9.

Despite the profound impact of preeclampsia on maternal and fetal health, its pathogenesis is not yet fully understood and is likely variable, limiting the development of treatment options. In conclusion, treatment of preeclampsia has been predominantly symptomatic and aimed at maintaining an acceptable blood pressure range, neuroprotection and seizure prevention, with immediate delivery at term or after 34 weeks for severe manifestations. However, cases of vascular insufficiency have been found to occur at all stages of preeclampsia, from placentation to the puerperium, and are likely due to a combination of inadequate trophoblast invasion, poor oxygen extraction by the placenta, and a proinflammatory immune environment. antiangiogenic factors, endothelial dysfunction and oxidative stress.

Due to the lack of robust studies assessing vascular parameters before pregnancy and before the onset of preeclampsia, it is unclear whether women who develop this syndrome have underlying vascular pathology or whether the possible vascular effects are simply a byproduct of increased trophoblast stress signaling. Mother. Both aspects are likely to play a role, and physiological abnormalities in preeclampsia begin long before clinical diagnosis. Therefore, it is important to improve early detection methods and screening tools. Although routine measurement of vasopressin levels during pregnancy is not yet used in clinical practice, it represents a promising opportunity to predict the future development of preeclampsia and provide more proactive care for these patients. In terms of molecular targets, less explored areas include the modulation of RGS proteins to mitigate the negative consequences of excessive GPCR induction by hormones such as angiotensin II, endothelin-1 and vasopressin, or the uptake of cellular stress leading to mitochondrial dysfunction leading to cellular dysfunction. Death, circulating DNA and subsequent TLR9 activation. Although much remains to be discovered, translational research, basic animal models, and mechanistic cell studies have already had a profound impact on the field, and new technologies such as trophoblast organoid cultures offer great potential for new ideas. Thus, collaboration across the spectrum, from the laboratory to the bedside, will accelerate

our understanding of preeclampsia as quickly as possible and potentially facilitate the development of new targeted treatments.

Birth conditions are favorable for the development of pleural effusion. Normal pregnancy may promote transudation of fluid into the pleural cavity due to increased hydrostatic pressure in the systemic circulation, increased blood volume, and decreased colloid osmotic pressure. Repeated Valsalva maneuvers may further contribute to pleural effusion.

Increased intrathoracic pressure and impaired lymphatic drainage of the pleural cavity due to increased systemic venous pressure. Atelectasis of the gravid uterus can also contribute to the formation of pleural fluid. The value of ultrasound in detecting pleural fluid is well known.

Treatment of hypertension during pregnancy depends primarily on expert opinion and observational studies because few randomized controlled trials have been conducted in this population, traditionally considered a vulnerable group by institutional review boards. An important factor is weighing the risks and benefits of treating high blood pressure in pregnant women for both the mother and the fetus. This, in turn, determines the exact blood pressure at which drug treatment in pregnant women begins.

After birth, the primary treatment of hypertensive disorders of pregnancy in most cases continues to be carried out by an obstetrician. Immediately after birth, the focus is on stabilizing the mother and normalizing her blood pressure with medication, if necessary. The American College of Obstetricians and Gynecologists (ACOG) recommends maintaining blood pressure below 150/100 during the postpartum period, although initiation of treatment, drug titration, and choice of antihypertensive drug are based on clinical judgment as there are no standardized treatments. Recommendations for specific antihypertensive medications or titration parameters for postpartum medications. Currently, women in the United States are typically discharged from the hospital 2 to 4 days after delivery, and ACOG recommends a single blood pressure measurement 3 to 10 days after delivery for women with hypertension during pregnancy. Women with persistent hypertension or those who need to take antihypertensive medications are generally more likely to be monitored for medications after delivery. However, this depends on the institution. The woman is then seen for a comprehensive postpartum visit, usually 4 to 6 weeks after birth, and referred to her primary care physician if additional need for antihypertensive medications arises.

Increasing evidence suggests a high rate of progression of chronic hypertension or persistent hypertension in the first year after hypertension during pregnancy. A recent study using ambulatory and inpatient blood pressure monitoring found that women with severe preeclampsia had persistent hypertension one year after delivery. These cases were detected only by APBM, suggesting that masked hypertension may significantly contribute to the increased risk of cardiovascular disease in this population. Factors appear to increase this risk including overweight and obesity, black race, and severity of hypertension during pregnancy.

The lifestyle interventions to improve cardiometabolic risk factors after complicated pregnancy were feasible and effective in the first year postpartum. The recently published SNAP-HT study demonstrated that regular titration of antihypertensive medications in the postpartum period not only shortens the duration of antihypertensive treatment, but can also lead to long-term improvements in blood pressure lasting up to 6 months postpartum. The authors suggested that this beneficial effect was secondary to more favorable cardiovascular remodeling. These results suggest that the first year postpartum may be critical for risk classification and easier

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identification of women with persistent or unresolved hypertension after hypertension during pregnancy.

Few health care providers offer postpartum counseling or cardiovascular disease risk screening, although the postpartum period may be a time when women become motivated to make lifestyle changes [26]. Although some health care providers are well aware of the risk of future cardiovascular disease and try to promptly educate patients, they face many barriers to reducing this risk. It is difficult to determine the appropriate time and place for counseling and implementation of recommended risk reduction measures. Much of this counseling occurs immediately after birth, which is often a stressful and emotional time for women. Given the birth of a newborn, numerous physical changes, pain and lack of sleep, it is not surprising that women do not retain all the information doctors give them during labor [27]. Although remote blood pressure monitoring may be a promising method for improving medication adherence in the postpartum period, blood pressure monitoring is often not reimbursed by health insurance, potentially harming women of lower socioeconomic status. Postpartum care following hypertension during pregnancy is often fragmented, and there is no clear transition from obstetrician to primary care physician or cardiologist [26]. This poor monitoring of care is compounded by underlying socioeconomic issues affecting care delivery during this period. The United States is one of the few developed countries without paid parental leave, which disproportionately affects the most disadvantaged women. Access to health care must also be considered, as many publicly insured women who were only covered during pregnancy lose coverage within 60 days of giving birth, significantly limiting their care following pregnancy complications, with conditions varying from state to state. States are different. The state is different. Significantly higher rates of posttraumatic stress disorder in women with hypertensive disorders during pregnancy. These women are less likely to return to the health care system for follow-up care after a traumatic birth. Postpartum screening as part of a trauma-informed model of care may be useful, but is untested to date.

Prenatal care focuses on caring for women between pregnancies with the overall goal of improving pregnancy outcomes for the woman and fetus. The Society of Maternal-Fetal Medicine (SMFM) and ACOG recommend prenatal care for women with hypertension disorders during pregnancy. They especially emphasize the importance of care during pregnancy to maximize a woman's health, not only between pregnancies and during subsequent pregnancies, but throughout her life. This prenatal care should actually begin during prenatal care during the first pregnancy, with SMFM recommending that during prenatal care providers discuss who will provide primary care immediately after birth, discuss contraceptive options, and provide proactive breastfeeding and maternal health counseling, and also discussed the context of prenatal care between pregnancy complications and maternal long-term health. At a full postpartum visit between 4 and 6 weeks, health care providers should assess pregnancy complications and their impact on the mother's future health, and ensure that the patient remains in primary care for additional care. In particular, for women whose pregnancy is complicated by preeclampsia or gestational hypertension, the SMFM recommends measuring blood pressure to rule out hypertension and maintaining blood pressure <120/80 mm Hg. Art. Consider starting treatment or contacting your primary care provider if blood pressure goals are not being achieved. They also recommend that women achieve a normal BMI and discuss taking aspirin in future pregnancies. In women with chronic hypertension, testing for ventricular hypertrophy, retinopathy, and renal disease should be

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considered in addition to the above recommendations in women with long-standing or uncontrolled hypertension.

Goal

Aim of the research was to study clinical case of postpartum preeclampsia and benign postpartum pleural effusion- timely recognition and management of the condition.

Case

A 38-year-old woman came to us with complaints: headache developed after caesarean section, slight deterioration of vision, episodes of mild respiratory insufficiency, small peripheral edema, chest discomfort, arterial hypertension within 140-160/90-95mm/Hg. Pregnancy and caesarean section went without complications. The increase of blood pleasure started 48 hours after the operation, no significant changes were observed in the laboratory during the hospital stay. she had been discharged on prescribed methyldopa at home.

Hypertension continued, the above-mentioned complaints were added, which became the reason for an outpatient visit to a cardiologist.

No arterial hypertension or any cardio pathology in the past history. One pregnancy and caesarean section 6 years ago without complications. The patient was a smoker, she refused any family history.

On Electrocardiography: normal sinus rhythm.

Echocardiography revealed: the dimensions of the heart chambers within the normal range, the function of the global contractility of left ventricle was normal, the ejection fraction 56%, no hemodynamically significant regurgitation was observed, the pericardium - free of fluid. 3-3 cm pleural effusion bilaterally has been revealed.

With laboratory control: complete blood analysis, electrolytes, complete urine analysis, creatinine, type B natriuretic peptide-proBNP, liver function tests - normal. The patient's condition was evaluated as postpartum preeclampsia and clinical management was done with the attending gynecologist.

Methyldopa was replaced by labetalol and blood pressure stabilized. Postpartum cardiomyopathy was ruled out, echocardiographic control was performed one and three weeks later, left ventricular contractility remained within normal limits, pleural effusion decreased and resolved, it was assessed as benign postpartum pleural effusion. Arterial blood pressure normalization occurred after 2.5-3 months on labetalol.

Discussion

Most often, the symptoms of preeclampsia appear during pregnancy [2], although some women develop preeclampsia after childbirth, including those who had a normal pregnancy, as it happened in our case. Postpartum preeclampsia mostly occurs within a few days of delivery, but can develop up to 6 weeks. Untreated preeclampsia can lead to stroke, seizures, and other serious complications [3].

A doctor should be consulted immediately if the systolic blood pressure reading is 140 mm Hg or higher and/or the diastolic blood pressure reading is 90 mm Hg or higher [4]. Preeclampsia should also be recognized immediately if the patient notices: changes in vision (blurring, sensitivity to light, spots in the field of vision), headache that does not resolve with medication, shortness of

breath, swelling of the face or hands, pain in the shoulder or abdomen, mostly in the right upper quadrant, nausea or vomiting, sudden weight gain (1.5 to 2 kg or more per week), decreased urination.

In our case, the patient did not have hypertension before delivery, nor did during first pregnancy, have not any complications during delivery. The blood pressure started increase 48 hours after cesarean section, blurred vision, progressive respiratory insufficiency, peripheral edema, chest discomfort developed in 72-96 hours, 3-3 cm pleural effusion bilaterally has been revealed and it should be considered as a benign postpartum pleural effusion [5,6,7].

Early recognition of postpartum preeclampsia and initiation of appropriate treatment is important. Postpartum preeclampsia can be treated with hypotensive tablet medications, sometimes intravenously (IV), to prevent seizures.

Preeclampsia is a progressive multisystem disorder characterized by the development of new-onset hypertension, proteinuria, or other important target organ dysfunction during the last half of pregnancy or the postpartum period. The progression of the disease from mild to severe can occur gradually or rapidly.

A major focus of routine prenatal care is monitoring patients for signs and symptoms of preeclampsia. If diagnosed during pregnancy, the only definitive treatment is delivery to avoid maternal or fetal complications from disease progression. The problem will eventually resolve with delivery, although target organ function may deteriorate in the first three days after delivery.

The timing of delivery is based on a combination of factors, including the severity of the disease, maternal and fetal condition and gestational age.

Postpartum maternal monitoring is important to identify the minority of patients whose blood pressure does not return to normal levels after delivery. Long-term follow-up of the mother is also important, as patients with a history of preeclampsia have a later risk of cardiovascular disease and mental disorders .

Most NOPP develops within 48 hours of delivery. But it sometimes develops up to six weeks after child birth or later. This is known as late postpartum preeclampsia.

NOPP detection is sometimes difficult. Most of women with NOPP have no signs or symptoms during pregnancy, as was in our case, and may not suspect a problem when they are focused on postpartum recovery and caring for their newborn.

Studies in this direction are rare. Possible risk factors: high blood pressure during the last pregnancy, arterial hypertension (gestational hypertension) developed after 20 weeks of pregnancy, obesity, multiple pregnancy - having twins, triplets or more increases the risk of preeclampsia. Chronic high blood pressure – uncontrolled high blood pressure before pregnancy increases the risk of gestational preeclampsia and postpartum preeclampsia.

Diabetes – type 1 or type 2 diabetes or gestational diabetes increases the risk of preeclampsia and postpartum preeclampsia.

In our case, the patient did not have any of the above risk factors. Symptoms of preeclampsia developed shortly after delivery and progressed rapidly. Early recognition and management of preeclampsia is important, as NOPP can be complicated by conditions such as postpartum eclampsia.

This is essentially postpartum preeclampsia with seizures. NOPP can permanently damage vital organs, including the brain (stroke), vision, liver and kidneys. Possible complications are: thromboembolism, HELLP syndrome, which involves hemolysis, increased liver enzymes, and thrombocytopenia. It can quickly turn into a life-threatening condition. Manifestations of this

syndrome are: nausea, vomiting, headache and pain in the upper right quadrant of the abdomen. Sometimes it can develop suddenly, even before high blood pressure is detected, or it can develop without any symptoms [8,9,10].

Conclusion

There is a need to raise awareness about postpartum hypertension, as NOPP can lead to serious complications if symptoms are not promptly assessed and treated. Thus, postpartum preeclampsia requires timely recognition and proper treatment.

Declaration of Interest Statement: No potential conflict of interest was reported by the authors.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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THE MANIFESTATION OF KEY ISSUE ASPECTS OF PHARMACISTS' OCCUPATIONAL FEATURES AND STUDY OF SOME DRIVING FORCES IMPACT ON PHARMACISTS' PROFESSION AND ROLE EXPANSION

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ABSTRACT

The main goal of the study was to analyze key issue aspects of pharmacists' occupational features and study of some driving forces impact on pharmacists' profession expansion. The study was a quantitative investigation and analysis of pharmacists' vocational perspectives impressions and evaluations of key issue of factors having influence on pharmacists' occupational development in Georgia, in general by using questionnaires. Were conducted a survey study. The in-depth interview method of the respondents was used in the study. The approved questionnaires were used (Respondents were randomly selected): Questionnaire for pharmacist specialist, 810 pharmacist specialists participated in the study. Were used methods of systematic, sociological (surveying, questioning), comparative, mathematical-statistical, graphical analysis. The data were processed and analyzed with the SPSS program. Were conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p< 0.05$ as significant for all analyses. The research implementation required the following sub studies: The scientific talks of pharmacists' vocational perspectives impressions and evaluation of key issue of factors having influence on pharmacists' occupational development in Georgia, in general. According the study results found: Common pharmacies have been providing health care for many years, via giving consultation, advice, providing and delivering medicine when needed, or referring patients to other health care professionals. This report, however, reflects and represent the embedding of a formalized approach whereby pharmacies are covering for these services, and where self-care through pharmacists is measured as an integral part of the health system. A pharmacist is a personality who is professionally competent and qualified to prepare and dispense medicine. The Pharmacist dispense drugs, check patient's health, and make sure that drugs do not interact in a harmful route. Pharmacist are drug experts eventually interested about their patients' wellness and health. Public health service interventions, higher level pharmaceutical care, rational pharmacotherapy and effective medicines supply chain management are main components of an accessible, sustainable, affordable and equitable health care system which ensures the efficacy, safety and quality of drugs. It is clear that pharmacy has a great role to play in the health sector reform process. The role of the pharmacist needs to be redefined and reoriented. Pharmacists have the capability and possibility to enhance therapeutic results and patients' quality of life within accessible resources, and must position themselves at the forefront of the health care system. The movement towards pharmaceutical care is a critical factor in this matter. Pharmacists also have a vital contribution to make to patient care through managing pharmacotherapy and concurrent non-prescription or alternative therapies. The pharmacists are health professionals who are dispensing prescription drugs to patients, also provide information about the medicines ordered by doctors. They explain the doctors' instructions to patients so that, people can safely and effectively use these medications. Another big issue is ensuring that drugs are used reasonably and rationally. Pharmacists have a deep

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knowledge of the chemistry and pharmacotherapy of different drugs and how they react to people, as well as how drugs interact with each other. Pharmacists must accurately measure and a package of medicine, providing its dosage and security to ensure patients proper and rational pharmacotherapy in general.

Keywords: Pharmacists', occupational, features, driving, forces, impact, pharmacists', profession, expansion.

Introduction

Pharmacists have a lot of public health functions that can benefit from the unique experience of pharmacists, which may include pharmacotherapy, pharmaceutical care, and pharmacy assistance. In addition to dispensing medicines, pharmacists have proved to be an accessible resource for information on health and medicines.

Being a health care professional means being part of a team that is focused on one goal- helping the patient achieve better health. Pharmacists are a part of this health care team, and their duty is to help the patients make the best use of their medication. Thus, within their profession, pharmacists have developed other categories of pharmacy workers to help get the work done more efficiently and allow pharmacists to be more focused on the patient The were found and estimated factors having influence on pharmacists' professional development, these factors were: Interesting and valuable (informative) work; The favorable (prosperous) psychological climate within the collective in the colleagues' team; The possibility of career growth (development); The possibility of professional education or training; The social importance of the profession; Independence in work [1-4].

The public and our patients should expect the highest possible pharmaceutical care from professional practitioners worldwide, without exception. The obviously evidence and confidence of competence, skills and capability that is corresponding with accelerating and master practice is a clear message to fostered public that pharmacists have this competence; professional distinction, credentialing and quality convinced of specialization are part of this evidence of competence, potential and capability. It is in the interest of patients, health systems and to pharmacists' profession that develop a common and shared understanding of what we mean by specialism and by forward practice". This is a key supervisor for future workforce perfection [5-7].

Education and advancement of long-term education are the cornerstones of the future pharmacy - today's students are supervisor in the pharmacy of tomorrow. This means that all parties involved in pharmaceutical education have a great responsibility for mastering new approaches and view for the training of future health care workers. Academic pharmacy must take a powerful position in forecasting essential changes in the world and developing strategies for improving the teaching of pharmacy in the interests of everyone's health. One of the most significant aspects is the development of knowledge, cognition and experience in the academic workforce [8-10].

A pharmacist a health care professional, which distributes medications to patients on prescription, on the order of a physician or another doctor. Pharmacists have a deep knowledge of the chemistry and Pharmacotherapy of different drugs and how they react to people, as well as how drugs interact with each other. Pharmacists must accurately measure and a package of medicine, providing its dosage and security due to the patient. While the pharmacist typically does not choose or prescribe medication, the pharmacist educates patients on how to take the medication and what reactions or problems should be avoided. Pharmacists also known as chemists (druggists) or they are health care professional specialists who working in pharmacy,

medical sciences, health care, focused on the safe and effective use of drugs. A pharmacist is a part of the health care brigade straight engaged in patient care [11-13].

Pharmacists are trained at the university grade degree level, to understand the biochemical and pharmacological mechanisms of effect of drugs, the use of drugs and therapeutic roles, side effects, possibility drug interactions, and inspection parameters. Pharmacists interpret and transmit this experience for patients, physicians and other medical professionals. Among other requirements for licensing in different countries require pharmacists to hold either a Bachelor degree of Pharmacy or Doctor of Pharmacy degree. The most general pharmacist positions that of the general pharmacist (also referred to as first-line retail pharmacist or pharmacist) or a hospital/clinic pharmacist, where they instruct, teach, advice and counsel on the correct use and side effects of drugs and medicines [14-16].

In most countries, the profession of pharmacist is subject to professional regulation. Depending on the legal framework of practice, pharmacists may promote to the destination (also known as pharmacist legislator) and the introduction of certain medications (eg, immunization) in some jurisdictions. Pharmacists can also practice in a diversity of other directions, including industry, studying, factories, wholesale trade, academia, research, universities, insurance, the military and government [17-19].

Pharmacists should see themselves as the main health care providers who can use their clinical experience in various public institutions. Pharmacists will always be an important health care provider based on their availability to patients through community pharmacy setting. This specific role of provider should never be reduced, as it serves the critical needs of patients (eg, dispensing and counseling for drug experience in nonprescription drugs, compounding, vaccinations, and the use of medication administration or monitoring devices) that not addressed by other health care providers [20-22]. However, this does not exclude pharmacists serving as suppliers of innovative alternative settings, such as outpatient clinics located in pharmacies and other retail outlets; in independent practice with a focus on medication management therapy, medication reconciliation, drug counseling or Pharmacogenomic; institution or organization, where they are responsible for the integration and promotion of patient care through the many other health care providers to facilitate continuity of care community; or organizations that coordinate research to improve practice through pharmacy practice based research networks. Pharmacy providers should look for opportunities to engage in professional activities between patient care, when and where they occur or as they develop in communities. For example, alternative practices may change to concentrate on providing pharmacy and health services for adults and retirement communities, given the growing number of them as Georgian population continues to age [22-24].

Pharmacy graduates who serve in the health services of Georgia, as these pharmacists to develop innovative practice settings, they should be drivers for expansion within the pharmacy practice in community, state and national levels. Pharmacy educators must ensure that graduates have the necessary knowledge, skills, attitudes/values, and practice experience, as well as confidence, drive, and entrepreneur spirit to be a driving force for change in order to facilitate these and other advances in the scope and type of community pharmacy practice [25-26].

Patient safety is a priority for all professionals - pharmacists - who care about the health. Patient safety is defined as the prevention of harm to patients, including by errors. For centuries, pharmacists were guardians / safeguards against "poisons" of substances that can cause harm to society. Now more than ever, pharmacist’s responsibility is receiving safely the medication to the patient. Hospitals and other institutions and facilities, such as outpatient clinics, drug-dependency

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treatment facilities, poison control centers, drug information centers, and long-term care facilities, may be operated by the government or privately. While many of the pharmacist's activities in such facilities may be similar to those performed by community pharmacists, they differ in a number of ways. Additionally, the hospital, clinic or institutional pharmacist has more possibility to interact closely with the prescriber and, therefore, to promote the rational prescribing and use of drugs in larger hospital and institutional pharmacies, is usually one of several pharmacists, and thus has a greater opportunity to interact with others, to specialize and to gain greater expertise, having access to medical records, is in a position to effect the option of drugs and dosage regimens, to monitor patient compliance and therapeutic response to drugs, and to recognize and report adverse drug reactions; can more easily than the community pharmacist assess and monitor patterns of drug usage and thus recommend changes where necessary serves as a member of policy-making committees, including those concerned with medicine choice, the use of antibiotics, and hospital infections and thereby actions of the preparation and composition of an essential-drug list or formulary is in a better position to educate other health professionals about the rational use of drugs, more easily participates in studies to determine the beneficial or adverse effects of drugs, and is involved in the analysis of drugs in body fluids ,can control clinical manufacture and acquisition of drugs to ensure the supply of high-quality products, takes part in the planning and implementation of clinical trials [28-31].

Goal

The main aim of the study was to analyze the key issue aspects of pharmacists' occupational features and study of some driving forces impact on pharmacists' profession expansion.

Methodology

Research objectives are materials of sociological research: the study was quantitative investigation by using survey (Questionnaire). The study was quantitative investigation by using survey (Questionnaire). The in-depth interview method of the respondents was used in the study. The approved questionnaires were used (Respondents were randomly selected. Questionnaire for pharmacist specialist, 810 pharmacist specialists participated in the study. We used methods of systematic, sociological (surveying, questioning), comparative, segmentation, mathematical-statistical, graphical analysis. The data was processed and analyzed with the SPSS program. Results and discussion: Questions and answers are given in the tables. On each question are attached diagrams or table. Questionnaire and diagrams are numbered. Study of the data was processed and analyzed with the SPSS program. We conducted descriptive statistics and re-gression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p < 0.05$ as significant for all analyses. The study's ethical items. In order to provide the study's ethical character each participant of it was informed about the study's goal and suggested of willingness of the work to be done. So, the respondents' written or oral compliance was got on that issue. All the studies were carried out by the selected organizations ad-ministrations' previous compliance. Were used Informed consent form for each respondent to participate in an anonymous survey. During the whole period of research, the participants incog-nita was also provided. For the international rules and criteria' conformity this human subject comprising given study was discussed and confirmed on the Bioethics Committee sessions of the YSMU. In order to meet the objectives, set in the research we also used the results obtained

through analysis of available official information, studies and opinions about pharmacists, as well as the methods of quantitative studies. The research implementation required the following sub studies: The key issue aspects of pharmacists' occupational features and study of some driving forces impact on pharmacists' profession expansion.

Results and discussion.

Pharmaceutical care is a ground-breaking concept in the practice of pharmacy which emerged in the mid-1980s. It stipulates that all practitioners should assume responsibility for the outcomes of drug therapy in their patients. It surrounds a variety of functions and services – some new to pharmacy, others traditional – which are determined and provided by the pharmacists serving individual patients. The concept of pharmaceutical care also includes affective commitment to the welfare of patients as individuals who require and deserve pharmacists' compassion, mercy, concern and trust. However, pharmacists often deny to accept responsibility for this power and extent of care. As a result, they may not adequately document, control and review the care given. Accepting such responsibility is essential to the practice of pharmaceutical care. Pharmaceutical care can be tendered to individuals and publics. "Population-based pharmaceutical care" uses demographic and epidemiological data to establish formularies or drug lists, develop and monitor pharmacy politics, develop and manage pharmacy networks, prepare and analyses reports of drug utilization/costs, conduct drug utilization reviews and educate providers on medicine policies and procedures [32-34].

Without individual pharmaceutical care, however, no system can manage drug therapy and monitor medicine-related illness effectively. The population-based functions identified by above need to occur either before or after patients are seen and provide useful information, but cannot replace patient-specific services while patients are being seen. Medicine related illnesses occur frequently even with medicines that are in a system's formulary or medicines list, since these medicines are often prescribed, administered or used inappropriately. Patients need pharmacists' maintenances at the time they are receiving care. Successful pharmacotherapy is specific for each patient. It includes individual drug therapy decisions, reaching concordance (an agreement between the patient and the health care provider on the therapeutic outcome and how it may be achieved), and critical patient monitoring activities. For each individual patient's pharmacotherapy treatment, the pharmacist develops a care schedule together with the patient. Patients can then contribute to successful outcomes by taking part of the responsibility for their own care and not relying solely on caregivers, in the former paternalistic style. Pharmaceutical care does not exist in isolation from other health care services. It must be provided in collaboration with patients, physicians, nurses and other health care providers. Pharmacists are responsible directly to patients for the cost, quality and results of pharmaceutical care does not exist in isolation from other health care services. It must be provided in collaboration with patients, physicians, nurses and other health care providers. Pharmacists are responsible directly to patients for the cost, quality and results of pharmaceutical care [35-37].

The forces behind the variations in pharmaceutical education are many and varied, and growing in both number and intensity. The major economic and political forces affecting the health care system in the most countries are also having an impact and influence on the practice of pharmacy. As an effect, radical changes are needed in pharmaceutical education. The role and function of pharmacists and pharmaceutical staff need to be reappraised and the educational outcomes of the evolving pharmacy curriculum should be clearly determined. The use of outcomes statements

would help to drive curriculum development. Educational outcomes can be used as a new organizing framework that integrates science, professional attributes, interprofessional practice, and professionalism across new major headings of pharmaceutical care, systems management, and public health, as they are in the practice of pharmacy. The educational change will require not only extensive curriculum revision and restructuring, but also a major commitment to faculty development to prepare teachers to educate pharmacists in a different way. The type and depth of didactic and experiential material to be included will be different. The amount and allocation of educational resources will have to change. Schools and colleges of pharmacy should create, establish and evaluate practice models that could be used within evolving health care environments. Courses should take into consideration the needs of the objective audience, learning outcomes, course content, learning and teaching methods, learning resources, participant assessment, course evaluation, and quality assurance when being introduced into the curriculum.

Pharmacy practice takes place at different levels. The ultimate aim of activities at all these levels is to benefit patients by improving and maintaining their health. Activities at individual patient level comprise all aspects of providing and managing a patient's drug therapy (i.e., pharmaceutical care, including clinical pharmacy services). At this level, decisions are made on issues of pharmaceutical care and triage (i.e., prioritization of care, patient follow-up and therapeutic outcome monitoring).

Patient safety is a priority for all professionals - pharmacists - who care about the health. Patient safety is defined as the prevention of harm to patients, including by errors. For centuries, pharmacists were guardians / safeguards against "poisons" of substances that can cause harm to society. Now more than ever, pharmacist's responsibility is receiving safely the medication to the patient.

Protecting the people is the primary goal of pharmacy boards. On a broad scale, this mission requires a pharmacist to attend university for a specific number of years and to pass the state competency examination. Boards also set the parameters for what happens if a law or regulation is violated, what penalties result, and what infractions can cause if a pharmacist lose his or her license.

Pharmacy is one of the most regulated professions in the western countries and pharmacist profession is one of the most ethically challenging position. In EU countries state boards regulate, administer and influence every phase of pharmacy practice, including the demands and licensing testing for pharmacist. In western countries each state board is staffed up of pharmacists who come from every practice area — hospitals, clinic, chains, independent pharmacies, pharmaceutical factory, industrial pharmacy — as well as at least one consumer (non pharmacist) representative. In most states, pharmacy board members are appointed by the government.

The health care brigade composes of the patient and all the health care professional specialists who have liability for patient care. This health care brigade demands to be well determined, and cooperation needs to be actively sought. Pharmacists have considerable character and role to play in this brigade. Pharmacists must demand to acclimatize their skills, knowledge, information and attitudes to this innovated role, which consolidates all traditional pharmaceutical sciences with hospital/clinical aspects of the patient care, clinical/hospital skills, management, administration and communication skills, active cooperation with medical brigade and solving of drug-related issues. If they are to be recognized as full members of the health care brigade, pharmacists will demand to adopt the essential attitudes required by health professional specialists laboring in this space: visibility, liability, duty, responsibility, accessibility in a working practice targeted at the

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general population, commitment to confidentiality and patient orientation. Pharmacists will demand to be competent, qualified, knowing and possess all that vision, opinion and a voice to fully integrate themselves into the health care brigade.

In western countries are actively working clinician pharmacist, pharmacist and family doctor system, it plays an important role in pharmaceutical care. In western countries and in many developing countries pharmacist professions a regulated sector in health, as well as family medicine. Pharmacist, as well as the family doctor, needs higher education, further Diploma, and continuing pharmaceutical education, Pharmacist's license and periodic accreditation. in pharmacy, on pharmacists position works only higher pharmaceutical education specialists, Who graduated by the state recognized and accredited universities, and colleges. In Georgia pharmacist further diploma , continuing pharmaceutical education, pharmacist licensing and accreditation regulatory legislative base is not perfect. Today, the pharmacist profession in Georgia is impaired, pharmacist profession is deleted from health adjustable medical fields, Therefore degree in pharmacy or higher education in pharmacy losing profession opinion and values. In Georgia not conducted pharmacists certification, re-certification, accreditation and licensing state programs. Therefore profession pharmacist specialty becomes given position by the pharmacy owner, and not only from the university awarded qualification. Because of the above reasons in Georgia in drugstores for pharmacist position is no longer necessary higher pharmaceutical education, in drugstore any person has the right to work as a pharmacist position, any educated person or a person without medical or pharmaceutical education may be given a "position" Pharmacist "according pharmacy owner desired, pharmacy profession granting needs 4-5 year study at medical and other universities.In Georgia drugstore pharmacist interpreted as the only drug-dealer-seller. Pharmacist as regulated medical specialists ignored in Georgian Health-care System. That is why higher pharmaceutical education system should be moved to a new model direction, which will be more focused on pharmacotherapy, pharmaceutical care, and clinical pharmacy. Therefore, in future pharmacist profession in Georgian health care system should become most important link. In the state health policy, it is necessary to develope pharmacist profession's concepts and common principles. pharmacist profession should become regulated health care job, look like family doctor. In Georgia should be developed and implemented pharmacists registration, licensing, and accreditation new standards accordance with international pharmaceutical programs. Also qualified pharmacist in Georgia should have the right to work as pharmacist in other European Countries. Georgian pharmacist Certificate should have recognition in western countries, and Georgia should create pharmacist registration standard which is exist in Great Britain and other Western countries.

As pharmacists proceed to become more clinically-oriented health care professionals, with increased responsibilities, liability and accountabilities for pharmaceutical care clear pathways for workforce development, coupled with professional recognition and credentialing of practitioners, is an important consideration. This represents a clear opportunity for transnational collaboration and further opportunities for transnational recognition of advanced capabilities for the pharmacy workforce. An obviously display and assurance of competence and facilities that is well-proportioned with progressive and expert practice is an obviously message to fostered public that pharmacists own this competence; occupational recognition, credentialing and quality assured specialism are part of this to show of competence, skills and capability. There is in the interest of patients, health systems and pharmacist profession that were develop a common and shared understanding of what we mean by specialization and by innovative practice. This is a key driver

for future workforce perfection. Pharmacists have a lot of public health functions that can benefit from the unique experience of pharmacists, which may include pharmacotherapy, pharmaceutical care, and pharmacy assistance. In addition to dispensing medicines, pharmacists have proved to be an accessible resource for information on health and medicines. The centralized position of the pharmacist in the society and clinical competence are invaluable. It is important to review and integrate public health practices into pharmacological training and pharmaceutical care. Encouraging cross-training will also increase the resources and help meet the needs of the workforce in the fields of pharmacy and public health. The Georgian Pharmacists Association has strongly supported the role of the pharmacist in public health. Through Trans disciplinary approaches, it is assumed that the pharmacist's contribution to public health, health care, health education, disease prevention and health promotion, public health promotion and the quality of health will help in achieving optimal public health outcomes.

The rational use of drugs remains the exception rather than the rule. For those people who do take medicines, more than half of all prescriptions are incorrect and more than half of the people involved fail to get them correctly. In additive, there is growing concern at the increase in the global spread of antimicrobial resistance, a major public health challenge. The global trend is for pharmacy to continue to become a more clinical, patient-facing profession, with enhanced responsibilities and accountabilities for pharmaceutical care in clinical environments; hence, clear pathways for workforce development, coupled with professional acknowledgment and credentialing of practitioners, becomes an important consideration. There is a clear opportunity for transnational collaboration and further opportunities for transnational recognition of advanced skills, capabilities for the pharmacy workforce management.

Responsible use of medicines implies that health-system stakeholder activities and capabilities are aligned to ensure that patients receive the right medicines at the right time, use them appropriately, and benefit from them. Bringing the right drugs to the patients who need them demands the engagement of all actors, including state, governments, and a vision on how to integrate society, public, people and private interests and to mobilize resources. While appropriate drug therapy is safer and more cost-effective than other treatment alternatives, there is no doubt that the personal and economic consequences of inappropriate drug therapy are enormous. It is important for public and people to be guaranteed that spending on pharmaceuticals represents good value for money. In view of their extensive academic background and their traditional role in preparing and providing medicines and informing patients about their use, pharmacists are well positioned to expect responsibility for the management of drug therapy.

Pharmacists, as well noted as druggists, who are health care team professionals, they working in pharmacy (drug-story), the field of health sciences focusing on safe and effective using drugs. The pharmacist is a part of the health care team directly engaged with patient care services. The pharmacists hold university degree level training and education to consider the pharmacological mechanisms and actions of drugs, pharmacology, pharmacotherapy, toxicology, drug uses, therapeutic roles, side effects of drugs, possible drug interactions, and checking parameters [3]. This is engaged to Botany, biology, anatomy, chemistry, physiology, histology, Biophysics and pathophysiology. Pharmacists interpret and communicate this particularized information to patients, physicians, doctors and other health care producers.

Being a health care professional means being part of a team that is focused on one goal: helping the patient achieve better health. Pharmacists are a part of this health care team, and their duty is to help the patients make the best use of their medication. This is a big job one that pharmacists

cannot do alone. Thus, within their profession, pharmacists have developed other categories of pharmacy workers to help get the work done more efficiently and allow pharmacists to be more focused on the patient.

Common pharmacies have been providing health care for many years, via giving consultation, advice, providing and delivering medicine when needed, or referring patients to other health care professionals. This report, however, reflects and represent the embedding of a formalized approach whereby pharmacies are covering for these services, and where self-care through pharmacists is measured as an integral part of the health system.

Pharmacists are health professionals who are dispensing prescription drugs to patients, also provide information about the medicines ordered by doctors. They explain the doctors' instructions to patients so that, people can safely and effectively use these medications. Another big issue is ensuring that drugs are used reasonably and rationally. This demands that patients get drugs assign to their clinical/hospital necessity, in doses that meet their own individual needs for the sufficient period of time, and at the lowest cost to them and their public. Pharmacists have a lot of public health functions that can benefit from the unique experience of pharmacists, which may include pharmacotherapy, pharmaceutical care, and pharmacy assistance. In addition to dispensing medicines, pharmacists have proved to be an accessible resource for information on health and medicines. Being a health care professional means being part of a team that is focused on one goal- helping the patient achieve better health. Pharmacists are a part of this health care team, and their duty is to help the patients make the best use of their medication. This is a big job one that pharmacists cannot do alone. Thus, within their profession, pharmacists have developed other categories of pharmacy workers to help get the work done more efficiently and allow pharmacists to be more focused on the patient. The were found and estimated factors having influence on pharmacists' professional development, these factors were: Interesting and valuable (informative) work; The favorable (prosperous) psychological climate within the collective in the colleagues' team; The possibility of career growth (development); The possibility of professional education or training; The social importance of the profession; Independence in work.

A pharmacist is a personality who is professionally competent and qualified to prepare and dispense medicine. The Pharmacist dispense drugs, check patient's health, and make sure that drugs do not interact in a harmful route. Pharmacist are drug experts eventually interested about their patients' wellness and health. Public health service interventions, higher level pharmaceutical care, rational pharmacotherapy and effective medicines supply chain management are main components of an accessible, sustainable, affordable and equitable health care system which ensures the efficacy, safety and quality of drugs. It is clear that pharmacy has a great role to play in the health sector reform process. To do it so, although, the role of the pharmacist needs to be redefined and reoriented. Pharmacists have the capability and possibility to enhance therapeutic results and patients' quality of life within accessible resources, and must position themselves at the forefront of the health care system. The movement towards pharmaceutical care is a critical factor in this matter. While efforts to communicate the proper information to patients are as significant as providing the medicine itself. Pharmacists also have a vital contribution to make to patient care through managing pharmacotherapy and concurrent non-prescription or alternative therapies.

On the question to what extent, you have realized your professional capabilities, skills and habits? Pharmacists' 18.4% answer -to the full extent, pharmacists' 46.3% answer -partially, more than

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50% of own potential, pharmacists' 24.7% answer- partially, less than 50% of own potential, pharmacists' 10.6% answer-cannot say.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor). Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Interesting and valuable (informative) work. On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Interesting and valuable (informative) work-pharmacists' 2.6% evaluate by 1 point, pharmacists' 4.9% evaluate by 2 points, pharmacists' 14.7% evaluate by 3 points, pharmacists' 42% evaluate by 4 points, pharmacists' 35.8% evaluate by 5 points.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The favorable (prosperous) psychological climate within the collective in the colleagues' team. On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The favorable (prosperous) psychological climate within the collective in the colleague's team. -pharmacists' 3.1% evaluate by 1 point, pharmacists' 4.2% evaluate by 2 points, pharmacists' 17.7% evaluate by 3 points, pharmacists' 35.6% evaluate by 4 points, pharmacists' 39.5% evaluate by 5 points.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The possibility of career growth (development). On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The possibility of career growth (development)-pharmacists' 5.1% evaluate by 1 point, pharmacists' 5.2% evaluate by 2 points, pharmacists 17.2% evaluate by 3 points, pharmacists' 39.6% evaluate by 4 points, pharmacists' 33% evaluate by 5 points.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) – "The possibility of professional education or training". On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The possibility of professional education or training-pharmacists '2.3 % evaluate by 1 point, pharmacists' 3.7% evaluate by 2 points, pharmacists' 15.3% evaluate by 3 points, pharmacists' 33.8% evaluate by 4 points, pharmacists' 44.8% evaluate by 5 points.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) – "The social importance of the profession". On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The social importance of the profession-pharmacists' 3.5% evaluate by 1 point, pharmacists' 3.8% evaluate by 2 points, pharmacists' 14% evaluate by 3 points, pharmacists' 36% evaluate by 4 points, pharmacists' 42.7% evaluate by 5 points.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) – "Independence in work". On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Independence in work-pharmacists' 3.8% evaluate by 1 point, pharmacists' 4.1% evaluate by 2 points, pharmacists' 14.6% evaluate by 3 points, pharmacists 34.9% evaluate by 4 points, pharmacists' 42.6% evaluate by 5 points.

In your opinion, at what level it is possible to cease education? On the question -In your opinion, at what level it is possible to cease education? Pharmacists' 4.3% answer -after getting specialist diploma (degree), pharmacists' 11.2% answer- after getting the specialist certificate, pharmacists' 84.4% answer -education should not be ceased

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On the question-have you used knowledge in the practice, obtained from professional publications? Pharmacists' 51.4 % answer yes, pharmacists' 40.7% answer –partially, pharmacists' 7.9% answer-no. See Illustration-4.

What issues (questions) of pharmaceutical activity are the most essential (relevant) for you? (You can specify several answers). On the question-What issues (questions) of pharmaceutical activity are the most essential (relevant) for you? Pharmacists' 64% answer new drugs (medications), about drugs generic, chemical and brand names, pharmacists' 59% answer psychology of communication (relations) with customers , pharmacists' 66.8% answer issues of pharmacotherapy of certain diseases, pharmacists' 68.9% answer the safety , effectiveness and quality of the drugs (medications), pharmacists' 70.6% answer pharmacology, pharmacodynamics and pharmacokinetics issues, pharmacists' 44.9% answer the normative legal regulation of pharmaceutical activity, pharmacists' 29.8 % answer drug technology issues, pharmacists' 13.6 % answer pharmacognosy, pharmacists' 19% answer pharmaceutical organization and economics and pharmaceutical business, pharmacists' 34.7% answer pharmacy management and pharmaceutical marketing, pharmacists' 11.1% answer pharmacochemistry, pharmacists' 11.9% answer toxicology, pharmacists' 33% answer clinical pharmacy, pharmacists' 60.1% answer pharmaceutical care, pharmacists' 9.5% answer pharmaceutical analysis, pharmacists' 6.2 % answer toxicological chemistry, pharmacists' 10.6% answer pharmaceutical technologies, pharmacists' 11.7% answer nutrition, pharmacists' 22% answer pharmaceutical cosmetics and perfume, pharmacists' 18% answer social pharmacy and public health, pharmacists' 17.3% answer computer technology and pharmaceutical information, pharmacists' 16.3% answer phytotherapy, pharmacists' 22.6% answer routes of drug administration, pharmacists' 19.5% answer drug forms and drug design, pharmacists' 24.2% answer drugs toxic effects, pharmacists' 29.3% answer rules of drug administration, pharmacists' 15.3% answer cost-effectiveness and cost-benefits of drugs, pharmacists' 32% answer terms and conditions of storage of drug (Conditions and shelf-life).

What is your attitude to qualification upgrading (improvement) study courses? On the question-What is your attitude to qualification upgrading (improvement) study courses? Pharmacists' 55.6% answer I learn with great pleasure, pharmacists' 38.6 % answer learning process rise interest to me, pharmacists' 5.8% answer -I have indifferent attitude toward learning.

Pharmacists should see themselves as the main health care providers who can use their clinical experience in various public institutions. Pharmacists will always be an important health care provider based on their availability to patients through community pharmacy setting. This specific role of provider should never be reduced, as it serves the critical needs of patients (eg, dispensing and counseling for drug experience in nonprescription drugs, compounding, vaccinations, and the use of medication administration or monitoring devices) that not addressed by other health care providers. However, this does not exclude pharmacists serving as suppliers of innovative alternative settings, such as outpatient clinics located in pharmacies and other retail outlets; in independent practice with a focus on medication management therapy, medication reconciliation, drug counseling or Pharmacogenomic; institution or organization, where they are responsible for the integration and promotion of patient care through the many other health care providers to facilitate continuity of care community; or organizations that coordinate research to improve practice through pharmacy practice based research networks. Pharmacy providers should look for opportunities to engage in professional activities between patient care, when and where they occur or as they develop in communities. For example, alternative practices may change to concentrate

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on providing pharmacy and health services for adults and retirement communities, given the growing number of them as Georgian population continues to age. Pharmacy graduates who serve in the health services of Georgia, as these pharmacists to develop innovative practice settings, they should be drivers for expansion within the pharmacy practice in community, state and national levels. Pharmacy educators must ensure that graduates have the necessary knowledge, skills, attitudes/values, and practice experience, as well as confidence, drive, and entrepreneur spirit to be a driving force for change in order to facilitate these and other advances in the scope and type of community pharmacy practice.

Hospitals and other institutions and facilities, such as outpatient clinics, drug-dependency treatment facilities, poison control centers, drug information centers, and long-term care facilities, may be operated by the government or privately. While many of the pharmacist's activities in such facilities may be similar to those performed by community pharmacists, they differ in a number of ways. Additionally, the hospital, clinic or institutional pharmacist has more possibility to interact closely with the prescriber and, therefore, to promote the rational prescribing and use of drugs in larger hospital and institutional pharmacies, is usually one of several pharmacists, and thus has a greater opportunity to interact with others, to specialize and to gain greater expertise, having access to medical records, is in a position to effect the option of drugs and dosage regimens, to monitor patient compliance and therapeutic response to drugs, and to recognize and report adverse drug reactions; can more easily than the community pharmacist assess and monitor patterns of drug usage and thus recommend changes where necessary serves as a member of policy-making committees, including those concerned with medicine choice, the use of antibiotics, and hospital infections and thereby actions of the preparation and composition of an essential-drug list or formulary is in a better position to educate other health professionals about the rational use of drugs, more easily participates in studies to determine the beneficial or adverse effects of drugs, and is involved in the analysis of drugs in body fluids ,can control clinical manufacture and acquisition of drugs to ensure the supply of high-quality products, takes part in the planning and implementation of clinical trials.

Conclusion.

A pharmacist is a personality who is professionally competent and qualified to prepare and dispense medicine. The Pharmacist dispense drugs, check patient's health, and make sure that drugs do not interact in a harmful route. Pharmacist are drug experts eventually interested about their patients' wellness and health. Public health service interventions, higher level pharmaceutical care, rational pharmacotherapy and effective medicines supply chain management are main components of an accessible, sustainable, affordable and equitable health care system which ensures the efficacy, safety and quality of drugs. It is clear that pharmacy has a great role to play in the health sector reform process. To do it so, although, the role of the pharmacist needs to be redefined and reoriented. Pharmacists have the capability and possibility to enhance therapeutic results and patients' quality of life within accessible resources, and must position themselves at the forefront of the health care system. The movement towards pharmaceutical care is a critical factor in this matter. While efforts to communicate the proper information to patients are as significant as providing the medicine itself. Pharmacists also have a vital contribution to make to patient care through managing pharmacotherapy and concurrent non-prescription or alternative therapies.

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There are no limitations that could affect the results of the study.

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ADVANTAGES OF DIGITAL RADIOGRAPHY (DR) OVER COMPUTED RADIOGRAPHY (CR) IN MEDICAL IMAGING

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ABSTRACT

This article conducts a thorough examination of the advantages associated with digital radiography (DR) in contrast to computed radiography (CR) within the realm of medical imaging. As technology has progressed, the landscape of radiography has shifted from traditional film-based methodologies to digital formats, representing a significant advancement in diagnostic radiology. This transition has been facilitated by the advent of digital radiography (DR) and computed radiography (CR) technologies, each presenting distinct capabilities and advantages. However, DR has emerged as the preferred option owing to its superior image quality, streamlined workflow, improved dose management, cost-effectiveness, and versatility in clinical applications. By conducting a comparative analysis of DR and CR systems across various parameters such as image quality, workflow efficiency, dose reduction, cost-effectiveness, and clinical utility, this article seeks to underscore the pivotal role played by DR in contemporary healthcare environments. Through a comprehensive exploration of technological advancements, obstacles, and future prospects, this article underscores the transformative influence of digital radiography on diagnostic precision, patient care, and healthcare outcomes.
Keywords: Digital Radiography (DR), Computed Radiography (CR), Medical Imaging, Image Quality, Workflow Efficiency, Dose Reduction, Cost-effectiveness, Clinical Versatility, Technology Advancements, Technological Innovations, Challenges and Limitations.

Introduction

In modern healthcare, medical imaging plays a crucial role by providing crucial insights into the complexities of the human body, facilitating accurate diagnosis, and aiding in treatment planning for clinicians. The evolution of radiography over the years has seen a significant transition from traditional film-based methods to more advanced digital imaging technologies. Among these advancements, digital radiography (DR) and computed radiography (CR) have emerged as leading modalities, fundamentally changing the landscape of diagnostic radiology. While both DR and CR are designed to capture and process X-ray images, they differ considerably in their underlying technology, workflow efficiency, and clinical applicability. In recent times, the advantages of digital radiography over computed radiography have become increasingly apparent. DR systems offer unmatched benefits in terms of image quality, workflow streamlining, radiation dose control, cost-effectiveness, and clinical adaptability. This article aims to explore the realm of digital radiography in detail, highlighting the numerous advantages it offers over computed radiography in the context of medical imaging. By examining the technological intricacies, clinical implications, and practical applications of DR, we seek to illuminate its transformative potential in enhancing diagnostic precision, elevating patient care standards, and shaping the future of radiological practice.

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Evolution of radiography

Historical Overview: Radiography, the method of visualizing internal body structures using X-rays, has been fundamental to medical diagnosis since Wilhelm Conrad Roentgen discovered it in 1895. Initially, radiographic images were recorded on photographic film, a procedure that required exposing X-ray film to radiation and processing it with chemical solutions. Transition to Digital Imaging: The emergence of digital technology transformed radiography, resulting in the creation of digital radiography (DR) and computed radiography (CR) systems. Unlike traditional film-based radiography, digital imaging involves directly capturing X-ray images in digital format, eliminating the need for film processing and allowing for immediate image interpretation.

Digital Radiography (DR): DR systems employ flat-panel detectors (FPDs) or charged-coupled devices (CCDs) to directly transform X-rays into digital signals. These detectors include a scintillator layer that converts X-ray photons into visible light. Subsequently, photodiodes or amorphous silicon sensors convert this light into electrical signals. Consequently, the produced digital images boast exceptional quality and are immediately viewable on computer screens. (**Figure 1**). [2], [6].

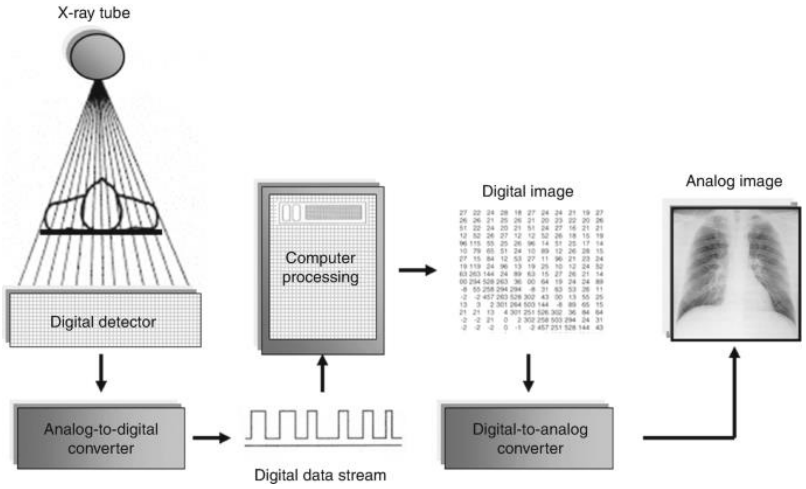

Figure 1: How do DR system work step-by-step.

Computed Radiography (CR): On the other hand, computed radiography (CR) systems utilize imaging plates coated with photostimulable phosphors, which are reusable. These phosphors store energy upon exposure to X-rays, and when the plate undergoes scanning by a laser in the CR reader, the stored energy is released as light. This emitted light is then transformed into digital signals, ultimately generating a digital image that is viewable on a monitor. (Figure 2).

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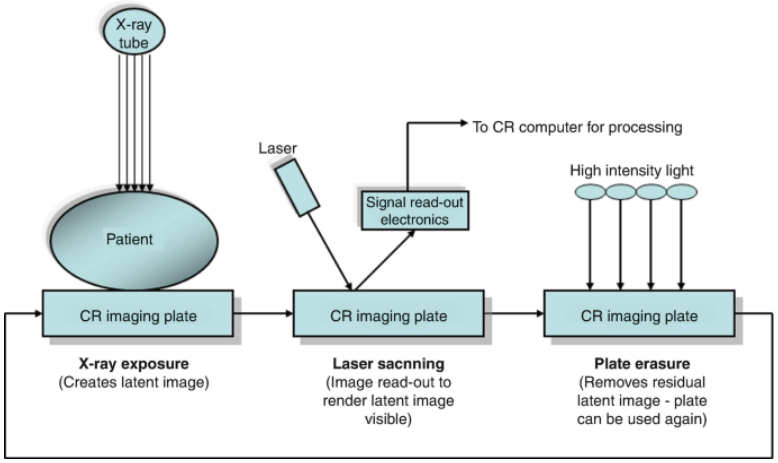

Figure 2: The work principle of CR system step-by-step.

Technological Advancements: Over time, there have been notable advancements in both DR and CR technologies, spurred by enhancements in detector design, image processing algorithms, and software integration. These developments have resulted in improved image quality, dose reduction capabilities, and workflow efficiency for both modalities. [3].
Transition from CR to DR: Although CR systems were instrumental in the shift toward digital imaging and provided benefits compared to conventional film-based radiography, the trend has shifted toward DR systems in recent years. DR systems directly convert X-rays into digital signals, bypassing the necessity for cassette manipulation and processing stages. Consequently, this facilitates a quicker workflow and enhances overall efficiency.

2. Image quality.
Parameters of Image Quality: Before exploring the contrast between DR and CR, it's crucial to grasp the fundamental factors that delineate image excellence:
Spatial Resolution: Spatial resolution pertains to the capability of an imaging system to differentiate between two neighboring structures. Enhanced spatial resolution facilitates the observation of finer anatomical features, thereby enhancing diagnostic precision. (**Figure 3**)

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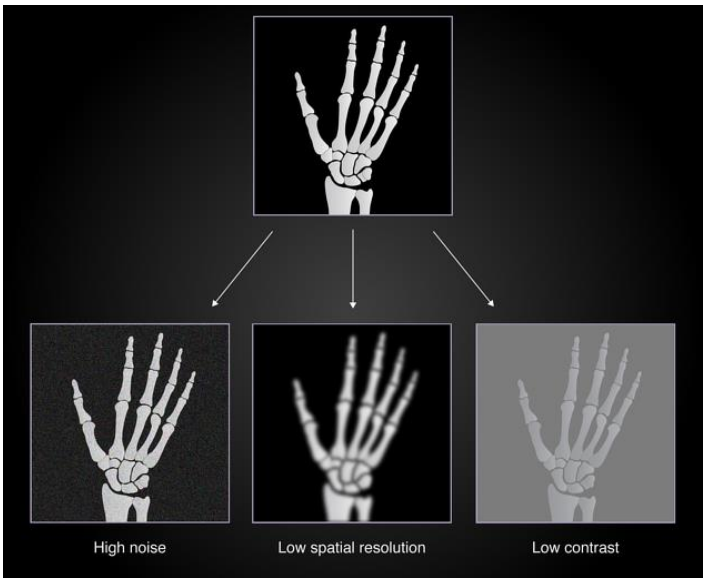

Figure 3: Spatial resolution refers to the ability of an imaging modality to differentiate two adjacent structures as being distinct from one another.

Contrast Resolution: Contrast resolution plays a vital role in discerning tissue variations by the imaging system. Enhanced contrast resolution enables clearer identification of subtle discrepancies in tissue density, thereby improving diagnostic precision.
Noise Reduction: Noise present in medical images can deteriorate the quality of the image and mask crucial anatomical details. Employing efficient noise reduction methods plays a significant role in enhancing the clarity of images and bolstering diagnostic certainty.
Comparative Analysis: Digital radiography (DR) and computed radiography (CR) employ distinct technologies for image acquisition and processing, which significantly impact image quality:
DR Image Quality: DR systems utilize direct conversion detectors such as amorphous selenium or cesium iodide to directly transform X-rays into digital signals. This direct conversion mechanism yields images characterized by exceptional spatial resolution and contrast. Moreover, the integration of advanced image processing algorithms in DR systems contributes to noise reduction, further augmenting image quality.
CR Image Quality: In contrast, computed radiography (CR) systems employ storage phosphor plates to capture X-ray images. These plates store the X-ray energy, which is subsequently retrieved and digitized using a CR reader. While CR systems generally deliver good image quality, they may demonstrate slightly inferior spatial resolution and contrast compared to DR due to the indirect conversion process and the potential degradation of phosphor plates over time. (Figure 4)

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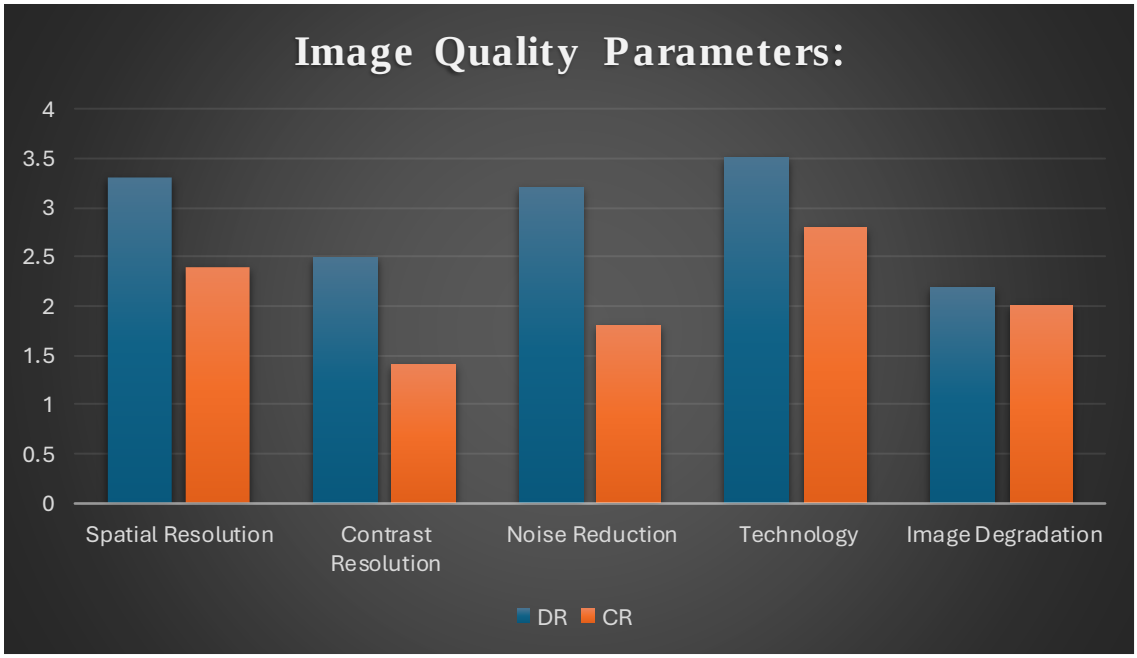

Figure 4: Some indicators are given that make it possible to compare DR and CR

Impact on Diagnostic Accuracy: The enhanced image quality offered by digital radiography (DR) holds substantial importance for diagnostic precision:
- Enhanced Clarity: DR systems empower radiologists to observe intricate anatomical structures with exceptional precision, resulting in more precise analysis of medical images.
- Enhanced Lesion Identification: The superior spatial and contrast resolutions of DR aid in identifying subtle lesions and irregularities, even in complex clinical contexts.
- Elevated Assurance: With the high-caliber images generated by DR systems, radiologists can confidently reach diagnostic conclusions, thereby minimizing the risk of misinterpretation or overlooking diagnoses. (Figure 5) [10],[11].

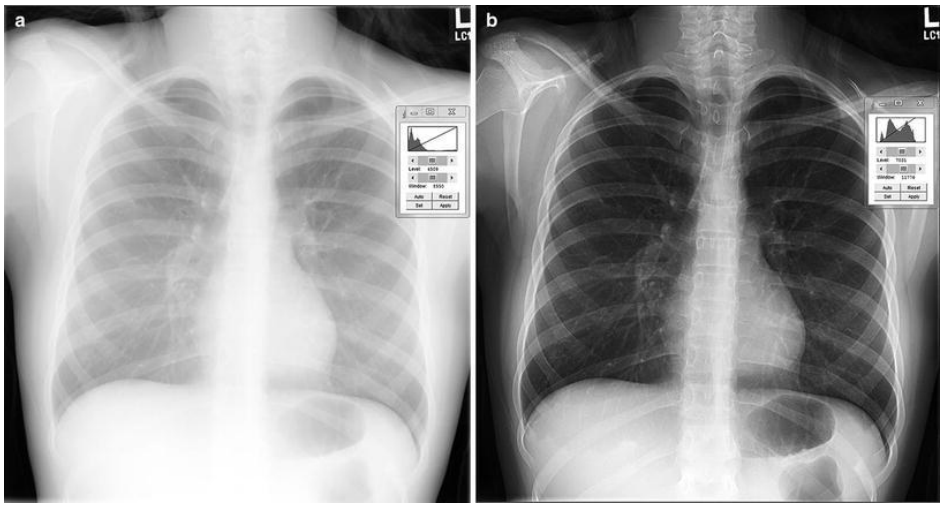

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Figure 5: The basic CR(a) and DR(b) results.

Workflow efficiency

In the field of medical imaging, the efficiency of workflow is crucial for timely diagnosis, effective treatment planning, and providing optimal patient care. Workflow processes, including image acquisition, processing, and interpretation, greatly influence clinical productivity and resource allocation. A comparison between digital radiography (DR) and computed radiography (CR) systems highlights the clear advantages of DR in terms of workflow efficiency.

Workflow Processes in DR and CR

Digital Radiography (DR): DR utilizes direct conversion technology, where X-ray photons are directly transformed into electrical signals through a flat-panel detector (FPD).

Once captured, the digital images become readily accessible for review on the workstation, removing the necessity for cassette handling or processing procedures.

Radiographers have the capability to acquire, examine, and adjust images in real-time, thereby improving workflow speed and efficiency. (Figure 6).

Figure 6: DR system in X-ray imaging.

Computed Radiography (CR): CR systems utilize a photostimulable phosphor plate enclosed within a cassette to capture X-ray images.

Following exposure, the cassette undergoes processing via a CR reader, which scans the latent image stored within the phosphor plate and transforms it into a digital form.

This processing stage results in a delay in image accessibility, as radiographers must await the completion of scanning and digitization by the CR reader. (Figure 7) [20].

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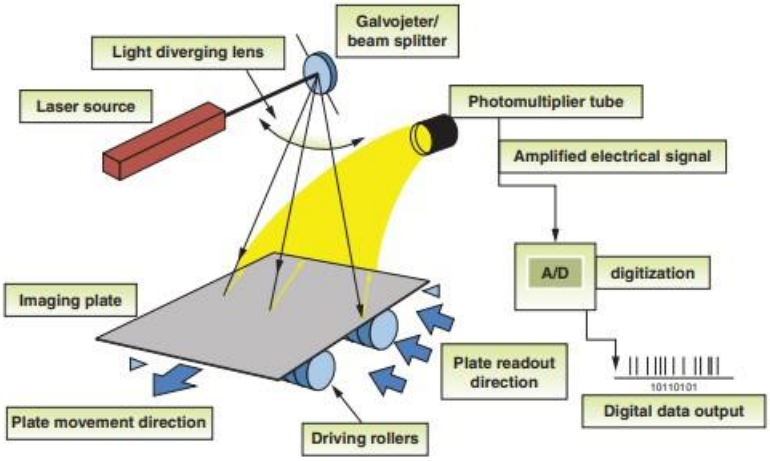

Figure 7: How is CR reader works.

Time-saving Benefits of DR

Instant Image Availability: The immediate availability of digital images for interpretation is one of the primary advantages offered by DR systems.

Within seconds of exposure, radiologists have access to high-quality images, facilitating swift diagnosis and treatment decisions.

This rapid availability of images significantly decreases patient waiting times and improves overall clinical workflow efficiency.

Elimination of Cassette Handling: In contrast to CR systems, which necessitate physical cassettes for image capture, DR systems completely eliminate the need for cassette handling.

By positioning the detector directly behind the patient, radiographers simplify the imaging process and mitigate the risk of cassette-related errors or inefficiencies.

The absence of cassette handling streamlines workflow tasks, allowing radiographers to prioritize patient care over logistical challenges. (Figure 8)

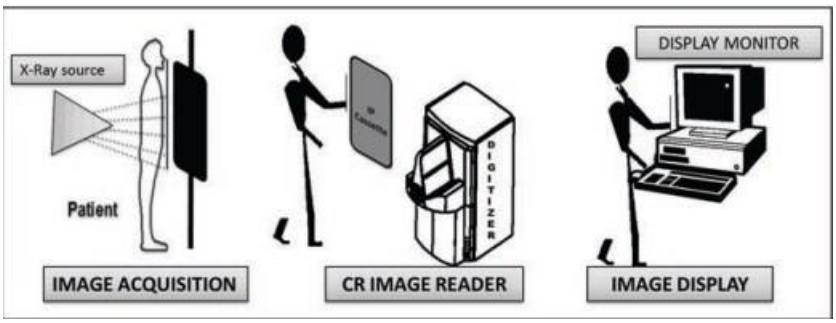

Figure 8: Flowchart shows workflow of computed radiography system.

Streamlining Diagnostic Workflow.

Improved Efficiency: Thanks to their rapid image capture and immediate availability, DR systems boost efficiency within clinical environments.

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Radiologists can efficiently assess and analyze a larger number of cases within shorter durations, resulting in enhanced throughput and patient management.
The efficient workflow supported by DR empowers healthcare institutions to optimize resource allocation and elevate overall operational effectiveness.
Clinical Decision Support: With digital radiography (DR) systems, radiologists can quickly access high-quality images, facilitating timely clinical decision support.
This enables physicians to promptly evaluate diagnostic findings, engage in consultations with colleagues, and initiate suitable treatment interventions, leading to enhanced patient outcomes.
The smooth incorporation of DR into clinical workflows promotes collaboration among multidisciplinary healthcare teams, thereby cultivating a patient-centred approach to delivering care.[13].

Dose reduction and radiation safety
Importance of Radiation Dose Management: Managing radiation dose is crucial in medical imaging to reduce potential health hazards linked to ionizing radiation. Overexposure to radiation can cause both deterministic effects, like tissue damage, and stochastic effects, such as the induction of cancer. Emphasizing radiation safety is vital for protecting patients' health by reducing their exposure to radiation during diagnostic examinations. Utilizing strategies for optimizing doses helps in preventing unnecessary radiation-related complications and long-term health issues. [12].
Strategies for Dose Reduction in DR Systems: An examination of dose optimization methods utilized in digital radiography, including an exploration of sophisticated functionalities such as automatic exposure control (AEC), iterative reconstruction algorithms, and real-time dose monitoring. (Figure 9) [16], [18].

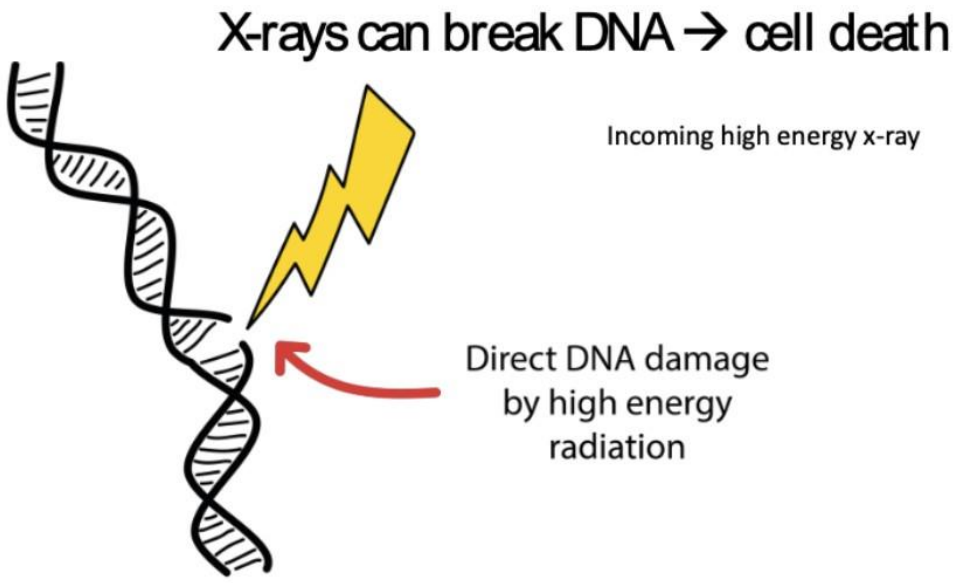

Figure 9: Radiation can harm our health.

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Comparative Analysis of Radiation Dose

Comparison of DR and CR systems concerning radiation dose levels. Discussion of research findings and empirical evidence illustrating the dose reduction capabilities of DR technology. (**Figure 10**) [7].

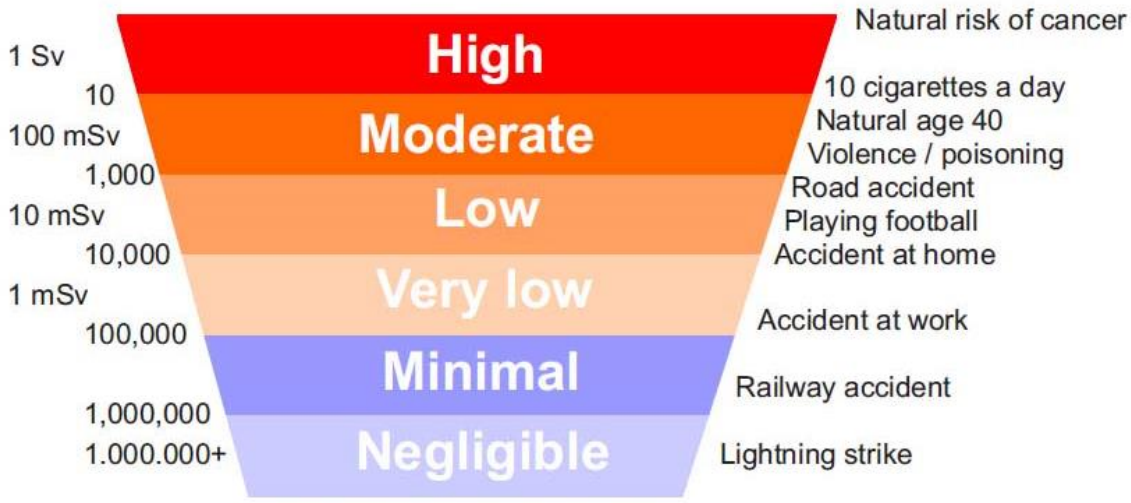

Figure 10: Comparative risk of exposure to X-rays.

Cost-effectiveness

Digital radiography (DR) and computed radiography (CR) systems not only differ in their technological aspects but also in their economic implications. It is crucial for healthcare facilities to understand the cost-effectiveness of these imaging modalities when making investment decisions. This section explores the factors influencing the cost-effectiveness of DR compared to CR.

One of the primary considerations in choosing between DR and CR is the initial investment cost. CR systems typically entail a lower upfront cost compared to DR systems. However, it is essential to analyze the long-term cost implications beyond the initial purchase. While DR systems may necessitate a higher initial investment, they often offer greater cost-effectiveness over time. [4],[8],[9].

Factors Influencing Cost-effectiveness: DR systems generally incur lower maintenance costs compared to CR systems. This is attributed to the simpler design of DR systems, which have fewer moving parts and do not rely on the physical processing of cassettes, thereby reducing the likelihood of mechanical failures and the need for repairs.

The efficiency gains associated with DR systems can result in significant cost savings over time. With DR, images become available for review immediately after exposure, streamlining the diagnostic workflow and alleviating staff workload. This increased efficiency translates into enhanced productivity and potentially lower labor costs. DR systems optimize resource utilization by reducing the time required for image acquisition, processing, and interpretation. Consequently,

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healthcare facilities can accommodate more patients within a given time frame, maximizing throughput and revenue generation.

The streamlined workflow and instant image availability of DR contribute to improved operational efficiency in healthcare settings. These factors underscore the long-term cost-effectiveness of DR systems compared to CR counterparts, making them an attractive investment for healthcare facilities seeking to optimize both clinical and economic outcomes. (Figure 11) [17].

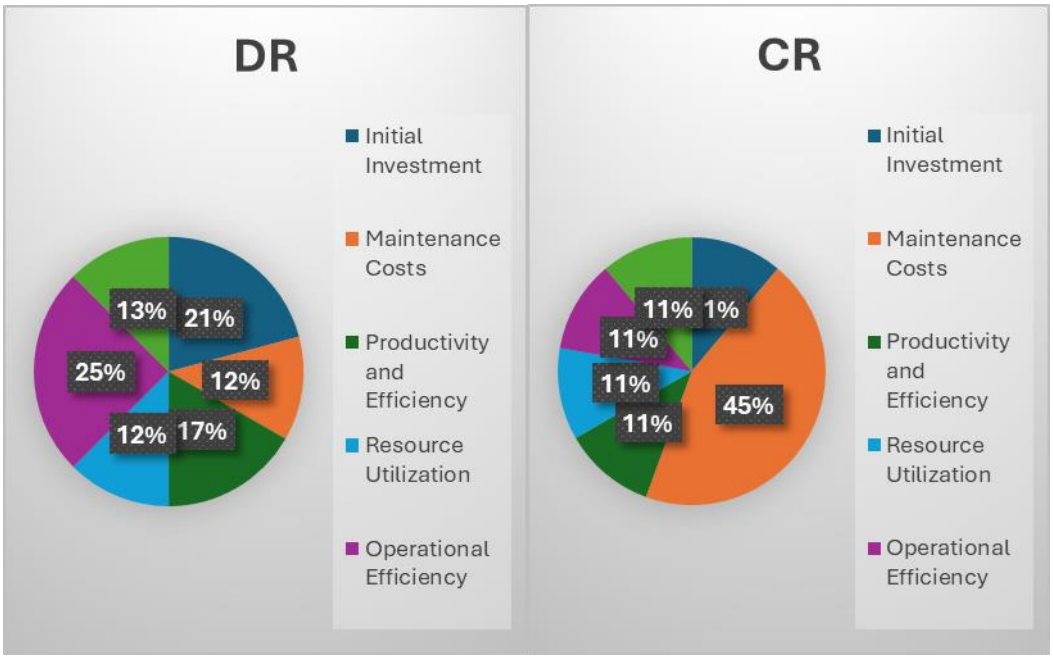

Figure 11. Comparison chart of factors influencing cost-effectiveness.

Technological innovations in digital radiography (DR)

Digital radiography (DR) technology has seen significant progress in recent times, transforming the landscape of diagnostic radiology. These advancements have positioned DR systems as frontrunners in medical imaging, providing unprecedented levels of image quality, workflow efficiency, and clinical applicability. This section delves into the pivotal technological innovations that are propelling the evolution of DR and shaping the future of medical imaging. [19].

Image Processing Algorithms: Image processing algorithms hold a critical role in optimizing image quality and minimizing artifacts in DR images. Advanced image reconstruction techniques, including iterative reconstruction algorithms, are instrumental in reducing noise and improving image clarity. Additionally, adaptive processing algorithms dynamically adjust image parameters based on anatomical regions, resulting in enhanced visualization of complex structures and subtle abnormalities.

Dose Optimization Technologies: Effective management of radiation dose is paramount in medical imaging, particularly in pediatric and radiation-sensitive populations. DR systems incorporate dose optimization technologies, such as automatic exposure control (AEC) and dose modulation algorithms, to customize radiation doses according to patient anatomy and imaging

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requisites. Real-time dose monitoring tools offer feedback to radiographers, facilitating dose adjustments to maintain image quality while minimizing radiation exposure.

Integration of Artificial Intelligence (AI): The integration of artificial intelligence (AI) and machine learning algorithms is increasingly prevalent in DR systems, augmenting diagnostic capabilities and streamlining workflow processes. AI-powered image analysis tools aid radiologists in image interpretation by automating tasks such as lesion detection, segmentation, and classification. Deep learning algorithms, trained on extensive datasets, contribute to enhanced diagnostic accuracy, reduced interpretation times, and improved clinical decision-making in radiology. [14],[15].

Mobile and Portable DR Solutions: Mobile and portable DR systems offer versatility and accessibility across various clinical settings, including emergency departments, intensive care units, and remote healthcare facilities. Their compact and lightweight designs enable point-of-care imaging, facilitating bedside examinations and expediting patient care. Furthermore, wireless connectivity and cloud-based image storage enhance data accessibility and foster collaboration among healthcare providers.

These technological innovations underscore the transformative potential of DR systems in revolutionizing medical imaging practices, promising enhanced diagnostic precision, streamlined workflows, and improved patient outcomes.

Conclusion

In conclusion, digital radiography (DR) systems present notable advantages in workflow efficiency over computed radiography (CR) systems. The immediate availability of digital images, removal of cassette handling, and streamlined diagnostic process all contribute to heightened clinical productivity, quicker turnaround times, and better patient care results. As medical facilities endeavor to optimize their operational effectiveness and provide top-tier imaging services, the integration of DR technology emerges as a fundamental aspect of contemporary radiology practice. While initial investment in digital radiography (DR) may be higher than that of computed radiography (CR), its enduring cost-effectiveness derives from reduced maintenance expenses, augmented productivity, and operational streamlining. By maximizing resource utilization and refining diagnostic workflows, DR systems play a pivotal role in enhancing patient care provision and bolstering economic viability in healthcare environments. Technological advancements in digital radiography (DR) are catalyzing transformative changes in diagnostic radiology, equipping healthcare providers with advanced imaging capabilities for precise diagnosis, treatment strategizing, and therapeutic monitoring. Through the utilization of state-of-the-art technologies, DR systems persist in expanding the horizons of medical imaging, shaping the trajectory of healthcare delivery, and elevating patient outcomes.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

Acknowledgment

The author would like to express gratitude to the care support workers and elderly individuals who participated in this study, sharing their invaluable insights and experiences. Their cooperation and openness have significantly contributed to the depth and richness of the research findings.

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ENVİRONMENTAL PROTECTİON AGAİNST THE EFFECTS OF CLİMATE CHANGE THE ROLE OF GIS İN İTS FORMATİON

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ABSTRACT

The article provides information about climate changes, which have become one of the global problems, and their impact on the living world, which worries the world community more and more. Unstable weather conditions are felt not only in Azerbaijan but also in several countries of the world and create problems. Increasing attention to these problems is manifested in the holding of a number of international events, including scientific and practical conferences. According to the latest assessment report of the Intergovernmental Panel on Climate Change, the average temperature on Earth has increased by 0.8 degrees in the last 100 years. The increase in temperature is mainly due to anthropogenic factors. The basis of anthropogenic factors are gases that create a thermal effect: carbon, methane, nitrogen oxide, nitrogen 1 oxide and chlorine-fluorine compounds. Space observations of the last 100 years show that the intensity and frequency of storms and blizzards have increased. Hot winds, hurricanes, and precipitation have intensified. At the same time, the number of flood events has also increased. If the surface of the ocean used to heat up to a depth of 1000 meters, then the warming reaches up to a depth of 2000 meters; resulting in hot currents becoming even hotter. That is, the main factor in the increase of all these natural disasters is climate change.

Azerbaijan has not been left out of the influence of global climate changes. In the last 100 years, average annual temperatures in the territory of Azerbaijan have increased by 0.4-1.3^0 C. The increase in temperature is unevenly distributed depending on the regions. In the last 10 years, the number and power of floods in small mountain rivers in the territory of Azerbaijan has increased. The issue of effective use of climate resources in agricultural production is one of the important tasks to solve the food problem. In order to implement it, it is necessary to deeply study the characteristics of our territory, to reveal the potential opportunities that ensure more efficient and rapid development of agriculture.

In this direction, the possibilities offered by Geographical Information Systems (GIS) are appreciated by think tanks of the world. Due to the capabilities of GIS, action plans can be prepared in the direction of preventing the consequences of global climate change, as well as the danger that may arise at a later stage.

GIS is the most efficient way to present information about geographic objects and to determine their position more quickly. GIS allows to analyze and model any geographical phenomenon - weather forecast, environmental changes, movement of lithospheric plates. It helps to solve the problem by connecting geographic information from different sources.

For this, GIS is the most accurate and perfect system that must be used to detect climate change in various areas and eliminate its consequences.

Keywords: Climate changes, environmental formation, GIS, average annual temperature, ecological crisis

Measures to combat the consequences of climate change, which have become one of the topics of wide discussion, increase attention to social and economic reforms. More than 6,500 think tanks operating around the world conduct research to establish modern effective communication, increase their influence and define standards for the measurement criteria of the achieved results. Against the consequences of climate change in the last 30 years; by creating a bridge between knowledge and policy in important areas such as international economy, environmental problems, poverty reduction, information and society, they have put forward a number of global initiatives that help to minimize the effects on the development line of countries, the evolution of the global economy and the lifestyle of ordinary people. Think tanks improve the process of making political decisions around the world by increasing international cooperation efforts, and by creating regional and international networks, they help in the creation and implementation of modern projects in the regions. Climate changes, which have become one of the global problems, and their impact on the living world are increasingly worrying the world community. Unstable weather conditions are felt not only in Azerbaijan, but also in several countries of the world and create problems. Increasing attention to these problems is manifested in the holding of a number of international events, including scientific and practical conferences. According to the latest assessment report of the Intergovernmental Panel on Climate Change, the average temperature on Earth has increased by 0.8 degrees in the last 100 years. The increase in temperature is mainly due to anthropogenic factors. The basis of anthropogenic factors are gases that create a thermal effect: carbon, methane, nitrogen oxide, nitrogen 1 oxide and chlorine-fluorine compounds. Space observations of the last 100 years show that the intensity and frequency of storms and blizzards have increased. Hot winds, hurricanes, and precipitation have intensified. At the same time, the number of flood events has also increased. If the surface of the ocean used to heat up to a depth of 1000 meters, then the warming reaches up to a depth of 2000 meters; resulting in hot currents becoming even hotter. That is, the main factor in the increase of all these natural disasters is climate change. Azerbaijan has not been left out of the influence of global climate changes. In the last 100 years, average annual temperatures in the territory of Azerbaijan have increased by 0.4-1.30C. The increase in temperature is unevenly distributed depending on the regions. In the last 10 years, the number and power of floods in small mountain rivers in the territory of Azerbaijan has increased. The issue of effective use of climate resources in agricultural production is one of the important tasks to solve the food problem. To implement it, it is necessary to deeply study the characteristics of our territory, to reveal the potential opportunities that ensure more efficient and rapid development of agriculture.

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THE MANIFESTATION OF KEY ISSUE ASPECTS OF SOME CHARACTERISTICS OF ENDOVASCULAR SURGERY AND TREATMENT STRATEGIES FOR GASTROINTESTINAL AND DUODENAL ULCER BLEEDING WITH BRIEF CASE REPORT

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[4]Multiprofile-Clinic «L&J».

ABSTRACT

Acute gastrointestinal bleeding is a common medical emergency that ranges from minor to potentially life-threatening bleeding. Endoscopy is the first-line diagnostic procedure for upper and lower gastrointestinal bleeding. Treatment options for acute GI bleeding include conservative management, therapeutic endoscopy, transcatheter embolization, and surgery. Transcatheter embolization and surgery are both options for recurrent GI bleeding when therapeutic endoscopy fails; However, both options are associated with several complications and risk of bleeding. The choice of management depends on the patient's status. Emergency surgery is usually associated with high rates of morbidity and mortality. Recently, superelective transcatheter embolization has become a safer procedure and is now widely used to treat acute gastrointestinal bleeding. This review article describes the role of interventional radiology in the management of acute GI bleeding. Improvements in catheter technology, development of more compatible embolization devices, and expansion of embolization techniques have led to angiography and embolization for the treatment of upper and lower gastrointestinal bleeding. Transcatheter embolization therapy for the treatment of acute GI bleeding is a safe procedure with high technical performance and clinical success, but it should be reserved as a treatment option for patients who have failed endoscopic and medical management. MDCT imaging is a useful tool for identifying the site of bleeding and evaluating the anatomical structure of the gastrointestinal tract in stable patients. Close working relationships between interventional radiologists, gastroenterologists, and diagnostic radiologists are essential for the optimal management of patients with GI bleeding. Endovascular embolization dramatically reduces the mortality rate in high-risk patients who require open surgery after failed endoscopy, further studies are needed to fully address these objectives.

Keywords: Endovascular surgery, gastrointestinal duodenal, ulcer bleeding, treatment.

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Introduction

Acute gastrointestinal bleeding is a common medical emergency that ranges from minor, uncontrollable bleeding to potentially life-threatening bleeding. The site of bleeding can be located anywhere in the gastrointestinal tract, which makes it difficult to determine its exact location. Patients with upper gastrointestinal bleeding usually have hematemesis or melena with the bleeding point proximal to the ligament of Treitz, while patients with lower gastrointestinal bleeding usually have melena or hematochezia with the bleeding point distal to the ligament of Treitz. Endoscopy is a first-line diagnostic procedure with 100% sensitivity to detect upper gastrointestinal bleeding; However, it has only 60% sensitivity for diagnosing lower gastrointestinal bleeding. Therapeutic options for treating acute GI bleeding include conservative treatment, therapeutic endoscopy, transcatheter embolization, and surgery. Transcatheter embolization and surgery are both options for recurrent GI bleeding [1-4]. When therapeutic endoscopy fails; However, both options are associated with several complications and risk of bleeding. The choice of management depends on the patient's status (for example, the degree of hemodynamic instability or hypotension, or whether resuscitation is required). Emergency surgery is usually associated with high rates of morbidity and mortality. However, recent technical improvements in superselective transcatheter embolization have increased the safety of the procedure, and it is widely used in the treatment of acute gastrointestinal bleeding. This review article describes the role of interventional radiology in the emergency management of acute GI bleeding [5-8].

Upper gastrointestinal bleeding is defined as bleeding originating from the distal esophagus, stomach, or duodenum (ie, proximal to the ligament of Treitz). The most common cause of upper GI bleeding is peptic ulcer disease, but the differential diagnosis is varied and includes benign and malignant tumors, ischemia, gastritis, arteriovenous malformations, Mallory-Weiss tears, trauma such as a Dieulafoy injury, and iatrogenic causes [9-12].

Upper gastrointestinal bleeding is a potentially fatal condition, so immediate management and accurate diagnosis of the location and etiology of bleeding is essential. The primary diagnostic procedure for upper gastrointestinal bleeding is endoscopy, which has high sensitivity and specificity for locating bleeding lesions in the upper gastrointestinal tract. Once a bleeding lesion is identified, therapeutic endoscopic techniques such as thermal coagulation or hemoclip placement can be used to achieve acute hemostasis. Endoscopic management achieves hemostasis in most patients, but 10% to 30% of patients experience recurrent bleeding for various reasons [13-16].

When hemostasis is not achieved with endoscopic management, other options are surgery and transarterial embolization. Surgery has long been the standard of care, but with the development of interventional radiology, more and more patients are now being referred for embolotherapy. Transarterial embolization can prevent unnecessary resection of the upper gastrointestinal tract and should be considered as an alternative to surgery [17-19].

Aim of the research was to study the key issue aspects of features of endovascular surgery and treatment for gastrointestinal and duodenal ulcer bleeding and brief case report.

Materials and Methods

The material of the article was the data from scientific publications, which were processed, analyzed, overviewed and reviewed by generalization and systematization. research studies are based on a review/overview assessment of the development of critical visibility and overlook of

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the modern scientific literature. use the following databases: (for extensive literature searches to identify key issue aspects of features of endovascular surgery and treatment for gastrointestinal and duodenal ulcer bleeding and brief case report). PubMed, Web of Science, Clinical Key, Tomson Reuters, Google Scholar, Cochrane library, and Elsevier foundations. national and international policies and guidelines were also reviewed and as well as grey literature.
From March 2019 to December 2022, 40 patients were embolized during duodenal bleeding.
These patients were divided into the following groups:

- ➢ Massive, active bleeding.
- ➢ Recurrence of bleeding in clinic and endoscopy was unsuccessful.
- ➢ Unstable hemodynamics and solid hemostasis could not be achieved during endoscopy.
- ➢ Failed to evacuate stomach contents and failed to see a bleeding ulcer.
- ➢ High risk of bleeding recurrence (Forest classification).
- ➢ Elderly and patients burdened with co-morbidities, with whom operative.

Result and Discussion

Lower gastrointestinal bleeding is defined as bleeding originating from a source distal to the ligaments of Treitz. About 80% of all lower GI bleeding comes from a colorectal source and 5% to 10% from a small intestinal source; 10% to 15% are classified as blood of upper gastrointestinal tract origin. A small bowel bleeding source is more likely than a colorectal bleeding source to be obscure or occult.
A common cause of lower GI bleeding is a colonic diverticulum. Differential diagnoses include colitis or enteritis, anorectal abnormalities (hemorrhoids, proctitis), tumors, arteriovenous malformations or angiodysplasia, and postpolyectomy bleeding.
Therapeutic colonoscopy is currently the first-line intervention for colonic bleeding. Colonoscopy is the diagnostic method of choice in patients with lower gastrointestinal bleeding, but therapeutic endoscopy can also be successful in a limited number of patients. Therapeutic colonoscopy fails in approximately 32% of cases due to the presence of stool or blood clots, or technical difficulties such as time required to prepare patients. Further disadvantages include the fact that small bowel bleeding cannot be accessed through colonoscopy and that colonoscopy is relatively ineffective when performed in patients with significant bleeding without bowel preparation. If bleeding cannot be stopped by therapeutic colonoscopy, transarterial embolization is the next line of therapy to control hemostasis. As with upper gastrointestinal bleeding, transarterial embolization is the first-line therapy for patients with lower gastrointestinal bleeding. The efficacy of transarterial embolization in the treatment of acute gastrointestinal bleeding when medical or endoscopic techniques are inadequate has been demonstrated in several large studies. For both upper and lower gastrointestinal bleeding, surgery is usually reserved as a last-line treatment for patients whose bleeding has failed to respond to previous treatments.
Lower gastrointestinal bleeding is defined as bleeding originating from a source distal to the ligaments of Treitz. About 80% of all lower GI bleeding comes from a colorectal source and 5% to 10% from a small intestinal source; 10% to 15% are classified as blood of upper gastrointestinal tract origin. A small bowel bleeding source is more likely than a colorectal bleeding source to be obscure or occult. A common cause of upper GI bleeding is colonic diverticula. Differential diagnoses include colitis or enteritis, anorectal abnormalities

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(hemorrhoids, proctitis), tumors, arteriovenous malformations or angiodysplasia, and postpolyectomy bleeding [20-24].

Therapeutic colonoscopy is currently the first-line intervention for colonic bleeding. Colonoscopy is the diagnostic method of choice in patients with lower gastrointestinal bleeding, but therapeutic endoscopy can also be successful in a limited number of patients. Therapeutic colonoscopy fails in approximately 32% of cases due to the presence of stool or blood clots. Technical difficulties, such as the time required to prepare patients. Further disadvantages include the fact that small bowel bleeding cannot be accessed through colonoscopy and that colonoscopy is relatively ineffective when performed in patients with significant bleeding without bowel preparation. If bleeding cannot be stopped by therapeutic colonoscopy, transarterial embolization is the next line of therapy to control hemostasis. As with upper gastrointestinal bleeding, transarterial embolization is the first-line therapy for patients with lower gastrointestinal bleeding. The efficacy of transarterial embolization in the treatment of acute gastrointestinal bleeding when medical or endoscopic techniques are inadequate has been demonstrated in several large studies. For both upper and lower gastrointestinal bleeding, surgery is usually reserved as a last-line treatment for patients whose bleeding has failed to respond to previous treatments [25-28].

In angiography, vascular access is usually obtained by transfemoral catheterization with a 4- or 5-Fr catheter and sheath. Diagnostic visceral arteriography, which includes angiography of the celiac trunk, superior mesenteric artery, and inferior mesenteric artery, is performed to examine the suspected vascular region, and then a microcatheter is inserted coaxially for superselective cannulation of the bleeding artery. In upper gastrointestinal bleeding, the source of the bleeding is usually identified by endoscopy. Therefore, angiography is most often performed only as a precursor to transcatheter embolotherapy. Angiograms are considered positive when they show direct angiographic evidence of active GI bleeding (eg, contrast medium extravasation) or indirect angiographic evidence of bleeding (eg, pseudoaneurysm). For embolization, the appropriate position of the catheter is selected, and transcatheter vessel occlusion is performed with embolized material. Embolization is carried out as selectively as possible, the catheter is technically possible near the site of bleeding. The goal is to achieve proximal and distal control of the bleeding lesion (embolization of both inflow and outflow vessels) to reduce the risk of recurrent bleeding via collateral circulation. Embolization will continue to the occlusive angiographic endpoint without antegrade arterial blood flow in the embolized artery. Post-embolization arteriography is performed to confirm completion of the procedure. The most common embolic material used to treat upper gastrointestinal bleeding is a fibrous platinum microcoil, which is usually placed in the bleeding artery distally proximal to the angiographic position [29-33].

Extravasation of the contrast medium is stopped and complete occlusion of the bleeding vessel occurs. Coiling of the gastroduodenal artery from the celiac axis may be inadequate because the gastroduodenal artery may be fed by collateral branches of the superior mesenteric artery. A "sandwich" technique has been proposed, in which the gastroduodenal artery is looped distally proximally. Sandwich occlusion can be used at the level of the gastroduodenal artery with the catheter directed toward the origin of the right gastroepiploic artery, and when the catheter is removed the coils are inserted into the proximal gastroduodenal artery. Complete embolization of the gastroduodenal artery, including proximal and distal embolization and exclusion of its two side branches, is the technical end point [34-35].

Selective superior mesenteric arteriography is performed after embolization to ensure that the bleeding site is not secured. If extravasation is detected, superselective catheterization of the lower pancreatic duodenal artery and side branch is performed with a microcatheter. Over the past 10 years, significant improvements in this technique have made superelective embolization a safer procedure by minimizing the risk of intestinal ischemia.

The development of sophisticated rotating wires and coaxial microcatheters, along with advances in digital fluoroscopic imaging, now allow for more precise vascular interventions. In a recent report, transarterial embolization for upper gastrointestinal bleeding was associated with a high technical success rate (93%) and a minimal complication rate (9%). In addition, a recently published international consensus recommendation considers transarterial embolization as an alternative therapy for the treatment of upper gastrointestinal bleeding in patients who have failed an endoscopic hemostatic procedure or who have recurrent bleeding [36-38].

Transarterial embolization for the treatment of lower GI bleeding was first introduced in 1974 and involved the non-elective injection of an autologous clot. In 1977, Gelfoam and Oxycel injection were described for embolization of diverticular bleeding. Although injection of autogal clot or gelatin sponge has been shown to achieve hemostasis, these early embolization techniques were characterized by high rates of intestinal infarction. The development of coaxial microcatheters has increased interest in the use of embolization to control lower GI bleeding. The use of a microcatheter, delivered via a 4- or 5-wire guide catheter, to a specific margin near the bleeding site in the arteries or vas rectus can be obtained to remove embolic material. Because this technique is superselective, the risk of intestinal infarction is significantly lower than nonselective embolic techniques or vasopressin infusion, and there are no vasopressin-related systemic side effects. In addition, the risk of bleeding from collateral vessels is reduced as embolic material is delivered to the site of bleeding.

The most common embolic materials for lower GI bleeding, used alone or in combination, are microcoil, polyvinyl alcohol (PVA) particles, and gelatin sponge. Microcoils are persistent embolic agents that can be superselectively placed near the bleeding site and are easily identified under fluoroscopy. However, due to the small caliber of the target vessels, positioning these coils correctly can be difficult. Coils can back out of small vessels and provoke ischemia if they enter a large feeding vessel. PVA is a permanent embolic agent that is less selective than microcol. The basis for PVA embolization with respect to flow is that PVA particles preferentially flow to the area of least resistance (ie, the bleeding site). Defrin et al demonstrated in 10 patients that lesions inaccessible by superelective catheterization could be safely embolized by flow-directed PVA embolization. However, a consensus on the optimal PVA particle size for embolization in lower GI bleeding has not yet been reached. Previous reports have recommended a PVA particle size of 300 to 500 μm, as early animal studies have shown that smaller particles may be associated with a higher risk of intestinal ischemia. The choice of embolic agent in relation to the characteristics of the bleeding vessel is important, but which embolic agent is best among coils, cyanoacrylate glue, gelatin sponge, and calibrated particles remains a matter of debate. In our department, microcoil, 1000 μm gelatin sponge particles, and cyanoacrylate glue are used to treat acute GI bleeding. Unlike PVA, the gelatin sponge is a temporary embolic agent that allows recanalization of the vessel from a few days to a few weeks. If the angiogram is negative for active bleeding, empiric embolization is performed based on discussion with the gastroenterologist or surgeon. For empiric embolization, if endoscopy showed that the bleeding source was located in the proximal stomach, the left gastric artery was selectively embolized. If endoscopy shows that the source of bleeding is

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in the distal stomach or duodenum, the gastroduodenal artery, the right gastroepiploic artery, the pancreaticoduodenum, or all three are selectively embolized. If endoscopic intervention fails to control bleeding, radioplaque clips are positioned as guides to the bleeding site via colonoscopy and transarterial embolization is performed.

Bleeding, deposition of coils is guided by endoscopy with pre-placed hemoclips. As a result, angiography and embolization of vessels causing GI bleeding have been gradually adopted and have revolutionized the management of lower GI bleeding.

Complications associated with embolization include angiography itself (eg, hematoma, arterial thrombosis, dissection, embolism, pseudoaneurysm) as well as intestinal infarction. Early transcatheter intervention involved vasopressin infusion, but the high rate of rebleeding and high complication rates led to its reduced use. Higher rates of complications and bleeding have been described in patients treated with vasopressin. Although the first embolic techniques improved hemostasis, their use was limited by the high incidence of intestinal infarction. Until the advent and development of microcatheter technology, transarterial embolization became a safer, more effective method for managing gastrointestinal bleeding. Improvements in microcatheter systems have enabled more selective delivery of embolic material near bleeding sites; This overcame the systemic side effects of vasopressin and resulted in a reduced risk of intestinal infarction and vascular bleeding. Recently, many reports have suggested that superelective embolization for the management of gastrointestinal bleeding rapidly stops bleeding with minimal risk of ischemia. However, the risk of ischemia after embolization is increased in patients with a history of surgical intervention in the same area or when the therapeutic intervention involves embolic agents that may advance into the vascular bed. Such agents include liquids (for example, fabric adhesives such as cyanoacrylate) or very small particles.

In stable patients, multidetector computed tomography (MDCT) imaging is a useful tool to identify bleeding sites and assess the anatomical structure of the gastrointestinal tract, thereby allowing for more targeted intervention. Scintigraphy of red blood cells has a sensitivity and specificity of more than 90%; However, its simulated resolution does not provide an accurate diagnosis. Computed tomography angiography (CTA) is also used (sensitivity up to 86%) in the diagnosis of acute GI bleeding and can be used to pinpoint the location and etiology of bleeding and thus direct further management. A positive MDCT angiogram may be useful in selecting patients suitable for rapid targeted embolization. Visualization of active extravasation of contrast medium in the gastrointestinal tract requires careful attention to technique, including the use of fine collimation, rapid administration of contrast medium, and appropriate scan times. Additionally, multimodal reconstruction and three-dimensional imaging are useful in determining the exact source of bleeding. Although further studies are needed to determine which course of action is best when bowel preparation is not possible, CTA may be useful in this situation to identify the site of bleeding [18,34].

The idea of embolization of duodenal bleeding as an alternative use of surgery belongs to Roche (1972). Since then, arterial embolization has been considered as an effective diagnostic and surgical method

Common causes of duodenal bleeding:

- Arteriovenous malformation
- Visceral aneurysms/pseudoaneurysm
- Angiodysplasia
- Aortoenteric fistula

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- Hemophilia
- Intestinal diverticula
- Inflammatory bowel disease (ulcer disease)
- Benign anorectal lesions

The main causes of duodenal bleeding. (See Illustration-1).

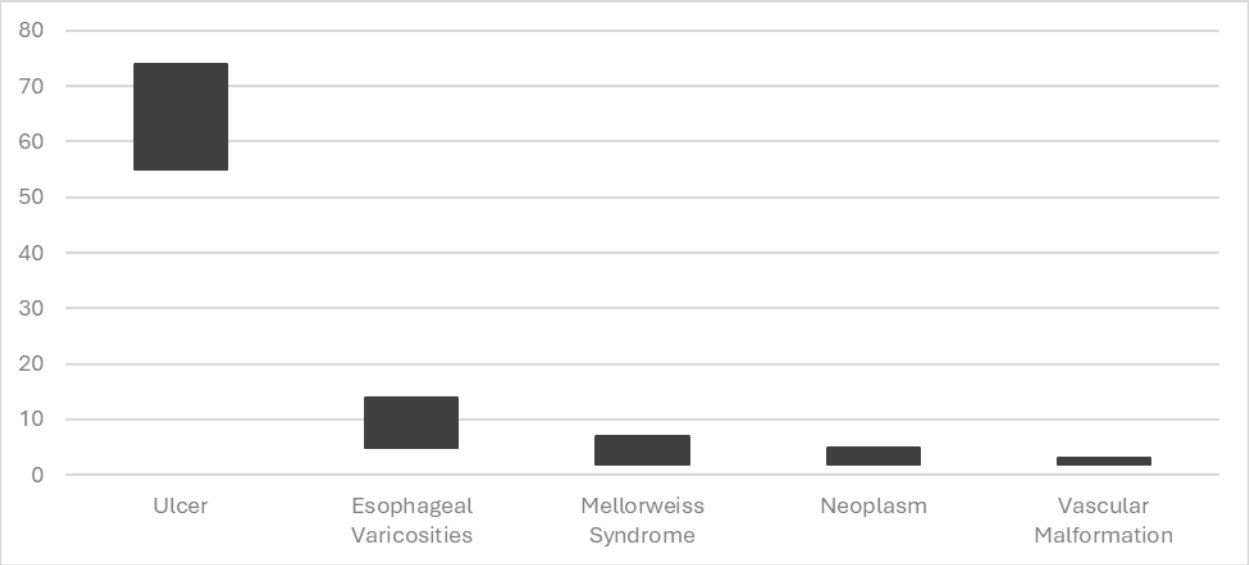

Illustration-1. Transcatheter arterial embolization for acute nonvariceal upper gastrointestinal bleeding: Indications, techniques and outcomes.

- Frequency of duodenal bleeding:
  - 375 cases per 100,000 population
  - Acute case of bleeding-75%
  - 70% of patients are >65 years old
  - Recurrent bleeding-25%
  - Mortality is 19-40%
  - Ratio male 2:1 female

- Clinical manifestations of duodenal bleeding
  - Hematemesis
  - Color brownish vomit
  - Melena
  - Anemia
  - Tachycardia (if blood loss > 500 ml)
  - Hypotension (if blood loss > 500 ml)
  - Systemic shock (if blood loss is more than 15% of circulating blood volume).

Diagnosis by fibrogastroscopy. See Photo-1-2.

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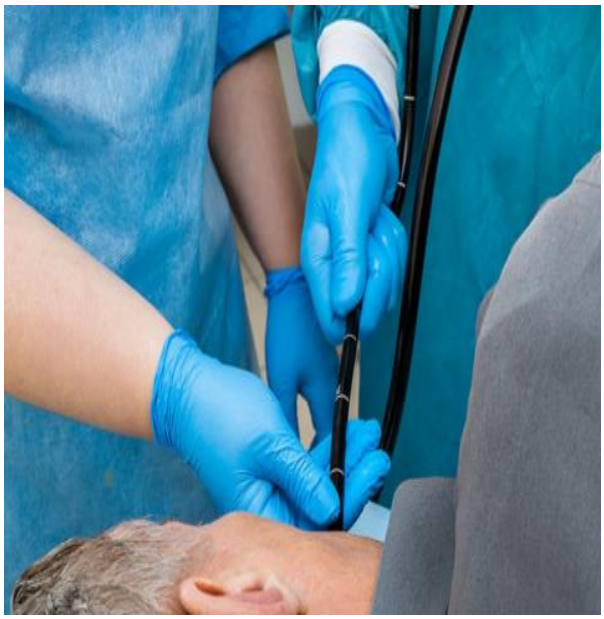

Photo-1-2. Fibrogastroscopy technics.

Angiography as a method of determining bleeding and result. (See Photo-3).

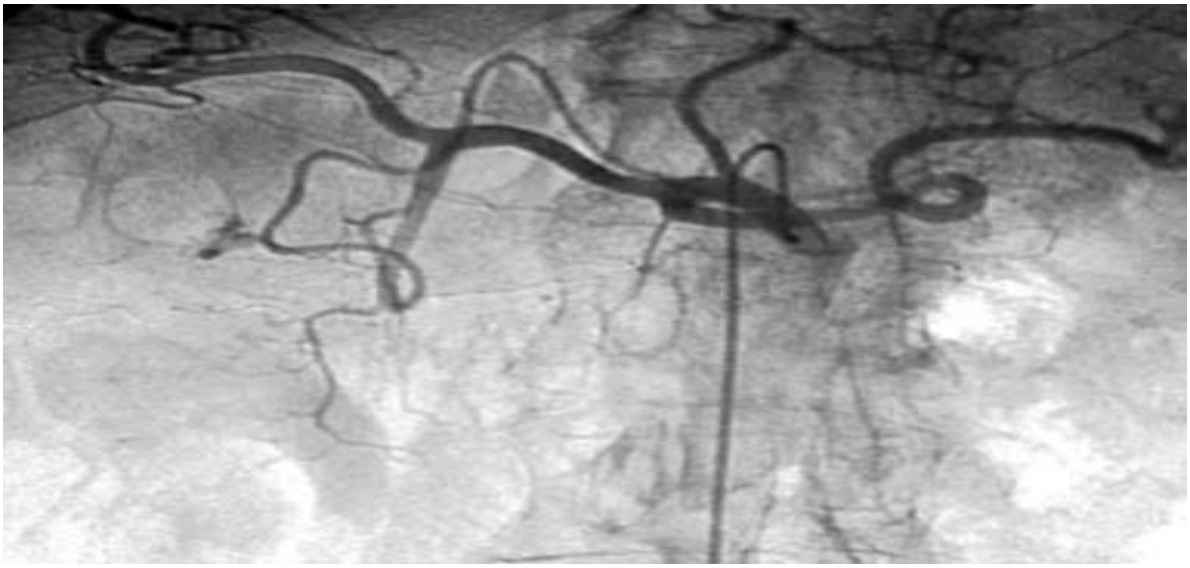

Photo-3. Angiography as a method of determining bleeding and result.
Angiographic signs of acute duodenal bleeding

- ❖ Direct:
  - ➢ Contrast extravasation into the intestinal lumen

- ❖ Indirect:
  - ➢ "Aneurysms/pseudoaneurysms
  - ➢ Asymmetry of the blood vessel

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- Arteriovenous/arterioportal shunting
- Neovascular

Our Purpose was to improvement of the results of surgical treatment of duodenal ulcer bleeding based on the use of endovascular embolization:

The task

- To determine indications for endovascular occlusion in ulcer patients complicated by gastroduodenal bleeding.
- The technique of endovascular interventions should be perfected.
- To evaluate the effectiveness of the endovascular occlusion method compared to the surgical method of treatment in high-risk patients.
- The tactics of surgical treatment of the mentioned patients should be developed based on the use of the endovascular occlusion method.

❖ Forrest's classification during endoscopy

- Forrest IA
- Forrest IB
- Forrest IIA
- Forrest IIB
- Forrest IIC
- Forrest III

Risk of rebleeding according to the Forrest classification. (See Illustration-2).

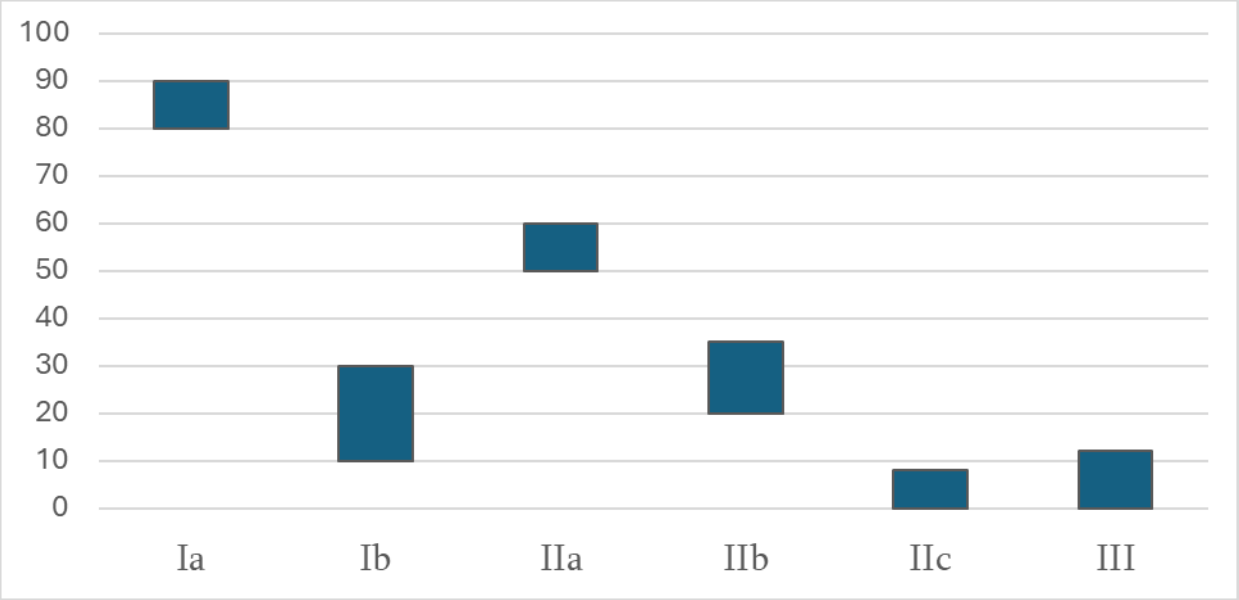

Illustration-2. Risk of rebleeding according to the Forrest classification.

❖ **Testimonials**

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- Low-risk patients - surgical treatment
- And high-risk patients - endovascular surgery
- Recurrent bleeding after surgery - endovascular surgery

The diagnosis and management of gastrointestinal (GI) bleeding are complicated and requires a multidisciplinary approach involving gastroenterologists, interventional radiologists, and surgeons.

- **Testimonials**

- With active bleeding (requiring 4 units of blood transfusion in 24 hours).
- With hemodynamic instability (low systolic pressure, pulse 100 or more, hypovolemic shock) - who did not have satisfactory results during endoscopic hemostasis, in this case it will be important to calculate the Rokall score.
- A high risk of rebleeding should be used in the Forrest classification. Forrest 1A, Forrest 1B Forrest 2A and Forrest 2B
- Co-morbidities that aggravate the patient's medical history.

Graphical comparison of mean age of TAE and surgical groups in included studies. See Illustartion-3.

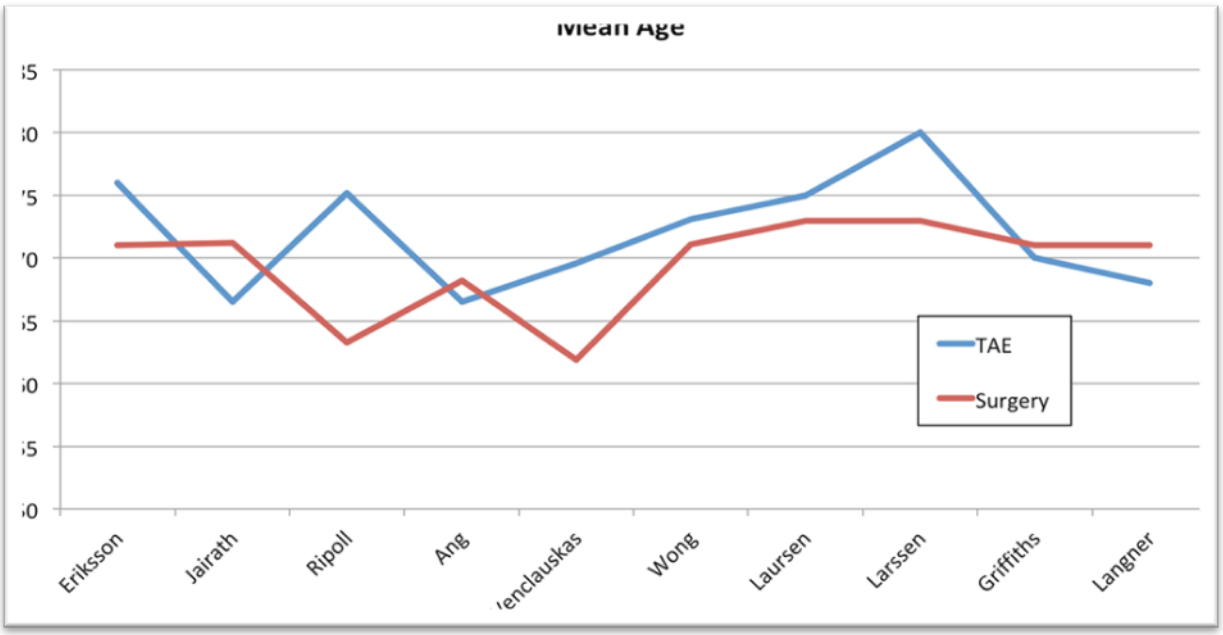

Illustration-3. Graphical comparison of mean age of TAE and surgical groups.

Material and methods**:** From March 2019 to December 2024, 40 patients were embolized during duodenal bleeding.
These patients were divided into the following groups:

- Massive, active bleeding;
- Recurrence of bleeding in clinic and endoscopy was unsuccessful;

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- Unstable hemodynamics and solid hemostasis could not be achieved during endoscopy;
- Failed to evacuate stomach contents and failed to see a bleeding ulcer;
- High risk of bleeding recurrence (Forest classification);
- Elderly and patients burdened with co-morbidities, with whom operative intervention represents a high risk of lethality.

Embolization performed according to Forrest's classification in 40 patients. See Illustration-4.

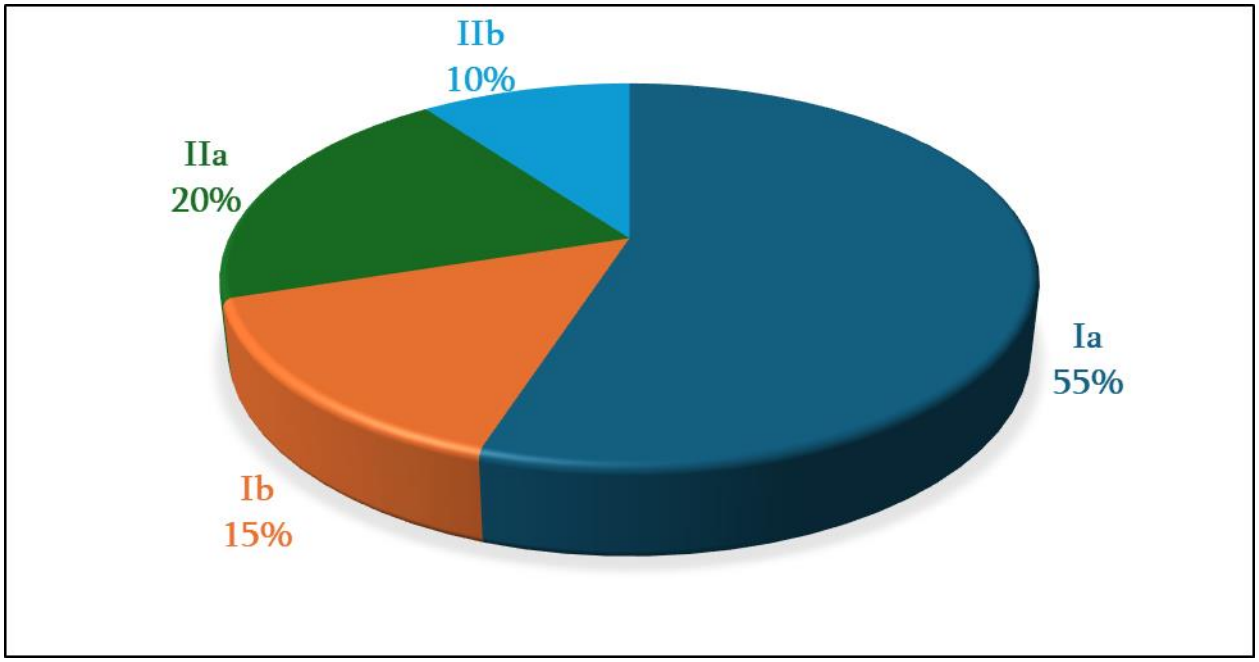

Illustration-4. Embolization performed according to Forrest's classification.

❖ Embolization methods
- Blind- embolization
- Empirical embolization

❖ Technical aspects of embolization
- Radial approach
- Femoral artery approach

❖ Factors influencing the choice of embolic agent
- Angiographic conclusion
- Vascular anatomy
- Vascular size
- Desired level of vascular occlusion
- Temporary or permanent occlusion is preferred
- Catheter position
- Operator experience

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Embolization techniques. (See Illustration-5).

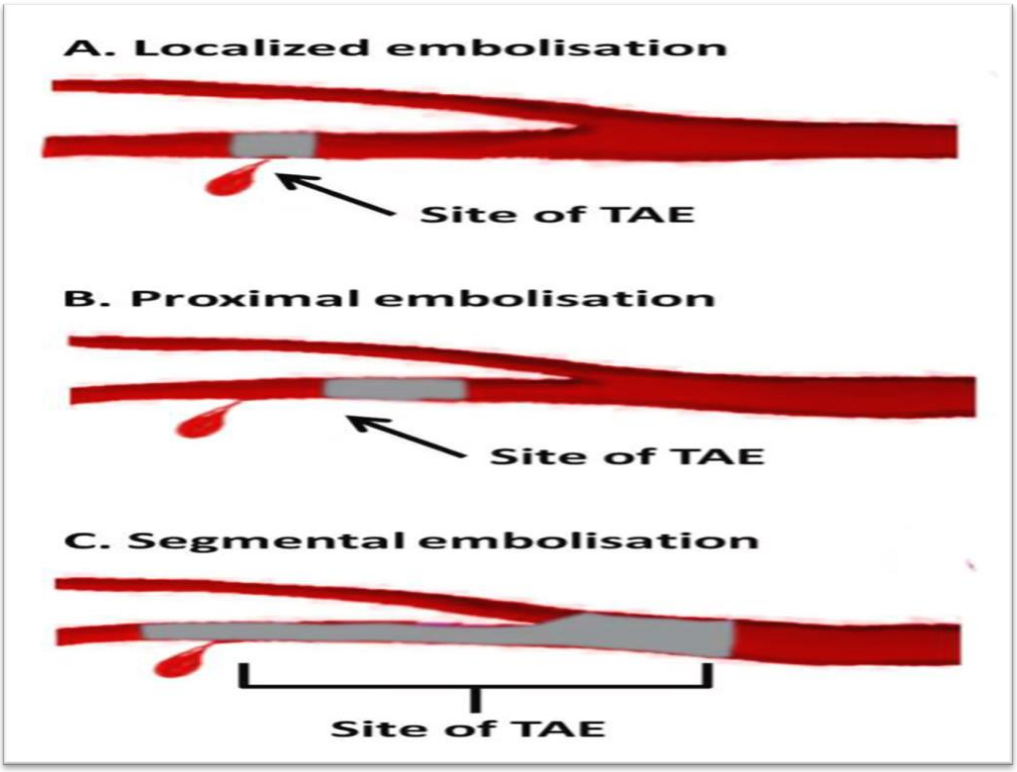

Illustration-5. Embolization techniques.

Embolization Sendvich technique. See Illustration-6.

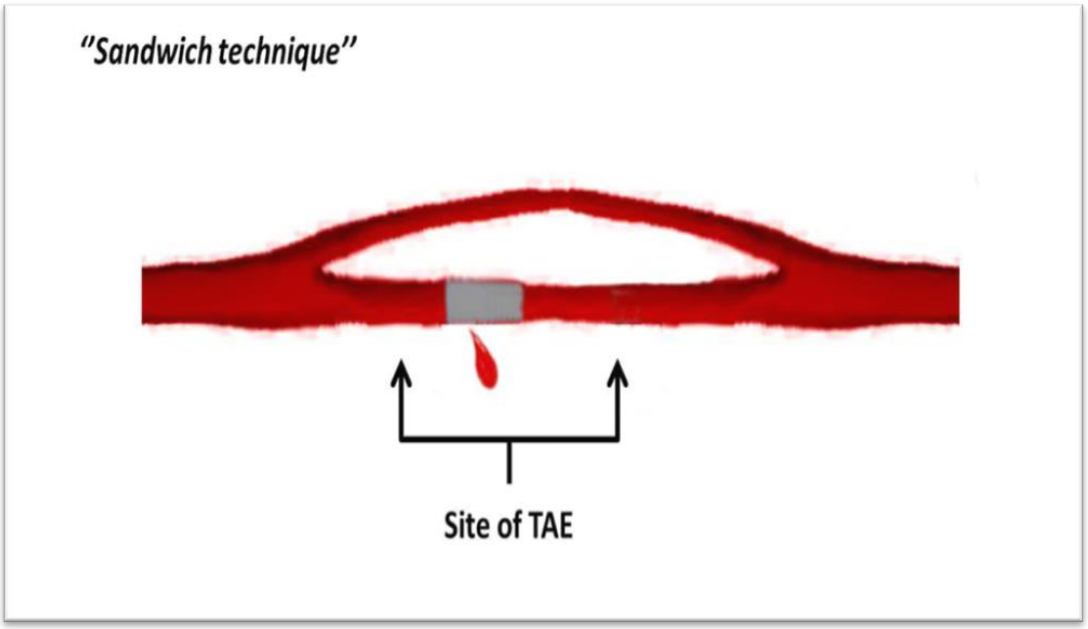

Illustration-6. Embolization Sendvich technique.

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❖ Study Results:
- ➢ Technical success in 39 patients (97.5%).
- ➢ Technical failure in 1 patient (2.5%).

Embolization results obtained on 40 patients. (See Illustration-7).

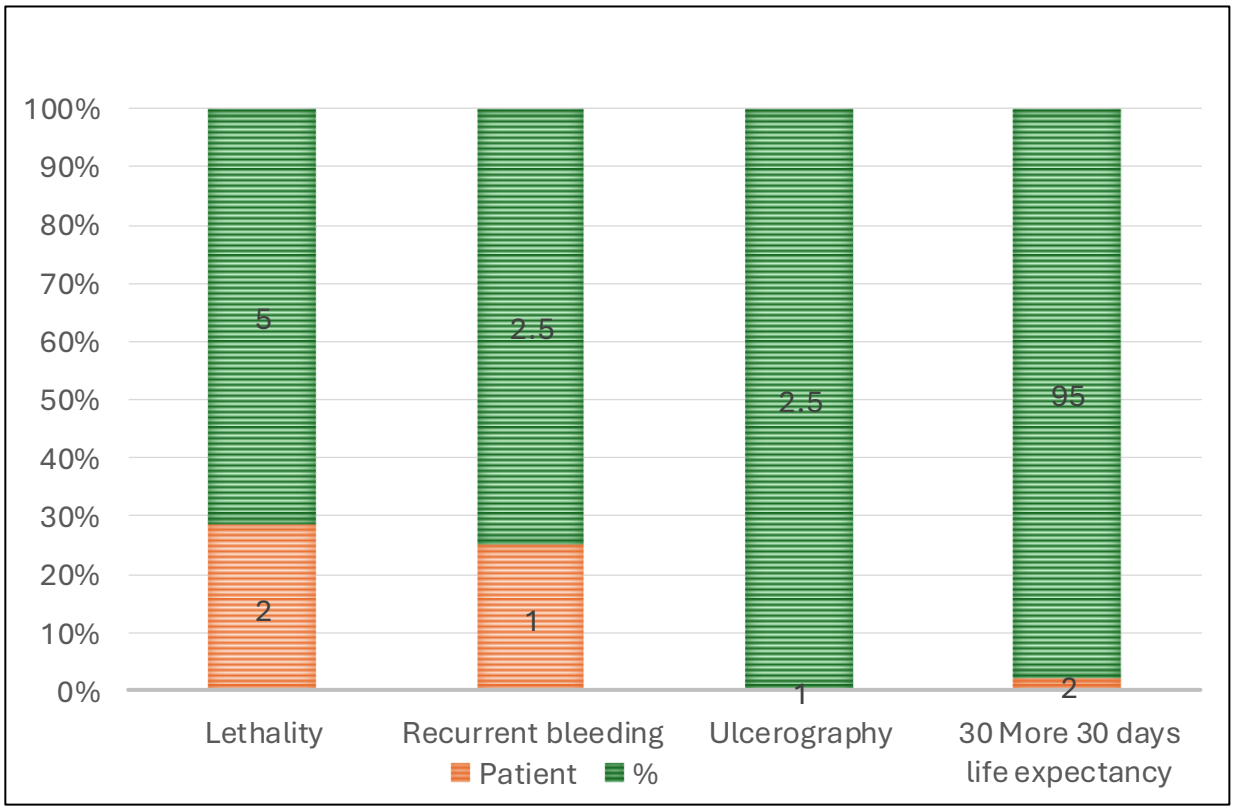

Illustration-7. Embolization results.

- Case description
- ➢ The patient is 78 years old
- ➢ Pain in the chest
- ➢ Marked respiratory failure
- ➢ Troponin 2.6 ug/L
- ➢ ST-elevation on the cardiogram

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Angiography results. See Photo-4.

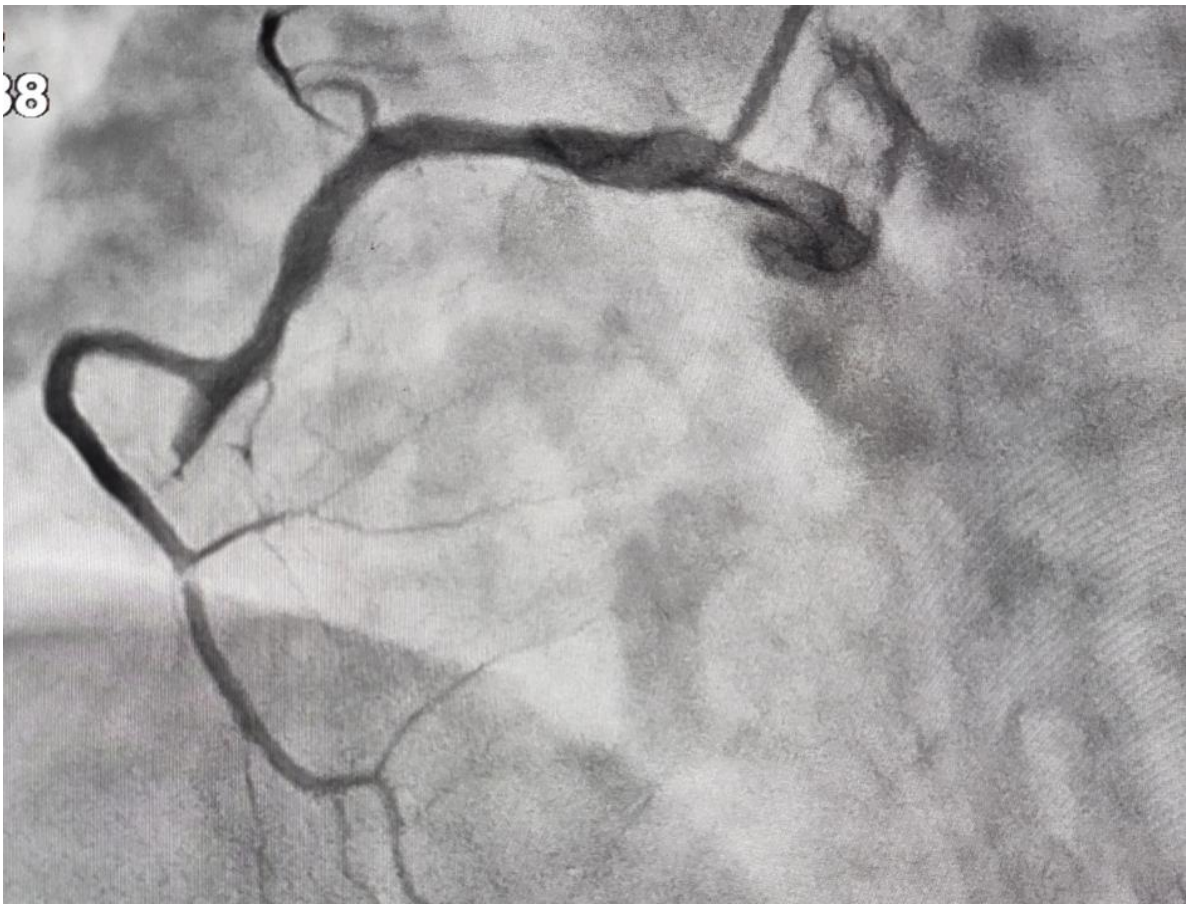

Photo -4. Angiography results.

- The following criteria are used to evaluate the effectiveness of endovascular hemostasis:
- Technical success - interruption of blood flow in the embolization zone.
- Clinical success - correction of bleeding recurrence and stabilization of hemodynamics
- Unsuccessful embolization.
- Studies show that coagulopathy is significantly associated with mortality after failed embolization.

The risk of rebleeding after successful embolization is three times greater in patients with coagulation problems, and for the same reason there is a 10-fold greater risk of death compared to patients with normal coagulation.

Conclusion

Improvements in catheter technology, development of more compatible embolization devices, and expansion of embolization techniques have led to angiography and embolization for the treatment of upper and lower gastrointestinal bleeding. Transcatheter embolization therapy for the treatment of acute GI bleeding is a safe procedure with high technical performance and clinical success, but

it should be reserved as a treatment option for patients who have failed endoscopic and medical management. MDCT imaging is a useful tool for identifying the site of bleeding and evaluating the anatomical structure of the gastrointestinal tract in stable patients. Close working relationships between interventional radiologists, gastroenterologists, and diagnostic radiologists are essential for the optimal management of patients with GI bleeding. Endovascular embolization dramatically reduces the mortality rate in high-risk patients who require open surgery after failed endoscopy, further studies are needed to fully address these objectives.

Acknowledgments
Declaration of Interest Statement. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. Conflict of interest-None.

Declaration of Interest Statement: No potential conflict of interest was reported by the authors.

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

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Introduction

Pre-implantation Genetic Diagnosis (PGD) is the diagnosis of genetic disorders in human embryos prior to implantation into the endometrium, i.e. before the phase of transfer on the program of in vitro fertilization (IVF). A biopsy of one blastomer in an embryo that is at the cleavage stage (6-10 blastomeres) or a biopsy of the trophectoderm (the outer layer of cells) at the blastocyst stage (day 5 of embryo development) is typically performed for analysis. The main advantage of PGD is that there is no selective termination of pregnancy when it is used and the chance of giving birth to a child without any diagnosed genetic diseases is quite high [1,3,15].

There are discrepant data in literature on the effectiveness of PGD as part of the program of assisted reproductive technologies (ART) [2,6,8].

According to some studies including ASRM (American Society for Reproductive Medicine) data, application of PGD doesn't increase the frequency of pregnancies with in vitro fertilization (IVF). This may be due to imperfection of the technique of the blastomer sampling procedure or the choice of a laboratory screening method to diagnose aneuploidy and microstructural chromosomal abnormalities simultaneously in all chromosomes. The method of array comparative genomichybridization (CGH) showed high performance for clinical studies on embryo transfer within ART (69-70%). While there is the high genetic abnormalities detection rate in PGD based on many studies, the frequency of pregnancies with this method doesn't exceed 30-40% [4,7,11].

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

Materials and methods.

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

All female patients underwent a special examination before IVF: the hormonal panel was studied (FSH, LH, estradiol, TSH, free T3, free T4, TSH, thyroperoxidase antibodies, prolactin, progesterone, Anti-Mullerian Hormone, testosterone) and infectious status (TORCH-complex infection, STDs), papanicolau test, peripheral karyotype, determination of the vitamin D level in the blood, hysterosalpingography, hysteroscopy with pathohistological examination of endometrial biopsy material. Males underwent mandatory sperm examination with morphological indicators of spermatozoa, genetic analysis of sperm (FISN) and DNA fragmentation. The immune system of spouses and their compatibility by the 2nd class of HLA genes were also examined.

The exclusion criteria were the females with monogenic diseases and males with significant pathozoospermia. Controlled ovarian hyperstimulation was performed according to the standard

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antagonist protocol from day 2-3 of the menstrual cycle with preparations of recombinant follicle-stimulating hormone combined with preparations of human menopausal hormone. Ultrasound monitoring of follicle growth was performed by transvaginal ultrasonography 4-5 times during the multifollicular ovarian stimulation. When the maximum follicle of 14-15 mm was reached, a gonadotropin-releasing hormone antagonist was administered at a dose of 0.25 mg.

Oocyte retrieval was performed in 35-36 hours after the administration of ovulation trigger. Immediately after receiving oocytes and spermatozoa, their morphological assessment was performed. Morphological analysis of oocytes and spermatozoa was carried out immediately after retrieval. Mature, immature and degenerative oocytes can be retrieved by puncturing follicles. More thorough assessment of the state of oocytes can be carried out only after purification before ICSI. The first polar cell is determined in mature oocytes ready for fertilization and designated as M II in the embryological protocol [1,13].

Intracytoplasmic sperm injection was performed for all patients (ISCI method). Two pronuclei form in the normal course of fertilization in 18-20 hours after ICSI (on the 1st day). In this case, 2pn rating is assigned to them. Further development of embryo cleavage occurs within 5-6 days. The embryo quality was assessed 40-42 hours (on Day 2), 72-74 hours (on Day 3), and 20 hours (on Day 5) after fertilization. Embryo cleavage should be symmetrical and equal. Embryos of poor quality were not transferred to the uterine cavity. They were left till Day 5 and then frozen or transferred upon normal blastocyst formation [5,10,14].

It is known that embryos form a blastocyst on Day 5. The quality of blastocysts was assessed by their size from 1 to 5; by the state of the inner cell mass - from " A " to " C "and surrounding cells – trophoblast (from" A "to"C"). The best blastocysts for transfer were those of size 3-5 with the multicellular ICM and trophoblast. Further development of the embryo occurs in the uterus after the implantation. For successful implantation, the blastocyst must exit the surrounding pellucid zone. This process is called hatching. In case of change in the pellucid zone and difficulties in the process of self hatching, auxiliary laser hatching is used [10,12,15].

Biopsy of the embryo was performed on Day 3 after the fertilization at phase 6-10 of blastomeres and blastocytes.

The FISH (fluorescence in situ hybridization) method was used to detect numerical and structural chromosomal abnormalities. This method involves DNA-probes which are a limited-size nucleotide sequence complementary to a specific region of nuclear DNA. The probe has a “tag”, i.e. it contains a nucleotide linked to fluorophore (a molecule capable of fluorescence).

After the procedure of hybridization with the formation of a hybrid DNA-probe and DNA-target molecule, fluorescence of specific DNA sequences on chromosomes or in nuclei can be observed on the study cytogenetic preparation by means of a fluorescent microscope [9,13].

Statistical data processing was performed using an application software package SPSS statistics 17.0. The Kruskal-Wallis test was used to evaluate the significance of intergroup differences in several independent samples.

In case of two samples the Mann-Whitney U-test was used for unlinked sequences. The inserted parts of genotypes were assessed for compliance with the Hardy–Weinberg principle by the X^2 criterion in comparison with expected genotype frequencies of equilibrium distribution. The significance of differences in the incidence of qualitative characters was determined by the criterion X^2.

Findings of Study.

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Mean age of females was 35.5 ±1.0. Infertility duration was 7.5 ±5 years. The patients were comparable (p>0.005) in their etiology of infertility, anamnestic data, mass-height index, structure of previous somatic and gynecological diseases, and surgical interventions. All patients had a normal karyotype.

The results of the study on the characteristics of embryos subjected to pre-implantation diagnosis are shown in Table 1. A total of 220 embryos were subjected to pre-implantation diagnosis: 111 embryos in Group A and 109 embryos in Group B. Patients of each study group were divided into subgroups by age: under the age of 35 and over 35. In Group A, among females aged <35, the number of embryos subjected to pre-implantation diagnosis was 52 and in females aged >35 the number of embryos subjected to pre-implantation diagnosis was 59. In Group B, 48 embryos were subjected to pre-implantation diagnosis in females aged <35 and 61 embryos in females aged >35.

The study findings showed that no pathology of embryos was observed both in females aged <35 and in females aged >35 in the group with successful IVF in 69.2% and 59.3% of cases respectively. These values are statistically significantly higher than similar values in the group of females with non-effective IVF results, respectively, 41.7% (p< 0.01) and 24.6 % (p < 0.01). Embryos with abnormalities were detected statistically more often in the group with negative IVF results (67.9%) than in the group of successful IVF (36.0%, p < 0.01).

Distribution of embryos with abnormalities showed that in the group of non-effective IVF results statistically significant increase in the relative incidence of embryo pathology was observed both in females aged <35 and in females aged >35 (58.3% and 75.4% respectively), as compared with the group of females with positive IVF outcomes in the relevant age group, 30.8% (p<0.001) and 40.7% (p<0.001) respectively (Table 1).

Table 1. Characteristics of embryos subjected to pre-implantation diagnosis.

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

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

Since the frequency of viable embryos formation varies in both groups, studying the frequency and nature of pathologies of viable embryos in these groups is of great interest. Viable embryos reached 35% in the group of females with positive IVF outcomes that was statistically more than in the group of negative IVF result – 20.3% (p<0.01) (Table 2). A detailed study of the frequency of viable embryos in patients of different age subgroups showed statistically significant high values among females aged > 35 with positive IVF outcomes (37.5%) in comparison with females of the same age with negative IVF outcomes (15.2%, p<0.05).

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The study of unviable embryos frequency showed a contrary picture. Unviable embryos were observed statistically more often in females aged >35 in the group with the negative IVF outcome (84.8%) as compared to females of the same age with the positive IVF outcome (62.5%, p<0.05). Among females aged <35, there was no relevant difference in the frequency of viable and unviable embryos between the study groups.

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

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

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

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

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

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

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

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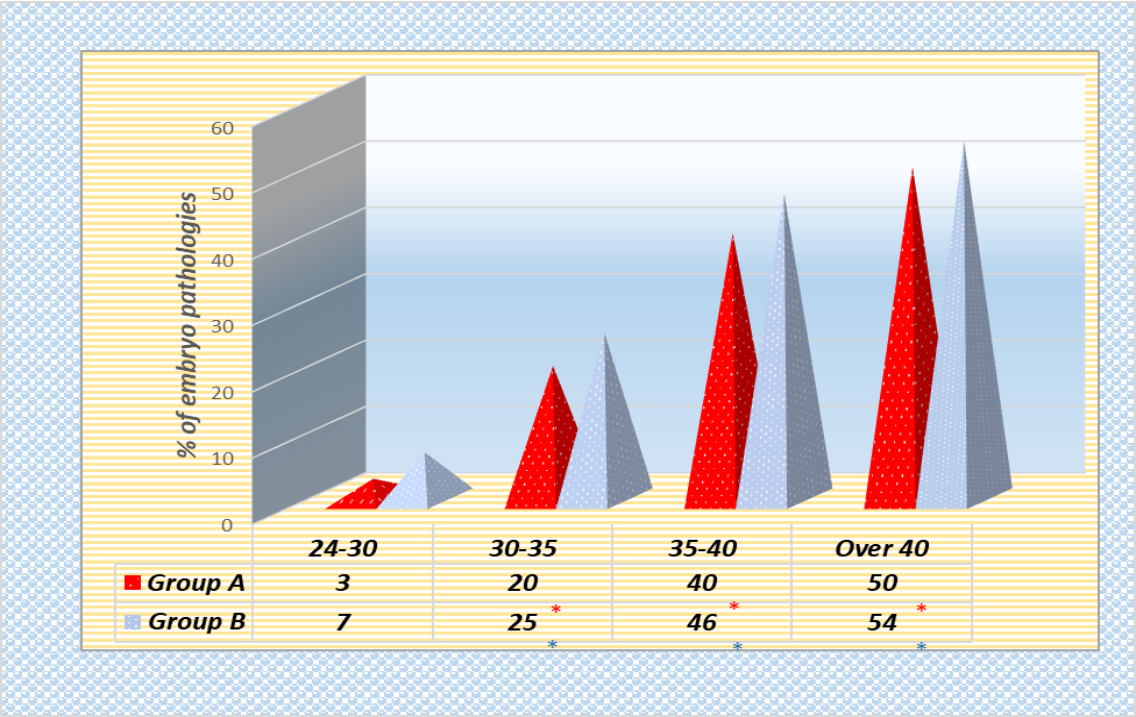

P < 0.01 as compared to the previous age within each group.

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

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

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

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Edwards syndrome (trisomy 18)	2	16.7	2	13.3	4	14.8
Polysomy Y (XYY)	1	8.3	2	13.3	3	11.1

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

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

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

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

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

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

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

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

risk of miscarriage and multiple pregnancies and to improve the chances of successful implantation and the birth of a healthy child.

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$$f(x) = a_0 + \sum_{n=1}^{\infty} \left(a_n \cos \frac{n\pi x}{L} + b_n \sin \frac{n\pi x}{L} \right) \qquad (1)$$

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Font	**Article Title**	**Headings**	**Subheadings**	**Reference list**	**Text**
	Times New Roman, 16 pt, Bold, centred	Times New Roman, 11 pt, Bold, Left aligned	Times New Roman, 10 pt, Bold, Left aligned	Times New Roman, 8 pt, Justified	Garamond, 11 pt, Justified
Line Spacing	1.15	1.15	1.15	1.15	1.15
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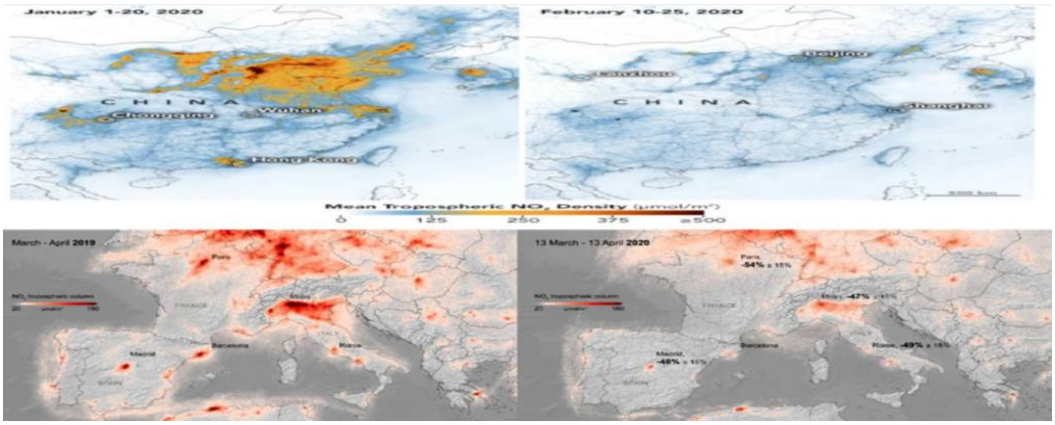

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