

Clinico - Functional Features Of The Condition Of The Cardiovascular System In Newborn Children With Delay Of Innerabetal Development

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Abstract:

Intrauterine growth retardation is an important problem in pediatrics, as it is an integral indicator of intrauterine dysfunction.

Purpose: to study the features of the clinical and functional state of the cardiovascular system in newborn children born with various types of intrauterine growth retardation.

Material and research methods: 70 newborns were examined. All children were divided into 2 groups: the 1st (main) amounted to 50 newborns with IUGR, of which: 1a - with the symmetric version of IUGR - 25, 1b - with the asymmetric version of IUGR - 25 children, in the 2nd group (comparisons) 20 premature infants without IUGR were included. All newborns underwent an echocardiographic examination of the heart.

Results: on the basis of clinical and instrumental studies, the features of the clinical and functional state of the cardiovascular system in newborn children born with various types of intrauterine growth retardation are presented. In children who had different types of intrauterine growth retardation, significantly significant features of cardiac activity and morphological and hemodynamic parameters of the heart at birth were proved. Children with a symmetric variant of IUGR are characterized by a slowed heart rhythm, which was recorded significantly more often than in children with a symmetric variant of IUGR.

Key words: newborn, intrauterine growth retardation, cardiovascular system.

1. RELEVANCE

The problem of intrauterine growth retardation (IUGR) of the fetus and the birth of children of low birth weight for gestational age does not lose its relevance, as these children have high morbidity and perinatal mortality, as well as the likelihood of developing serious chronic diseases in the future [6,15].

The frequency of IUGR in a population is highly variable and depends on a number of reasons. According to WHO, the proportion of children with IUGR among newborns is from 5 to 16%. In developed Western countries, birth of small children is registered in 4-12% of cases of all births, in Central Asia it reaches 31.1%, in the USA - 10-15%, in Russia - 2.4-17%, and in Kazakhstan 20 000 small children. The perinatal mortality of small children is 6-

10 times higher than that of newborns with normal body weight, and the perinatal morbidity is from 70 to 80% and is an important social and economic problem for the state due to the high costs of nursing, rehabilitation and social adaptation of such children [1,2,7].

According to foreign literature, IUGR is detected in children of healthy mothers in 5–7% of cases, and in mothers with a history of history up to 25% [11].

The prevalence of IUGR in preterm infants is usually higher and, according to some estimates, ranges from 4% to 60%, about 23% of IUGR is found among children with very low body weight and about 38% with extremely low body weight (ELBW) [3,16,17].

The formation of the IUGR is a complex multi-stage and time-prolonged process, depending on a complex of factors: genealogical, biological and socio-environmental. The leading role in the pathogenesis of IUGR belongs to the violation of the uteroplacental circulation, which leads to hypoxia, a cascade of metabolic and functional disorders in the fetus and newborn [4,8]. Also, the most significant risk factors for the occurrence of IUGR are: maternal factors, which include chronic arterial hypertension or arterial hypertension associated with pregnancy, preeclampsia, gestational diabetes mellitus, lung disease, anemia, chronic renal failure, antiphospholipid syndrome, malnutrition and bad habits; fetal factors, including genetic diseases, congenital malformations, intrauterine infection, multiple pregnancy; placental factors, such as placental insufficiency and placental infarction [5,7,12].

In children with IUGR, morphological features and functions of internal organs are formed, which subsequently increase the risk of diseases of the central nervous and cardiovascular systems and metabolic diseases [9].

In the last decade, there has been an increase in the frequency of cardiovascular pathology in children (arterial hypertension, cardiomyopathy, cardiac arrhythmias, neurocirculatory dystonia, metabolic myocardial disorders), the origins of which lie in the pathology of the antenatal and early neonatal period of development [goat]. It has been proven that fetal hypoxia leads to delayed and asynchronous maturation of the cardiovascular system, a violation of morphogenesis, the formation of the cardiac conduction system, neurohumoral regulation of vascular tone, including in the coronary bed, and a decrease in metabolism in cardiomyocytes [13,14]. Studies have shown that intrauterine growth retardation leads to a decrease in the number of cardiomyocytes, a decrease in glycogen and, as a consequence, to a violation of hemodynamics and myocardial contractility after birth. Children with IUGR have a delay in closing the ductus arteriosus up to 1.5–2 years, persisting signs of pulmonary hypertension up to 3 years, various rhythm disturbances, myocardial dystrophy, as well as a high risk of sudden death syndrome in the first months of life. In subsequent years of life, the risk of developing hypertension, coronary heart disease and cardiac arrhythmias increases [10].

Thus, timely diagnosis and adequate correction of cardiovascular disorders in newborns with intrauterine growth retardation may become a major factor in reducing the frequency and severity of cardiovascular disease in older children. In this regard, the features of adaptation of the cardiovascular system in the neonatal period in children born with IUGR, the characteristics of clinical and functional disorders in various options for intrauterine growth retardation require a more detailed study.

The aim of our study was to study the characteristics of the clinical and functional state of the cardiovascular system in newborn babies born with various types of intrauterine growth retardation.

2. MATERIAL AND METHODS.

In this study, 70 newborns were examined. All newborns were divided into groups: the 1st (main) amounted to 50 newborns with IUGR, of which: 1a - with a symmetric version of IUGR - 25 children, 1b - with an asymmetric version of IUGR - 25 children, 2nd group (comparisons) amounted to 20 premature infants without IUGR. Assessment of the condition of newborns was carried out on the Apgar scale. Morphofunctional and neuromuscular maturity of the newborn was evaluated on a Ballard scale. In all newborns, an echocardiographic examination of the heart was performed using an ACUSON-128 XP / 10c company with a vector sensor with a frequency of 2.5 and 4.0 MHz. The data obtained were statistically processed using the programs developed in the EXCEL package using a library of statistical functions with calculation of arithmetic mean (M), standard deviation (δ), standard error (m), relative values (frequency,%), student criterion (t) with calculating the probability of error (P).

2. RESULTS AND DISCUSSIONS.

At the first stage, we analyzed the frequency of occurrence of congenital heart defects in newborns with different variants of IUGR (Table 1.).

Table 1.
The frequency of congenital heart defects in newborns
in the observation groups (%)

Variety of CHD	1- group		Total n-50	2nd comparative group n-20
	Symmetric option 1a n-25	Asymmetric option 1b n-25		
DIVS	8,0±3,7	4,0±2,7	6,0±3,4	–
DIAS	4,0±2,7	–	2,0±2,0	–
ODA	28,0±6,1 *	16,0±5,0	22,0±6,0	5,0±3,0
OOW	76,0±5,8 ^	60,0±6,7	68,0±6,7	80,0±5,4
Pulmonary stenosis	–	–	–	10,0±4,1
Single ventricle of the heart	–	–	–	5,0±3,0

Note. DIVS – defect of the interventricular septum, DIAS - defect of the interatrial septum, ODA — open ductus arteriosus, OOW — open oval window. * - P <0,01– significance of differences between Ia and the comparison group; ^ - P <0,01– significance of differences between subgroups.

Our studies have shown that among the CHD in the observed children, the most common metastatic cancer, OOW, ODA. Among newborns with a symmetric variant of IUGR, DMS was 2 times more common than among children with an asymmetric variant of IUGR (4%).

Only one child (4%) met with a symmetric variant of IUGR. We found that ODA in newborns with a symmetric variant of IUGR was found more significantly than in children of the comparison group ($P < 0.01$).

In the comparison group, the largest number of children with OOW was noted - 80%. In the main group, ODAs were most often detected in newborns with a symmetric variant of IUGR and their number was significantly higher than among children with an asymmetric variant of 60%. In addition, we found that in newborns of the comparison group, defects such as pulmonary stenosis and a single ventricle of the heart were detected.

Thus, in newborns with a symmetric variant of IUGR in 100% of cases, pathology from the cardiovascular system was detected, and in 16% of them there was a combined pathology. In children with an asymmetric variant of IUGR, pathology from the cardiovascular system was found in 80% of cases.

We conducted a clinical examination of the cardiovascular system of the observed newborn babies (Table 2).

As a result of the studies, it was revealed that in newborns of the main group systolic murmur is much more marked than in newborns of the comparison group. In this case, the frequency of systolic noise in newborns of the main group with a symmetric version was detected much more often than in children with an asymmetric variant of IUGR. Muffled heart sounds were practically found in the vast majority of newborns of all groups and the frequency of occurrence did not differ significantly. Some predominance of this trait was noted in children with an asymmetric variant of IUGR compared with children with a symmetric version of IUGR.

Table 2.

Comparative characteristics of clinical signs from the cardiovascular system in the observed children (%)

Clinical signs	1- group		Total n-50	2nd comparative group, n-20
	Symmetric option 1a n-25	Asymmetric option 1b n-25		
Systolic murmur	72,0±6,1	56,0±6,8	64,0 ±6,9	55,0±6,8
Muffled heart sounds	80,0±5,4	88,0±4,4	82,0±5,3	85,0±4,9
Bradycardia	52,0±6,8 ^	16,0±5,0	34,0±6,8	—
Tachycardia	36,0±6,5 *	40,0±6,7 **	38,0±7,0	20,0±5,4

Note: ^ - $P < 0.001$ – significance of differences between subgroups; * - $P < 0.05$ – significance of differences between the 1st and the comparison group. ** - $P < 0.05$ – significance of differences between the 1st and the comparison group.

A study of the cardiovascular system in premature infants with IUGR revealed the following patterns. We have studied the dependence of the frequency of heart rhythm changes according to auscultation on the form of intrauterine growth retardation. It was revealed that in the main group in children with a symmetric variant of IUGR, bradycardia was detected significantly more often than among children with an asymmetric variant of IUGR ($P < 0.001$). In the main group, in children with an asymmetric variant of IUGR, tachycardia

prevailed, which was observed in $40 \pm 7.8\%$ of children, which was significantly more than in the comparison group ($P < 0.05$).

Thus, for children with a symmetric variant of IUGR, a slowed heart rhythm is characteristic, which was recorded significantly more often than in children with an asymmetric variant of IUGR ($P < 0.001$), and for children with an asymmetric version of tachycardia ($P < 0.05$).

Along with this, we also studied the frequency of occurrence of other clinical signs characterizing the condition of newborns with IUGR depending on its clinical variant (Table 3).

Table 3.
The frequency of clinical signs in newborns, depending on the clinical variant of IUGR (%)

Clinical symptoms	1– group		Total n-50	2nd comparative group, n-20
	Symmetric option 1a n-25	Symmetric option 1a n-25		
Cyanotic skin	20,0±5,4	24,0±5,8	22,0±6,0	25,0±5,9
Pallor of the skin	68,0±6,3	76,0±5,8	72,0±6,5	75,0±5,9
Subictericity of the skin	24,0±5,7	32,0±6,3 **	28,0±6,5	10,0±4,1
Acrocyanosis	8,0 ±3,7	16,0±5,0	12,0±4,7	15,0±4,9
Perioral cyanosis	28,0±6,1	24,0±5,8	26,0±6,3	20,0±5,4
Marbling	12,0±4,4	12,0±4,4	12,0±4,7	–
Wheezing	56,0±6,8 *	44,0±6,8 **	50,0±7,2	20,0±5,4
Dyspnea	52,0±6,8	40,0±6,7	46,0±7,2	45,0±6,8

Note: * - $P < 0.05$ - significance of differences between 1a and the comparison group; ** - $P < 0.05$ - significance of differences between 1b and the comparison group;

The cyanoticity of the skin was relatively more common in newborns with an asymmetric version of IUGR than in children with a symmetric version of IUGR, and this symptom did not have significant differences with the comparison group. A significant part of the children of the main group and the comparison group revealed pallor of the skin.

However, it was found that pallor of the skin was significantly more likely to occur in children with an asymmetric variant than in children of the comparison group ($P < 0.05$). In the group of children with a symmetric variant of IUGR, pallor of the skin was detected in 68% of children.

Our study showed that newborns with a pronounced sub-bacterial skin were significantly more among children with an asymmetric variant of IUGR ($P < 0.05$) than among children in the comparison group/

In children with an asymmetric variant of IUGR, acrocyanosis was observed 2 times more often than in premature babies with a symmetric version of IUGR. Such signs as, perioral cyanosis, shortness of breath and wheezing were found with the greatest frequency in the group of children with a symmetric variant of IUGR.

Wheezing in children with an asymmetric variant of IUGR was significantly more likely to occur than in children with a symmetric version of IUGR ($P < 0.05$).

Thus, damage to the cardiovascular system in the observed children was clinically manifested in the form of cyanotic skin, pallor of the skin, acrocyanosis, perioral cyanosis, marbling, small bubbling rales in the lungs. It was established that the severity of clinical signs of damage to the cardiovascular system was more detected in newborns with an asymmetric variant of IUGR.

To characterize functional disorders of the heart in newborns who underwent chronic and acute hypoxia, we also analyzed the data of echocardiography studies (Table 4).

Table 4.
Comparative analysis of echocardiography data in infants with IUGR depending on the clinical variant

Indicators	Symmetric option 1a n-25	Symmetric option 1a n-25	2nd comparative group, n-20
FDS LV	16,0±0,3	14,6±0,3*	16,6±0,9
FDV LV	3,9±0,5	3,3±0,2	3,5±1,0
FSS LV	10,5±0,3	9,8±0,3	10,8±0,8
TPW LV	2,4±0,1	2,2±0,1	2,4±0,1
TIVS	3/6	3/7	3/7
EF	65,3±0,4	64,7±0,3	63,8±0,4
RV	11,4±0,1	10,9±0,1*	11,0±0,1
A/P	62/37	57/34	60/32

Note. FDS LV- the final diastolic size of the left ventricle, FDV LV - the final diastolic volume of the left ventricle, FSS LV - the final systolic size of the left ventricle, TPW LV- the thickness of the posterior wall of the left ventricle, TIVS - the thickness of the interventricular septum, EF - the expulsion fraction, RV - the right ventricle; * - $P < 0.001$ significance of differences between subgroups.

One of the important indicators characterizing hemodynamic disturbances in newborns who underwent hypoxia in the perinatal period is a change in the final diastolic size. In our observations, it was found that the indicator of the final diastolic size of the left ventricle (FDS LV) was significantly lower ($P < 0.001$) in children with an asymmetric variant and amounted to 14.6 ± 0.3 . The average values of FDS LV in children with a symmetric variant of IUGR and in children of the comparison group did not have significant differences and amounted to 16.0 ± 0.3 mm and 16.6 ± 0.9 mm, respectively.

At the same time, hemodynamic disturbances in newborns that developed in adverse conditions may manifest as a change in the final diastolic volume of the left ventricle (FDV LV). The lowest value of FDV LV was found in children with an asymmetric variant of IUGR and amounted to 3.3 ± 0.2 mm. In children with a symmetric variant of IUGR, the FDV LV was slightly higher (3.9 ± 0.5 mm) than in children of the comparison group (3.5 ± 1.0 mm). The smallest value of the final systolic size of the left ventricle was found by us in children with an asymmetric variant of IUGR. This indicator in children with a symmetric variant of IUGR did not have significant differences with the comparison group.

The thickness of the posterior wall of the left ventricle in children with an asymmetric version of IUGR was slightly lower than in children with a symmetric version of IUGR and than in children of the comparison group.

An important indicator of myocardial contractility is such an indicator as the fraction of ejection. In our observations, this indicator in children with an asymmetric version of IUGR was 64.7 ± 0.3 mm, and in children with a symmetric version of IUGR 65.3 ± 0.4 , which did not differ significantly from the comparison group (63.8 ± 0.4 mm).

The obtained echocardiography data in the observed children showed that the size of the right ventricle (RV) was significantly smaller ($P < 0.001$) in newborns with an asymmetric version of IUGR and amounted to 10.9 ± 0.1 mm. In children, the right ventricular size was 11.4 ± 0.1 mm in a symmetric version of IUGR, which practically did not differ from the indicator of the comparison group 11.0 ± 0.1 .

Thus, in children born with IUGR, especially with the asymmetric variant, a decrease in contractile function and impaired myocardial relaxation ability are noted, which can affect the rate of intracardiac blood flow. A change in the ratio of the phases of the filling of the left ventricle indicates a violation of the relaxation ability of the myocardium. Changes in intracardiac hemodynamics have a negative effect on systemic blood flow, contributing to a decrease in the blood supply to organs and tissues, causing an aggravation of hypoxic changes. It should be noted that a violation of the myocardial relaxation ability in combination with a change in intracardiac blood flow can lead to a deterioration in the blood supply to the myocardium. The recorded less pronounced changes in echocardiographic parameters in children who had a symmetric type of intrauterine growth retardation are probably due to the fact that the fetus, which is under the influence of unfavorable factors from an early date, adapts to them and the postpartum adaptation of the circulatory system is less noticeable.

In children who had different types of intrauterine growth retardation, significantly significant features of cardiac activity and morphological and hemodynamic parameters of the heart at birth were proved. Children with a symmetric variant of IUGR are characterized by a slowed heart rhythm, which was recorded significantly more often than in children with a symmetric variant of IUGR.

BIBLIOGRAPHY:

- [1] Kant, N., Saralch, S., & Singh, H. (2011). Ponderomotive self-focusing of a short laser pulse under a plasma density ramp. *Nukleonika*, 56, 149-153.
- [2] Patyar, S., & Patyar, R. R. (2015). Correlation between sleep duration and risk of stroke. *Journal of Stroke and Cerebrovascular Diseases*, 24(5), 905-911.
- [3] Khamparia, A., & Pandey, B. (2015). Knowledge and intelligent computing methods in e-learning. *International Journal of technology enhanced learning*, 7(3), 221-242.
- [4] Singh, A., Lin, Y., Quraishi, M. A., Olasunkanmi, L. O., Fayemi, O. E., Sasikumar, Y., ... & Kabanda, M. M. (2015). Porphyrins as corrosion inhibitors for N80 Steel in 3.5%

- NaCl solution: Electrochemical, quantum chemical, QSAR and Monte Carlo simulations studies. *Molecules*, 20(8), 15122-15146.
- [5] Singh, S., Kumar, V., Upadhyay, N., Singh, J., Singla, S., & Datta, S. (2017). Efficient biodegradation of acephate by *Pseudomonas pseudoalcaligenes* PS-5 in the presence and absence of heavy metal ions [Cu (II) and Fe (III)], and humic acid. *3 Biotech*, 7(4), 262.
- [6] Mia, M., Singh, G., Gupta, M. K., & Sharma, V. S. (2018). Influence of Ranque-Hilsch vortex tube and nitrogen gas assisted MQL in precision turning of Al 6061-T6. *Precision Engineering*, 53, 289-299.
- [7] Prakash, C., Singh, S., Pabla, B. S., & Uddin, M. S. (2018). Synthesis, characterization, corrosion and bioactivity investigation of nano-HA coating deposited on biodegradable Mg-Zn-Mn alloy. *Surface and Coatings Technology*, 346, 9-18.
- [8] Feng, X., Sureda, A., Jafari, S., Memariani, Z., Tewari, D., Annunziata, G., ... & Sychrová, A. (2019). Berberine in cardiovascular and metabolic diseases: from mechanisms to therapeutics. *Theranostics*, 9(7), 1923.
- [9] Bashir, S., Sharma, V., Lgaz, H., Chung, I. M., Singh, A., & Kumar, A. (2018). The inhibition action of analgin on the corrosion of mild steel in acidic medium: A combined theoretical and experimental approach. *Journal of Molecular Liquids*, 263, 454-462.
- [10] Sidhu, G. K., Singh, S., Kumar, V., Dhanjal, D. S., Datta, S., & Singh, J. (2019). Toxicity, monitoring and biodegradation of organophosphate pesticides: a review. *Critical Reviews in Environmental Science and Technology*, 49(13), 1135-1187.
- [11] Nanda, V., & Kant, N. (2014). Enhanced relativistic self-focusing of Hermite-cosh-Gaussian laser beam in plasma under density transition. *Physics of Plasmas*, 21(4), 042101.
- [12] Kotla, N. G., Gulati, M., Singh, S. K., & Shivapooja, A. (2014). Facts, fallacies and future of dissolution testing of polysaccharide based colon-specific drug delivery. *Journal of Controlled Release*, 178, 55-62.
- [13] Farooq, R., & Shankar, R. (2016). Role of structural equation modeling in scale development. *Journal of Advances in Management Research*.
- [14] Singh, S., Ramakrishna, S., & Gupta, M. K. (2017). Towards zero waste manufacturing: A multidisciplinary review. *Journal of cleaner production*, 168, 1230-1243.
- [15] Mahla, S. K., Dhir, A., Gill, K. J., Cho, H. M., Lim, H. C., & Chauhan, B. S. (2018). Influence of EGR on the simultaneous reduction of NO_x-smoke emissions trade-off under CNG-biodiesel dual fuel engine. *Energy*, 152, 303-312.
- [16] Nanda, V., Kant, N., & Wani, M. A. (2013). Self-focusing of a Hermite-cosh Gaussian laser beam in a magnetoplasma with ramp density profile. *Physics of Plasmas*, 20(11), 113109.
- [17] Kaur, P., Singh, S. K., Garg, V., Gulati, M., & Vaidya, Y. (2015). Optimization of spray drying process for formulation of solid dispersion containing polypeptide-k powder through quality by design approach. *Powder Technology*, 284, 1-11.
- [18] Sharma, D., & Saharan, B. S. (2016). Functional characterization of biomedical potential of biosurfactant produced by *Lactobacillus helveticus*. *Biotechnology Reports*, 11, 27-35.
- [19] Wani, A. B., Chadar, H., Wani, A. H., Singh, S., & Upadhyay, N. (2017). Salicylic acid to decrease plant stress. *Environmental Chemistry Letters*, 15(1), 101-123.
- [20] Mishra, V., Patil, A., Thakur, S., & Kesharwani, P. (2018). Carbon dots: emerging theranostic nanoarchitectures. *Drug discovery today*, 23(6), 1219-1232.

- [21] Kumar, V., Pitale, S. S., Mishra, V., Nagpure, I. M., Biggs, M. M., Ntwaeaborwa, O. M., & Swart, H. C. (2010). Luminescence investigations of Ce³⁺ doped CaS nanophosphors. *Journal of alloys and compounds*, 492(1-2), L8-L12.
- [22] Pudake, R. N., Swaminathan, S., Sahu, B. B., Leandro, L. F., & Bhattacharyya, M. K. (2013). Investigation of the *Fusariumvirguliformefvtox1* mutants revealed that the FvTox1 toxin is involved in foliar sudden death syndrome development in soybean. *Current genetics*, 59(3), 107-117.
- [23] Kapoor, B., Singh, S. K., Gulati, M., Gupta, R., & Vaidya, Y. (2014). Application of liposomes in treatment of rheumatoid arthritis: quo vadis. *The scientific world Journal*, 2014.
- [24] Haldhar, R., Prasad, D., & Saxena, A. (2018). Myristica fragrans extract as an eco-friendly corrosion inhibitor for mild steel in 0.5 M H₂SO₄ solution. *Journal of Environmental Chemical Engineering*, 6(2), 2290-2301.
- [25] Bordoloi, N., Sharma, A., Nautiyal, H., & Goel, V. (2018). An intense review on the latest advancements of Earth Air Heat Exchangers. *Renewable and Sustainable Energy Reviews*, 89, 261-280.
- [26] Sharma, P., Mehta, M., Dhanjal, D. S., Kaur, S., Gupta, G., Singh, H., ... & Chellappan, D. K. (2019). Emerging trends in the novel drug delivery approaches for the treatment of lung cancer. *Chemico-biological interactions*, 309, 108720.
- [27] Goga, G., Chauhan, B. S., Mahla, S. K., & Cho, H. M. (2019). Performance and emission characteristics of diesel engine fueled with rice bran biodiesel and n-butanol. *Energy Reports*, 5, 78-83.
- [28] Umashankar, M. S., Sachdeva, R. K., & Gulati, M. (2010). Aquasomes: a promising carrier for peptides and protein delivery. *Nanomedicine: Nanotechnology, Biology and Medicine*, 6(3), 419-426.
- [29] Sharma, A., Shree, V., & Nautiyal, H. (2012). Life cycle environmental assessment of an educational building in Northern India: A case study. *Sustainable Cities and Society*, 4, 22-28.
- [30] Kaur, T., Kumar, S., Bhat, B. H., Want, B., & Srivastava, A. K. (2015). Effect on dielectric, magnetic, optical and structural properties of Nd-Co substituted barium hexaferrite nanoparticles. *Applied Physics A*, 119(4), 1531-1540.
- [31] Datta, S., Singh, J., Singh, S., & Singh, J. (2016). Earthworms, pesticides and sustainable agriculture: a review. *Environmental Science and Pollution Research*, 23(9), 8227-8243.
- [32] Vij, S., & Bedi, H. S. (2016). Are subjective business performance measures justified?. *International Journal of Productivity and Performance Management*.
- [33] Chawla, R., & Sharma, S. (2017). Molecular dynamics simulation of carbon nanotube pull-out from polyethylene matrix. *Composites Science and Technology*, 144, 169-177.
- [34] Prakash, C., & Uddin, M. S. (2017). Surface modification of β -phase Ti implant by hydroxyapatite mixed electric discharge machining to enhance the corrosion resistance and in-vitro bioactivity. *Surface and Coatings Technology*, 326, 134-145.
- [35] Saxena, A., Prasad, D., & Haldhar, R. (2018). Investigation of corrosion inhibition effect and adsorption activities of *Cuscuta reflexa* extract for mild steel in 0.5 M H₂SO₄. *Bioelectrochemistry*, 124, 156-164.
- [36] Prabhakar, P. K., Kumar, A., & Doble, M. (2014). Combination therapy: a new strategy to manage diabetes and its complications. *Phytomedicine*, 21(2), 123-130.
- [37] Wheeler, K. C., Jena, M. K., Pradhan, B. S., Nayak, N., Das, S., Hsu, C. D., ... & Nayak, N. R. (2018). VEGF may contribute to macrophage recruitment and M2 polarization in the decidua. *PLoS One*, 13(1), e0191040.

- [38] Singh, A., Lin, Y., Ansari, K. R., Quraishi, M. A., Ebenso, E. E., Chen, S., & Liu, W. (2015). Electrochemical and surface studies of some Porphines as corrosion inhibitor for J55 steel in sweet corrosion environment. *Applied Surface Science*, 359, 331-339.
- [39] Gill, J. P. K., Sethi, N., Mohan, A., Datta, S., & Girdhar, M. (2018). Glyphosate toxicity for animals. *Environmental Chemistry Letters*, 16(2), 401-426.
- [40] Kumar, V., Singh, S., Singh, J., & Upadhyay, N. (2015). Potential of plant growth promoting traits by bacteria isolated from heavy metal contaminated soils. *Bulletin of environmental contamination and toxicology*, 94(6), 807-814.
- [41] Patel, S. (2012). Potential of fruit and vegetable wastes as novel biosorbents: summarizing the recent studies. *Reviews in Environmental Science and Bio/Technology*, 11(4), 365-380.
- [42] Srivastava, G., Das, C. K., Das, A., Singh, S. K., Roy, M., Kim, H., ... & Philip, D. (2014). Seed treatment with iron pyrite (FeS₂) nanoparticles increases the production of spinach. *RSC Advances*, 4(102), 58495-58504.
- [43] Nagpal, R., Behare, P. V., Kumar, M., Mohania, D., Yadav, M., Jain, S., ... & Henry, C. J. K. (2012). Milk, milk products, and disease free health: an updated overview. *Critical reviews in food science and nutrition*, 52(4), 321-333.
- [44] Vaid, S. K., Kumar, B., Sharma, A., Shukla, A. K., & Srivastava, P. C. (2014). Effect of Zn solubilizing bacteria on growth promotion and Zn nutrition of rice. *Journal of soil science and plant nutrition*, 14(4), 889-910.
- [45] Lin, Y., Singh, A., Ebenso, E. E., Wu, Y., Zhu, C., & Zhu, H. (2015). Effect of poly (methyl methacrylate-co-N-vinyl-2-pyrrolidone) polymer on J55 steel corrosion in 3.5% NaCl solution saturated with CO₂. *Journal of the Taiwan Institute of Chemical Engineers*, 46, 214-222.
- [46] Mahesh, K. V., Singh, S. K., & Gulati, M. (2014). A comparative study of top-down and bottom-up approaches for the preparation of nanosuspensions of glipizide. *Powder technology*, 256, 436-449.
- [47] Singh, G., Gupta, M. K., Mia, M., & Sharma, V. S. (2018). Modeling and optimization of tool wear in MQL-assisted milling of Inconel 718 superalloy using evolutionary techniques. *The International Journal of Advanced Manufacturing Technology*, 97(1-4), 481-494.
- [48] Chauhan, C. C., Kagdi, A. R., Jotania, R. B., Upadhyay, A., Sandhu, C. S., Shirsath, S. E., & Meena, S. S. (2018). Structural, magnetic and dielectric properties of Co-Zr substituted M-type calcium hexagonal ferrite nanoparticles in the presence of α -Fe₂O₃ phase. *Ceramics International*, 44(15), 17812-17823.
- [49] Sharma, A., Shahzad, B., Kumar, V., Kohli, S. K., Sidhu, G. P. S., Bali, A. S., ... & Zheng, B. (2019). Phytohormones regulate accumulation of osmolytes under abiotic stress. *Biomolecules*, 9(7), 285.
- [50] Balakumar, P., Chakkarwar, V. A., Kumar, V., Jain, A., Reddy, J., & Singh, M. (2008). Experimental models for nephropathy. *Journal of the Renin-Angiotensin-Aldosterone System*, 9(4), 189-195.
- [51] Singh, A., Lin, Y., Liu, W., Kuanhai, D., Pan, J., Huang, B., ... & Zeng, D. (2014). A study on the inhibition of N80 steel in 3.5% NaCl solution saturated with CO₂ by fruit extract of *Ginkgo biloba*. *Journal of the Taiwan Institute of Chemical Engineers*, 45(4), 1918-1926.
- [52] Kaur, T., Kaur, B., Bhat, B. H., Kumar, S., & Srivastava, A. K. (2015). Effect of calcination temperature on microstructure, dielectric, magnetic and optical properties of Ba_{0.7}La_{0.3}Fe₁₁Co_{0.7}O₁₉ hexaferrites. *Physica B: Condensed Matter*, 456, 206-212.

- [53] Singh, P., Singh, A., & Quraishi, M. A. (2016). Thiopyrimidine derivatives as new and effective corrosion inhibitors for mild steel in hydrochloric acid: Electrochemical and quantum chemical studies. *Journal of the Taiwan Institute of Chemical Engineers*, 60, 588-601.
- [54] Anand, A., Patience, A. A., Sharma, N., & Khurana, N. (2017). The present and future of pharmacotherapy of Alzheimer's disease: A comprehensive review. *European journal of pharmacology*, 815, 364-375.
- [55] Saxena, A., Prasad, D., Haldhar, R., Singh, G., & Kumar, A. (2018). Use of *Sida cordifolia* extract as green corrosion inhibitor for mild steel in 0.5 M H₂SO₄. *Journal of environmental chemical engineering*, 6(1), 694-700.
- [56] Ahmadi, M. H., Ghazvini, M., Sadeghzadeh, M., Alhuyi Nazari, M., Kumar, R., Naeimi, A., & Ming, T. (2018). Solar power technology for electricity generation: A critical review. *Energy Science & Engineering*, 6(5), 340-361.
- [57] Kant, N., Wani, M. A., & Kumar, A. (2012). Self-focusing of Hermite–Gaussian laser beams in plasma under plasma density ramp. *Optics Communications*, 285(21-22), 4483-4487.
- [58] Gupta, V. K., Sethi, B., Upadhyay, N., Kumar, S., Singh, R., & Singh, L. P. (2011). Iron (III) selective electrode based on S-methyl N-(methylcarbamoyloxy) thioacetimidate as a sensing material. *Int. J. Electrochem. Sci*, 6, 650-663.
- [59] Mehta, C. M., Srivastava, R., Arora, S., & Sharma, A. K. (2016). Impact assessment of silver nanoparticles on plant growth and soil bacterial diversity. *3 Biotech*, 6(2), 254.
- [60] Gupta, V. K., Guo, C., Canever, M., Yim, H. R., Sraw, G. K., & Liu, M. (2014). Institutional environment for entrepreneurship in rapidly emerging major economies: the case of Brazil, China, India, and Korea. *International Entrepreneurship and Management Journal*, 10(2), 367-384.
- [61] Singh, A., Lin, Y., Obot, I. B., Ebenso, E. E., Ansari, K. R., & Quraishi, M. A. (2015). Corrosion mitigation of J55 steel in 3.5% NaCl solution by a macrocyclic inhibitor. *Applied Surface Science*, 356, 341-347.
- [62] Ansari, K. R., Quraishi, M. A., Singh, A., Ramkumar, S., & Obote, I. B. (2016). Corrosion inhibition of N80 steel in 15% HCl by pyrazolone derivatives: electrochemical, surface and quantum chemical studies. *RSC advances*, 6(29), 24130-24141.
- [63] Jnawali, P., Kumar, V., & Tanwar, B. (2016). Celiac disease: Overview and considerations for development of gluten-free foods. *Food Science and Human Wellness*, 5(4), 169-176.
- [64] Saggu, S., Sakeran, M. I., Zidan, N., Tousson, E., Mohan, A., & Rehman, H. (2014). Ameliorating effect of chicory (*Chichorium intybus* L.) fruit extract against 4-tert-octylphenol induced liver injury and oxidative stress in male rats. *Food and chemical toxicology*, 72, 138-146.
- [65] Bhatia, A., Singh, B., Raza, K., Wadhwa, S., & Katare, O. P. (2013). Tamoxifen-loaded lecithin organogel (LO) for topical application: development, optimization and characterization. *International Journal of Pharmaceutics*, 444(1-2), 47-59.
- [66] Singh, A., Lin, Y., Liu, W., Yu, S., Pan, J., Ren, C., & Kuanhai, D. (2014). Plant derived cationic dye as an effective corrosion inhibitor for 7075 aluminum alloy in 3.5% NaCl solution. *Journal of Industrial and Engineering Chemistry*, 20(6), 4276-4285.
- [67] Raza, K., Thotakura, N., Kumar, P., Joshi, M., Bhushan, S., Bhatia, A., ... & Katare, O. P. (2015). C60-fullerenes for delivery of docetaxel to breast cancer cells: a promising

- approach for enhanced efficacy and better pharmacokinetic profile. *International journal of pharmaceutics*, 495(1), 551-559.
- [68] Prabhakar, P. K., Prasad, R., Ali, S., & Doble, M. (2013). Synergistic interaction of ferulic acid with commercial hypoglycemic drugs in streptozotocin induced diabetic rats. *Phytomedicine*, 20(6), 488-494.
- [69] Chaudhary, A., & Singh, S. S. (2012, September). Lung cancer detection on CT images by using image processing. In *2012 International Conference on Computing Sciences* (pp. 142-146). IEEE.
- [70] Mishra, V., Bansal, K. K., Verma, A., Yadav, N., Thakur, S., Sudhakar, K., & Rosenholm, J. M. (2018). Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. *Pharmaceutics*, 10(4), 191.
- [71] Singh, A. (2012). Hydroxyapatite, a biomaterial: its chemical synthesis, characterization and study of biocompatibility prepared from shell of garden snail, *Helix aspersa*. *Bulletin of Materials Science*, 35(6), 1031-1038.
- [72] Arora, S., & Anand, P. (2019). Binary butterfly optimization approaches for feature selection. *Expert Systems with Applications*, 116, 147-160.
- [73] Chhikara, N., Kushwaha, K., Sharma, P., Gat, Y., & Panghal, A. (2019). Bioactive compounds of beetroot and utilization in food processing industry: A critical review. *Food Chemistry*, 272, 192-200.
- [74] Singh, S., Kumar, V., Chauhan, A., Datta, S., Wani, A. B., Singh, N., & Singh, J. (2018). Toxicity, degradation and analysis of the herbicide atrazine. *Environmental chemistry letters*, 16(1), 211-237.
- [75] Baranwal, T., & Pateriya, P. K. (2016, January). Development of IoT based smart security and monitoring devices for agriculture. In *2016 6th International Conference-Cloud System and Big Data Engineering (Confluence)* (pp. 597-602). IEEE.
- [76] Trukhanov, S. V., Trukhanov, A. V., Salem, M. M., Trukhanova, E. L., Panina, L. V., Kostishyn, V. G., ... & Sivakov, V. (2018). Preparation and investigation of structure, magnetic and dielectric properties of (BaFe₁₁. 9Al₀. 1O₁₉) 1-x-(BaTiO₃) x bicomponent ceramics. *Ceramics International*, 44(17), 21295-21302.
- [77] Singh, S., Singh, N., Kumar, V., Datta, S., Wani, A. B., Singh, D., ... & Singh, J. (2016). Toxicity, monitoring and biodegradation of the fungicide carbendazim. *Environmental chemistry letters*, 14(3), 317-329.
- [78] Bhyan, B., Jangra, S., Kaur, M., & Singh, H. (2011). Orally fast dissolving films: innovations in formulation and technology. *Int J Pharm Sci Rev Res*, 9(2), 9-15.
- [79] Saxena, A., Prasad, D., Haldhar, R., Singh, G., & Kumar, A. (2018). Use of Saraca ashoka extract as green corrosion inhibitor for mild steel in 0.5 M H₂SO₄. *Journal of Molecular Liquids*, 258, 89-97.
- [80] Panghal, A., Janghu, S., Virkar, K., Gat, Y., Kumar, V., & Chhikara, N. (2018). Potential non-dairy probiotic products—A healthy approach. *Food bioscience*, 21, 80-89.
- [81] Kumar, D., Agarwal, G., Tripathi, B., Vyas, D., & Kulshrestha, V. (2009). Characterization of PbS nanoparticles synthesized by chemical bath deposition. *Journal of Alloys and Compounds*, 484(1-2), 463-466.
- [82] Ansari, K. R., Quraishi, M. A., & Singh, A. (2015). Corrosion inhibition of mild steel in hydrochloric acid by some pyridine derivatives: an experimental and quantum chemical study. *Journal of Industrial and Engineering Chemistry*, 25, 89-98.
- [83] Singh, P. S., Singh, T., & Kaur, P. (2008). Variation of energy absorption buildup factors with incident photon energy and penetration depth for some commonly used solvents. *Annals of Nuclear Energy*, 35(6), 1093-1097.

- [84] Ansari, K. R., Quraishi, M. A., & Singh, A. (2015). Isatin derivatives as a non-toxic corrosion inhibitor for mild steel in 20% H₂SO₄. *Corrosion Science*, 95, 62-70.
- [85] Singh, A., Lin, Y., Ebenso, E. E., Liu, W., Pan, J., & Huang, B. (2015). Ginkgo biloba fruit extract as an eco-friendly corrosion inhibitor for J55 steel in CO₂ saturated 3.5% NaCl solution. *Journal of Industrial and Engineering Chemistry*, 24, 219-228.
- [86] Dey, A., Bhattacharya, R., Mukherjee, A., & Pandey, D. K. (2017). Natural products against Alzheimer's disease: Pharmaco-therapeutics and biotechnological interventions. *Biotechnology Advances*, 35(2), 178-216.
- [87] Ansari, K. R., Quraishi, M. A., & Singh, A. (2015). Pyridine derivatives as corrosion inhibitors for N80 steel in 15% HCl: Electrochemical, surface and quantum chemical studies. *Measurement*, 76, 136-147.
- [88] Patel, S. (2012). Threats, management and envisaged utilizations of aquatic weed *Eichhornia crassipes*: an overview. *Reviews in Environmental Science and Bio/Technology*, 11(3), 249-259.
- [89] Mia, M., Gupta, M. K., Singh, G., Królczyk, G., & Pimenov, D. Y. (2018). An approach to cleaner production for machining hardened steel using different cooling-lubrication conditions. *Journal of Cleaner Production*, 187, 1069-1081.
- [90] Kondrateva T.S. Biopharmaceutical studies of children's suppositories with phosphothiamine. Pharmacy.-Moscow, 1990.-No.5.-P.14-15.
- [91] Maksudova F.Kh., Kariyeva E.S., Tursunova M.Kh. Study of the pharmacological properties of the combined gel of sodium diclofenac and benzketozone. /Infection, immunity and pharmacologists I.- Tashkent.-2015.-№5.C.160-163 /
- [92] Maksudova F. Kh., Kariyeva E. S. In vitro equivalence evaluation of diclofenac sodium generic medicinal preparation. // Pharmacy, a scientific and practical journal, special issue, St. Petersburg, 2016, pp. 461-464.
- [93] Piotrovsky V.K. Model and model-independent methods for describing pharmacokinetics: advantages, disadvantages and interrelation. // Antibiotics and medical biotechnology. -Moscow, 1997.-№7.P.492-497.
- [94] Kukes V.G., Sychev D.A. Clinical pharmacology. 5th ed., Moscow, 2017, p. 478.
- [95] Tillaeva U. M., Azizov U. M. Development of a methodology for isolating the amount of fensulcal determination from a biological object. Materials of the scientific-practical conference "Actual issues of education, science and production in pharmacy. Tashkent, 2009.-P.172 .
- [96] Tillaeva U.M. Standardization and quality control of fensulcal in soft dosage forms. // Authors' dissertation for the study of the academician of the candidate of pharmaceuticals. Sciences . Tashkent. 2011.23 s.
- [97] Golovkin V.A. On the importance of pharmacokinetics modeling for increasing the efficiency of biopharmaceutical research. // Optimization of drug supply and ways to increase the effectiveness of pharmaceutical science : Sat. Tez.dokl.-Kharkov, 1986.-P.61-62.
- [98] Stefanova A.V. Preclinical studies of medicines. Kiev. -2002. -650 p.
- [99] Altynbayeva G.B., Bozhbanbayeva N.S., Adilbekova I.M., Zhexengul S.S. Modern ideas about the birth of children with low weight the assessment of their development // Bulletin of KazNMU. 2017; (1): 185 – 187.
- [100] Belousova T.V., Andryushina I.V. Intrauterine growth retardation and its effect on the health status of children in subsequent periods of life. The possibilities of nutritional correction // Questions of modern pediatrics. 2015; V14: (1): 23-30.

- [101] Bliznetsova E.A., Antonova L.K., Kulakova N.I. Features of the course of the neonatal period in premature infants with intrauterine growth retardation // *Neonatology: news, opinions, education*. 2017; (3): 83–88.
- [102] Chernenkov Yu.V., Nechaev V.N., Dudukina E.S. Features of newborn children with intrauterine growth retardation // *Saratov Journal of Medical Scientific Research*. 2017; 13 (1): 62-67.
- [103] Deepak Sharma, Sweta Shastri and Pradeep Sharma. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects // *Pediatrics*.– 2016; (10): 67–83.
- [104] Derevtsov V.V. Some health aspects of children born with different types of intrauterine growth restriction during the early neonatal period // *Kazan Medical Journal*. 2017; V98: (1): 44 – 52.
- [105] Goryunova A.G., Simonova M.S., Murashko A.V. Fetal growth retardation syndrome and adaptation of placenta. *Arkhiv Akusherstva i Ginekologii im. V.F. Snegiryova (V.F. Snegirev Archives of Obstetrics and Gynecology, Russian journal)*. 2016; 3(2): 76—80. (In Russ.). DOI: 10.18821/2313-8726-2016-3-2-76-80
- [106] Khodjamova N.K., Rakhmonkulova Z.J., York Stein., Fazliddinova S.F. The value of antenatal risk factors in the formation of intrauterine growth retardation // *Eurasian Journal of Pediatrics*. 2020; 1(4): 20-28.
- [107] Kopobaeva I.L., Borovskaya K.A., Velikanova M.S. Perinatal delivery outcomes with intrauterine growth retardation // *Journal of Western Kazakhstan*. 2015; 2 (46): 91-94.
- [108] Kozlova L.V., Ivanov D.O., Derevtsov V.V., Priima N.F. Changes in the cardiovascular system in children born with fetal growth retardation in the first half of life. *Russian Bulletin of Perinatology and Pediatrics*. 2016; 6 (61): 59–67.
- [109] Levine T.A., Grunau R.E., McAuliffe F.M., Pinnamaneni R. et al. Early childhood neurodevelopment after intrauterine growth restriction: a systematic review // *Pediatrics*. - 2015.- Vol. 135. - №1. - P. 126–141.
- [110] Nardoza, L.M.M., Caetano, A.C.R., Zamarian, A.C.P. et al. Fetal growth restriction: current knowledge. *Arch Gynecol Obstet*. 2017; (295): 1061–1077. <https://doi.org/10.1007/s00404-017-4341-9>
- [111] Petrova I.N., Trubachev E.A., Kovalenko T.V., Ozhegov A.M. Features of adaptation of the cardiovascular system in the neonatal period in children with intrauterine growth retardation // *Russian Bulletin of Perinatology and Pediatrics*. 2016; (3): 40-45.
- [112] Rakhmankulova Z.Zh., Fayzieva Z.B., Gulyamova M.A., Khojimetova Sh.Kh. Priority risk factors and the structure of congenital heart defects in newborns with enrichment of the pulmonary circulation. // *Scientific and practical journal "Doctor graduate student", Voronezh*. 2015; 3 (70): 241-245.
- [113] Ryumina I.I., Kirillova E.A., Narogan M.V., Grosheva E.V., Zubkov V.V. Feeding and postnatal growth of preterm infants with intrauterine growth retardation // *Neonatology: News, Opinions, Training*. 2017; (1): 98–107.
- [114] Zamaleeva R.S., Maltseva L.I., Cherepanova N.A., Frizina A.V., Lazareva V.K., Yupatov E.Yu., Kogan Ya.E., Fattakhova F.A. . The state of the problem of treatment and prediction of fetal growth retardation // *Practical medicine*. 2016; 1 (93): 41-44.
- [115] Ulyanina E.V., Akhmadeev N.R., Khayrullina G.R. Pathology of the placenta with fetal growth retardation - echographic and morphological signs of a critical condition // *Kazan Medical Journal*. 2016; 97 (6): 869-872.