

Features of Adaptive Shifts in the Autonomic Regulation of the Heart Rate of Newborns Born to Women with Preeclampsia in the Dynamics of the Early Neonatal Period

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Abstract: The work under study consisted in determining the informativeness of a complex of research methods in the "mother-fetus-newborn" system to determine the adaptive capabilities of the cardiovascular system and were expressed in the following provisions:

The need to take into account the postnatal gestational age (PGV) and physiological immaturity of full-term and premature infants in the interpretation and differential diagnosis of clinical and neurological disorders in the general adaptation of newborns.

Keywords: physiological immaturity, preeclampsia, functional failure.

Introduction

Preeclampsia (PE), preeclampsia of pregnant women, OPG-preeclampsia (edema, proteinuria, hypertension) are the syndrome of multiple organs, and polysystemic functional failure that develops during pregnancy [1,3,5,7,11]. PE in pregnant women is not an independent disease, but a syndrome caused by a mismatch in the capabilities of the adaptive systems of the body of women to adequately meet the needs of the developing fetus [2, 4]. It has been shown that this discrepancy develops through varying degrees of diffusion-perfusion insufficiency of the placenta [6, 7,10]. PE continues to be one of the most frequent and formidable complications of pregnancy and childbirth, leading to a disruption in the health of the mother, fetus and newborn [9]. In addition, PE is the most mysterious condition, due to the lack of an answer to the questions: why PE develops only during pregnancy, occurs with a living fetus and only in humans, does not occur in nature in animals and in fetal anencephaly [11].

According to the literature, PE is detected in 18-22% of pregnant women [3, 4,12], and in

specialized hospitals intended for high-risk groups of women, its frequency reaches 28-30% [4]. The growing frequency of PE is largely explained by an increase in the growth of extragenital diseases (EHD) in the population of women of reproductive age, such as kidney disease, endocrinopathy, arterial hyper- and hypotension, diabetes mellitus, obesity, anemia, heredity for PE, genetic forms of thrombophilia [2,7]. According to some researchers, an increase in the frequency of PE is also associated with the changed socio-economic living conditions of the population [10].

Materials and Methods

To solve the set goals and objectives of this work, we conducted a comparative study of pregnant women, women in labor, and their fetuses with clinical and laboratory signs of PE (main group, n = 97) and without manifestations of the latter (control group, n = 30). Pregnant women were observed and examined in the conditions of antenatal clinics, antenatal departments, according to the order of the Ministry of Health of the Republic of Uzbekistan No. 425 dated September 25, 2005 "On the introduction of modern technologies to improve the efficiency of providing care to pregnant women in primary health care institutions of the Republic of Uzbekistan."

The studies were carried out on the basis of our own observations and data from medical records - "individual card of pregnant women and women in labor" (form No. 111 / U), "Exchange card of a maternity hospital, maternity ward of a hospital" (f No. 113 / U), "Medical card of an outpatient patient» (f # 025 / U), "Card of dispensary observation" (f # 030 / U), birth histories, newborns, the conclusion of specialists on paraclinical research methods.

To establish and form a clinical diagnosis of PE, the currently generally accepted classification of PE according to the Gooke scale modified by G.M. Savelyeva et al. Was used. [10], taking into account the assessment of elevated systolic (SBP), diastolic pressure (DBP), the presence of edema, proteinuria, gestational age (in weeks), when the sign of PE was first established, intrauterine growth retardation (delay in a week), the presence of background and extragenital diseases before and during pregnancy. After receiving paraclinical indicators and data from instrumental studies, an additional assessment of the severity of PE was carried out according to the A.M. Vinzileos scale [1].

Results and Discusions

As known, the birth of a child leads to a qualitatively new level of activity of organs and systems, necessary for adaptation to postnatal life [8]. In this regard, the main task of this sub-chapter was to study the adaptive capabilities of newborns born to women with PE using the method of cardiointervalography (CIG), the data of which are given in Table. 1. As can be seen from the data table. 1, in newborns born to women without signs of PE, on days 2-4, compared with 5-7 days of life, a shortening of RR cardiocycles ($P < 0.001$) is found, with a lower heart rate variability (HR) - Δx , σ ($P < 0.001$), and high indicators ($P < 0.001$), the autonomic response index (ARI), the vegetative rhythm index (VRI), and the indicator of the adequacy of regulation processes (IARP), stress index (SI). These data indicate a high mobilization of the adaptive capabilities of newborns born to women without manifestations of PE, activation of the sympathetic division of the ANS, and

reflect their "stressful" response to childbirth and the transition to new conditions of postnatal existence. In these newborns, by 5-7 days of life, an increase in the value of cardiocycles RR occurs, therefore, a decrease in heart rate ($P < 0.001$), Δx and σ ($P < 0.001$), with a insignificant decrease in the amplitude of the mode (IOM), ARI, VRI, IARP and SI ($P < 0.001$). These data indicate a shift in the autonomic balance towards the prevalence of the parasympathetic division of the ANS, in particular, the autonomous circuit of regulation of the heart rhythm by the sinus node [3].

Table 1

Cardiointervalography (CIG) indices in the examined newborns depending on the day of postnatal life ($M \pm m$)

№	Indicators of CIG	Control group n=21		Treatment group n=62		P ₁	P ₂
		2 – 4 days	5 – 7 days	2 – 4 days	5 – 7 days		
1.	M av, sec	0,44±0,01	0,55±0,005***	0,464±0,004	0,482±0,01	<0,05	<0,001
2.	Δx , sec	0,12±0,003	0,142±0,002***	0,134±0,002	0,141±0,005	<0,001	<0,001
3.	σ , sec	0,024±0,002	0,032±0,001***	0,028±0,001	0,027±0,001	>0,05	>0,05
4.	IOM, %	40,2±1,66	29,8±0,44***	37,1±0,81	23,7±1,42***	>0,05	<0,001
5.	ARI, con. u.	404,8±14,4	195,0±3,08***	207,8±3,91	173,7±6,76***	<0,001	<0,05
6.	VRI, con. u.	25,0±1,18	11,4±0,31***	19,9±0,38	15,5±1,04***	<0,001	<0,001
7.	IARP, con.u.	98,0±4,26	51,8±1,12***	151,3±3,16	47,7±1,95***	<0,001	>0,05
8.	IN, con. u.	371,5±24,4	84,3±14,7	364,7±27,3	120,7±39,1***	>0,05	>0,05
9.	σ / M avg	0,055±0,002	0,054±0,002	0,060±0,001	0,056±0,001**	<0,05	>0,05
10.	$\Delta x / M$ avg	0,273±0,001	0,258±0,007	0,284±0,004	0,293±0,004	<0,001	<0,001

Note: 1. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ - statistically significant within the group

2. P₁ - P₂ - statistical reliability of indicators of the control and main group of newborns on days 2-4 and 5-7 of life

Consequently, in newborns born to women with PE, the adaptive reactions of SR on days 2-4 of their life occur against the background of lower activity of the sympathetic nervous circuit of heart rate regulation. In newborns of the main group, on the 5-7th day of their life, there is a decrease in IOM, ARI, IARP, and σ / M_{av} ($P < 0.001$). These data indicate the inadequacy of regulation (dysregulation) processes between the activity of the sympathetic division of the ANS and the leading level of functioning of the heart rhythm - the sinus node. This is confirmed by severe bradycardia ($RR \geq 0.58$ sec) in 3 (4.84%) newborns born to women

with PE, impaired automatism of the sinus node ($\Delta x \geq 0.16$ sec, $CV \geq 8.0\%$) in 4 (6.45%), against the background of a significant predominance of the parasympathetic division of the ANS ($\Delta \geq 0.06$ sec), $IOM \leq 30.0\%$, $IN \leq 150.0$ conventional units. Also, in 8 (12.9%) cases, a significant increase in IU (≥ 500 conventional units) was found, against the background of an increase in σ / Mav (≥ 0.08 conventional units) and $\Delta x / Mav$ (≥ 0.40), indicating the multidirectional shifts in the ANS, dysregulation of the heart rhythm and the presence of arrhythmias. IOM children in the control group, only 1 (4.76%) case revealed moderate sinus bradycardia ($RR = 0.58$, heart rate = 103 beats/min) in a child with a bodyweight (2750.0 grams) inappropriate for gestational age (39 weeks). Consequently, dysregulatory changes in the heart rate of newborns in the main group are 5 times more common (24.2%) than in children of the control group (4.76%, $P < 0.01$). It is known that chronic (intrauterine) fetal hypoxia, as a consequence of the mother's PE, causes long-term structural changes in the fetoplacental system. Apparently, this creates conditions for persistent suppression of the sympathetic division of the ANS. It persists for a long time after birth, being the basis for the formation of an impaired sympathetic response to environmental stimuli during the neonatal period and in later periods of ontogenies. One of the delayed consequences of preserved autonomic dysregulation is the formation of persistent vegetative-visceral and vegetative-sulistic disorders, which require in-depth studies. Table 2 shows the CIG indices of the examined newborns on the 2nd-4th day of their life at different times of the day.

Table 2

Indicators of cardiointervalography (CIG) in newborns of the control and the treatment group at different times of the day
 (2-4 days of life)

№	Indicators of CIG	6 hours		12 hours		18 hours		24 hours	
		Control group	Treatment group						
1.	M av., sec	0,388±0,026	0,462±0,022 *	0,400±0,011	0,469±0,019**	0,425±0,02	0,448±0,019	0,458±0,012	0,435±0,01
2.	Δx, sec	0,125±0,011	0,114±0,006	0,100±0,007	0,149±0,011***	0,09±0,01	0,114±0,014	0,195±0,024	0,116±0,011**
3.	σ, sec	0,024±0,002	0,023±0,003	0,019±0,002	0,029±0,002**	0,02±0,003	0,023±0,002	0,039±0,005	0,023±0,003**
4	Mo, sec	0,415±0,024	0,464±0,022	0,393±0,013	0,473±0,029**	0,430±0,026	0,442±0,022	0,430±0,011	0,436±0,011
5	IOM, %	36,0±2,68	49,0±4,59	42,3±2,11	28,9±2,4***	40,3±6,09	43,2±3,92	42,0±2,59	45,3±4,06
6	ARI, con.	304,1±32,0	632,8±44,1	466,7±34,7	236,1±18,6***	690,0±33,1	601,3±50,5	235,0±21,8	565,0±44,8***
7	VRI, con.	21,3±2,31	24,3±3,99	27,7±1,11	16,5±0,99***	36,5±2,25	28,1±2,04**	13,5±0,93	26,5±1,49***
8	IARP, con	92,5±8,21	106,0±6,79	110,2±7,52	74,6±2,79***	101,5±6,75	101,2±15,4	95,8±4,58	105,3±10,7
9	IS, con.	395,1±41,2	679,1±31,0***	610,8±35,7	257,5±27,5***	911,7±41,3	725,6±49,9**	272,3±16,0	673,1±102,5***
10	σ / M avg	0,069±0,009	0,049±0,009	0,049±0,004	0,065±0,099	0,044±0,007	0,049±0,007	0,084±0,008	0,052±0,006**
11	Δx / M avg	0,348±0,036	0,246±0,036	0,249±0,019	0,325±0,048	0,272±0,016	0,251±0,026	0,421±0,009	0,263±0,033***
12	CV, %	6,92±0,74	4,91±0,74	4,96±0,38	6,46±0,83	4,43±0,62	4,48±0,44	8,88±0,82	5,58±0,66**

Note: * P <0.05, ** P <0.01, *** P <0.001 compared with the control group

As can be seen from the data in the table 2, in newborns born to women with PE, compared with children in the control group, at 6 o'clock in the morning the value of the cardiac cycle increased - RR, instantaneous oscillation amplitude (IOM) % ($P < 0.05$), ARI, SI and $\Delta x / Mav$ ($P < 0.01-0.001$). By 12 o'clock in the afternoon in these children, the cardiac cycle is even more lengthened - RR ($P < 0.01$), Δx , σMO ($P < 0.01-0.001$) increases, and IOM, ARI, VRI, IARP and SI ($P < 0.001$). By 18 hours, the CIG indices in both groups of newborns had relatively stabilized, however, the newborns of the main group have low values of CMR and IN ($P < 0.01$). At 24:00 in the newborns of the main group, the values of Δx , σ , σ / Mav , $\Delta x / Mav$, CV% decreased ($P < 0.01-0.001$), and the indicators of ARI, VCR, and SI increased ($P < 0.001$).

We have analyzed the diurnal dynamics of the derived indicators of CIG of newborns on days 2-4 of their life, the results of which are presented in table 3. At the same time, it was noted that in newborns of the control group, the indicator of daily variability (CVD) in terms of Dx (heart rate variability) is highest at night - 24 hours (152.5%), compared to 12-18 hours of daytime (78.1 -70.3%, $P < 0.01-0.001$). In accordance with the shifts in Dx in newborns of the control group at 6 and 24 hours of the day, low values of ARI (71.7-55.4%), VLF (85.9-54.4%), and SI (72.2-49, 3%), with sufficient adequacy of the processes of regulation of the heart rhythm - IARP (92.5-95.8%). These data indicate that in newborns of the control group, already by 2-4 days of their life, the activation of the parasympathetic division of the ANS begins at night, as evidenced by the decrease in the indicators of ARI, VRI, and SI. At the same time, in the newborns of the control group, in the daytime (12 hours), especially by 18 hours, there is a high mobilizing force of the sympathetic division of the ANS, which is evident from the data of high values of ARI (110.1-162.7%), CMV (111.7 -147.2%) and SI (111.6-166.5%).

Table 3
 Diurnal dynamics of CIG derivatives in examined newborns on days 2-4 of life

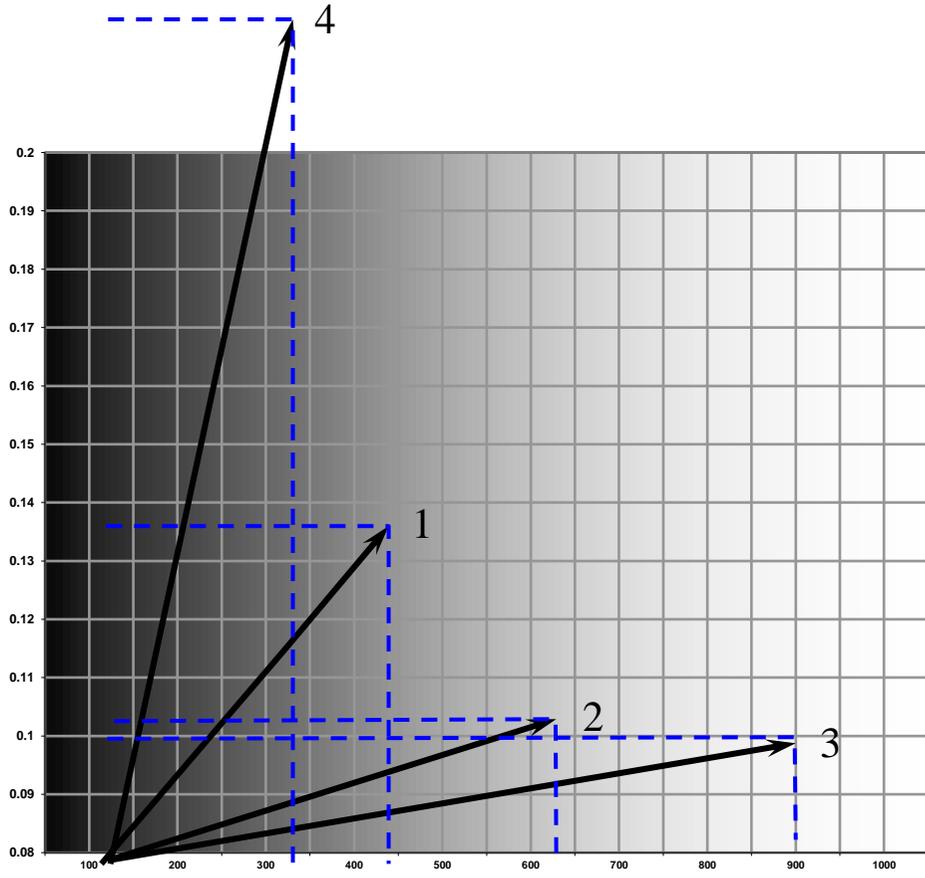
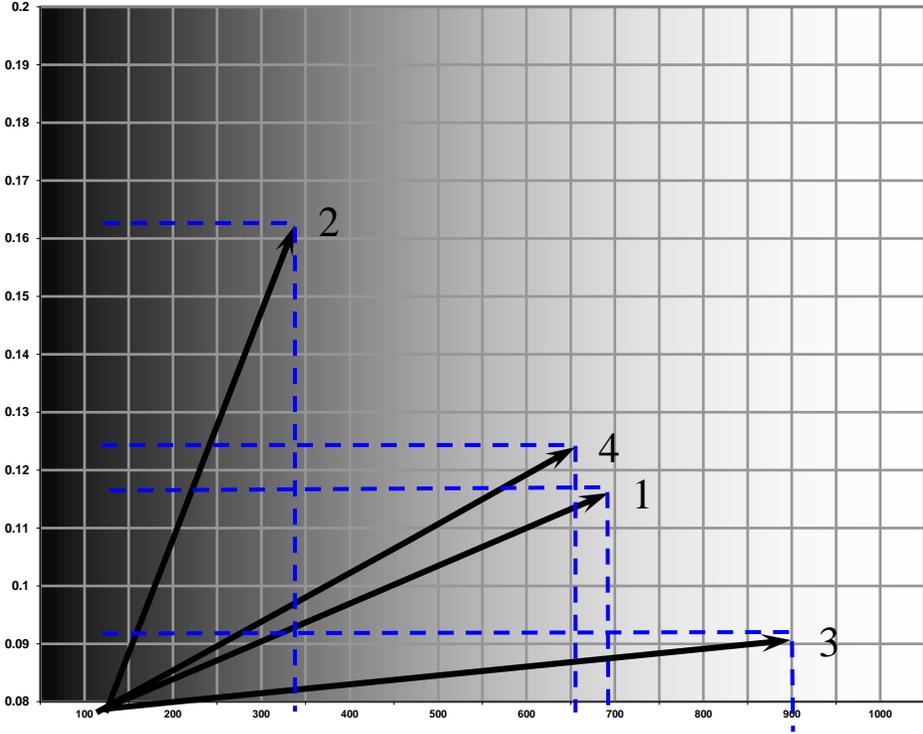
№	Indicators CIG	Indicators of daily variability (IDV)								Coefficient of daily periodicity (CDP)		Indicators of daily adaptability (IDA)	
		6		12		18		24					
		C	T	C	T	C	T	C	T	C	T	C	T
1	Mo, sec	99,5	102,2	94,2	104,2*	103,1	97,4	103,1	96,0	1,03	0,98	-5,9	1,94
2	Δx , sec	97,7	92,7	78,1	121,1*	70,3	92,7*	152,3	94,3*	1,68	0,87	-20,0	30,7
3	IOM,%	89,6	117,8*	105,2	69,5*	100,2	103,8	104,5	108,9	0,94	1,31	17,5	-41,0
4	ARI, conventional units	71,7	124,4*	110,1	46,4*	162,7	118,2*	55,4	111,0*	0,46	1,43	53,5	-62,7
5	VRI, conventional units	85,9	101,7*	111,7	69,0*	147,2	117,6*	54,4	110,9*	0,38	1,14	30,0	-32,1
6	IARP, conventional units	92,5	109,5*	110,2	77,1*	101,5	104,5	95,8	108,9*	0,89	1,2	19,1	-29,6
7	SI, conventional units	72,2	116,3*	111,6	44,3*	166,5	124,3*	49,7	115,3*	0,44	1,37	51,6	-62,1

It is noteworthy that in the newborns of the control group, the indicators of daily frequency (IDF), as the ratio of CIG indicators at night (24-6 hours) to daytime (12-18 hours), are the highest in terms of Δx (1.68), and according to the data of ARI, VLF and SI (0.46, 0.38 and 0.44) low ($P < 0.001$).

Indicators of daily adaptability (IDA), reflecting the ratio of the difference in CIG values at 12 and 6 hours. to the data of the 6-hour indicator (%) in these children is also the highest according to the data of Δx (-20.0%), ARI (53.5%), CMR (30.0%), and SI (54.6%).

As can be seen from the data table 3, IDV indicators of CIG in newborns born to women with PE differ significantly from those of children in the control group. Thus, the highest values of PSA were revealed for Δx (121.1%), and low values - for values of IOM (69.5%), ARI (46.4%), VRI (69.0%) and SI (44, 1%) at 12 noon ($P < 0.001$). The periods with the

highest activity of the parasympathetic division of the ANS, detected in children of the control group (6 and 24), in the newborns of the main group were replaced with an increase in ARI (124.4- 111.0%), VRI (110.9%) and SI (116, 3%). From these data, it follows that in the newborns of the main group, according to the IDV data, desynchronois is traced in the daily activity of the parasympathetic (at night) and the activity of the sympathetic component of the ANS (daytime). This is proved in these children by an increase in the CSP, i.e. a decrease in Δx (0.87), an increase in ARI (1.45), VRI (1.14) and SI (1.57), and inadequacy of processes in the regulation of heart rhythm - IARP (1.2). Also, these children have significantly reduced IDA in terms of IOM (-41%), ARI (-62.7%), CMR (-32.1%), IARP (-29.6%) and SI (-62.1%), against the background of increased Dx values (30.0%), appointee to a decrease at night. These shifts in every way reflect the daily dynamics of Δx (variation range) and SI (degree of centralization of heart rate control) (Fig. 1).



As can be seen from the data in Fig. 1, in newborns of the control group, the most optimal ratio of Δx and SI occurs at 6 a.m., with the daytime activity of sympathetic regulation over the heart rate (decrease in Δx , increase in SI) with a maximum of acrophase at 6 p.m. In these children, at 24 hours, the least activity of the sympathetic (low IN SI and the greatest of the parasympathetic division of the ANS (Δx high) occurs. Unlike children in the control group, in children of the main group, the greatest activity of the sympathetic division is observed at 6, 18, and 24 hours (high IU), which by 12 noon are replaced by a significant "drop" in the activity of the sympathetic, and an increase in the parasympathetic division of the ANS (low Δx). At the same time, the value of Δx , reflecting the state of adaptation of the heart rate to external stimuli, is significantly lower (≤ 0.15 sec) than in children of the control group (0.195 sec).

Concluion

Thus, a comparison of the parameters of CIG, rhythmograms, histograms and ACF of the heart rate function in newborns during the first week of their lives suggests that the main regularity in the formation of regulatory mechanisms in the early neonatal period is a change in the level of organization of functions from the central type of regulation to the beginning. activation of cholinergic (parasympathetic) activity, i.e. processes of autonomous regulation. These conclusions are based on the fact that in newborns of the control group by the 5-7th day of life, rhythmic fluctuations of the heart rate are quite clearly formed, in connection with the optimal ratio of respiratory (ORP) and slow-wave structures (SWS), indicating a dynamic relationship between the central links in the regulation of the cardiovascular system. In the newborns of the main group, such a pattern is not observed, i.e. there is no activation of parasympathetic influences on the heart rate in the second half of the day (ORP does not increase), the share of MB-II order is high, indicating a high level of regulation of the heart rate, leading to a decrease in the activity of the autonomous circuit over the sinus rhythm. In this regard, it can be assumed that the ratio of ORP and SWS in the wave structure of the heart rhythm, their shift during the day in newborns of the control group is an indicator of the adequacy of the regulation of the heart rate by the central nervous system, and a decrease in ORP and an increase in SWS-I order, as a prognostically unfavorable parameter of the heart rate, indicating a violation of adaptation, the development of dysadaptive phenomena.

Acknowledgment

The use of the method of cardiointervalography (CIG) in newborns in the early neonatal period makes it possible to determine the regularities of the formation of regulatory mechanisms of the heart rhythm, i.e. a change in the level of organization by function from the central type of regulation and sympathicotonia during the day, to the predominance of parasympathetic activity and processes of autonomous regulation at night.

CIG derivatives, as an indicator of diurnal variability (ORP), diurnal periodicity (DP),

and an indicator of daily adaptation (IDA), being highly informative parameters in studying the reactivity of daily compensation, proven valuable information on assessing the formation of postnatal adaptation in newborns.

In newborns born to women without signs of preeclampsia and extragenital diseases, the early neonatal period is characterized by synchronization of the daily activity of the sympathetic and parasympathetic VNS link in the daytime and at night

References

- [1]. Berner-Trabska M, Kowelska-Koprck U., Karowicz-Bilinska A et al. The course of pregnancy and perinatal period in overweight or obese pregnant women with regard to the condition of the newborn - own experience. //Gynecol. Pol. - 2009.- v.80, №11, p. 845-850.
- [2]. Bohlmann M.K., Tritzechinq B., Lucolders D.W., Hornemann A. Impact of assisted reproduction on obstetrics and neonatology.//J. Geburtshilfe Neonatal-2009-v.213,-S. 213-216
- [3]. Dilfuzahon Mamarasulova, Abdulla Abduhakimov, Doniyor Tursunov, Dilbarkhon Urmanbaeva, Oybek Jalolov, Zuhridin Isaev / Comparative Analysis of the Mortality Structure of the Population of Andijan Region for 2016-2018/ Journal of Cardiovascular Disease Research, Vol 11, Issue 2, April June, 2020/ DOI: 10.31838/jcdr.2020.11.02.01
- [4]. Isakova et al.: To examine clinical characteristics for the detection of cervical cancer, according to a checkup in Andijan region /International Journal of Current Research and Review.P 28-32 /DOI: <http://dx.doi.org/10.31782/IJCRR.2020.12146>
- [5]. Mikolajczyk R.T., Zhang J., Ford J., Grewel J. Effects of inter pregnancy interval on blood Pressure in conceptive Pregnancies.// Am. J. Epidemiol., 2008, v. 165, p. 422-426.
- [6]. Ortigosa Rocha C., Bitter R.E., Zugaib M. Neonatal outcomes of late-preterm birth associated or not with intrauterine growth restriction.//Obstet Gynecol Int.- 2010, v. 129, №3, p.1 18-124.
- [7]. Ortigosa Rocha C., Bitter R.E., Zugaib M. Neonatal outcomes of late-preterm birth associated or not with intrauterine growth restriction.//Obstet Gynecol Int.- 2010, v. 129, №3, p.1 18-124.
- [8]. Puorrat O., Pierre F. Late prognosis after pre-eclampsia.//Ann. Fr. Anesth. Reanim.,2010,v.29,№8, p.155-160.
- [9]. Puorrat O., Pierre F. Late prognosis after pre-eclampsia.//Ann. Fr. Anesth. Reanim.,2010,v.29,№8, p.155-160.
- [10]. Rasmussen S., Irgens L.M. Pregnancy- induced hypertension in women Who Were Born Small.// Hypertension, 2007, v.49, p.806-812.
- [11]. Fakhriddin Abdikarimov, Kuralbay Navruzov. Mathematical method of calculating the volume of the cavities of the heart ventricles according to echocardiography. European Journal of Molecular & Clinical Medicine, 2020, Volume 7, Issue 8, pp. 1427-1431.
- [12]. Rasmussen S., Irgenst M. History of Fetal Growth Restriction is More Strongly Associated with Severe Rather Than Milder Pregnancy -Induced hypertension. //Hypertension, 2008, v.51, p. 1231-1238.
- [13]. Rasmussen S., Irgenst M. History of Fetal Growth Restriction is More Strongly Associated with Severe Rather Than Milder Pregnancy -Induced hypertension. //Hypertension, 2008, v.51, p. 1231-1238.
- [14]. Fakhriddin Abdikarimov, Kuralbay Navruzov. Mathematic modeling of pulsation movement of blood in large arteries. European Journal of Molecular & Clinical Medicine, 2020, Volume 7, Issue 8, pp.1438-1444.