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EFFECT OF CYTOMEGALOVIRUS INFECTION ON INFANT NERVOUS SYSTEM DAMAGE

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Abstract: purpose: to determine the role of cytomegalovirus infection in the damage of the nervous system of babies. **Material and methods:** based on the analysis of the examination results of 130 newborns in the Samarkand regional perinatal center and maternity complex No. 1 in the city of Samarkand in 2022-2023. **Results:** based on the results of laboratory and instrumental examination of observed babies. **Conclusion:** in the analysis of results of neurosonography dopplerometry in infants born to mothers with SMVI, it was determined from the results of the analysis that along with pathological changes in the brain, the resistance of cerebral arterial blood vessels increased, and the speed of blood vessels in the vein of Galena decreased.

Key words: Cytomegalovirus, infants, nervous system, neurosonography with dopplerometry.

Intrauterine infection takes one of the leading places in perinatal mortality. Cytomegalovirus infection (CMVI) ranks first among fetal infections and is considered one of the main causes of the formation of various defects. One of the features of SMVI is its ability to parasitize inside the cell and remain in the human body for a long time with periodic reactivation and development. Cytomegalovirus (SMV) belongs to the family of herpes viruses and is its 5th representative (Human Herpes virus - 5) and is the causative agent of diseases characterized by polymorphic clinical symptoms and its variability.[1,11,13]

SMVI is divided into congenital and acquired (primary, secondary) types. SMVI is a common viral infection caused by cytomegalovirus (human cytomegalovirus), which can cause damage to internal organs and the central nervous system (in immunocompromised people and with damage to the fetus) from asymptomatic to severe general damage. manifests itself in appearances. Congenital cytomegalovirus infection is the result of transplacental transfer of the pathogen to the fetus (during primary infection of a non-immune pregnant woman or reactivation of previously infected SMV infection during pregnancy or when an immune pregnant woman is infected with another strain of cytomegalovirus infection). Mother-to-fetus transmission is more likely to occur during the intranatal period (in the presence of intrapartum cytomegalovirus infection)[2,3].

SMVI refers to persistent infections, the course of which is closely related to various relationships between mild and severe general organ damage and macroorganism. SMVI can be acute (active), chronic (with relapses) and manifests in congenital and acquired forms. Cytomegaloviruses are characterized by irregular production of viral bodies in the body and the ability to increase chronic infection, which contributes to the formation of various somatic pathologies [12]. Infection with SMVI in the fetus largely depends not on the presence of the virus in the mother's body, but on the activity of the infectious process during pregnancy [7]. The presence of SMVI in the blood leads to the infection of the placenta, its damage and subsequent infection of the fetus. SMVI can also damage smooth muscle cells, young cells of the bone marrow, and the retina [4].

Cytomegalovirus infection (CMVI) is an urgent problem of perinatology, which complicates pregnancy, delivery and neonatal period, and leads to severe fetal malformations that lead to serious complications and death [12]. An important factor in its spread is the fact that most adults are asymptomatic, and there is little awareness of the risk of infection in fetuses and newborns. [5].

The variety of clinical manifestations of the disease is determined by the ability of SMV to infect the fetus at any stage of pregnancy [3,5].

When the fetus is infected in the early period of pregnancy, various defects are formed in the central nervous system, cardiovascular system, kidney and other organs. When infected in the late period of pregnancy, damage to various organs and systems is detected in newborns. 40-90% of newborns with congenital SMVI have long-term neurological complications and hearing loss, as well as damage to the organs of vision.

In terms of teratogenicity, cytomegalovirus (SMV) ranks second after rubella. The ability of SMV to live and multiply in various cells of the human body allows us to talk about its pantropy, and the specific immunosuppressive effect of SMV is second only to HIV infection [10]. If a pregnant woman is infected during early pregnancy, various defects of the central nervous system, cardiovascular system, kidneys and other organs may develop. When infected late in pregnancy, the active form of SMVI can cause long-term neurological consequences and hearing loss in newborns, as well as damage to the organs of vision [11].

In newborns, SMVI is fatal in 80% of cases without specific therapy in the general care clinic, and severe complications can be detected in 50% of infants even if they survive the disease [8]. The most common complications in the surviving children are mental retardation, convulsion syndromes, mental retardation and retardation of psychomotor development, difficulties in speech formation, atrophy of the optic nerve, and calcifications in the brain [6].

The purpose of the work: to determine the role of cytomegalovirus infection in the damage of the nervous system of infants.

Materials and testing methods : Clinical testing materials were collected in the perinatal center of the Samarkand region and maternity complex No. 1 in the city of Samarkand during 2022-2023. Our investigation is based on the analysis of the results of examination of 130 newborns. The main group included 90 babies born to mothers with cytomegalovirus infection, and the control group included 40 babies born to healthy mothers without cytomegalovirus infection. Newborn babies born are the results of the examination. The infants, in turn, were studied in subgroups based on gestational age. Group I includes 60 full-term infants of the main group; Group II included 30 premature babies of the main group. The control group, in turn, was divided into two groups depending on the gestational age, group III - 20 full-term babies; Group IV consists of 20 "conditionally healthy" newborns born prematurely.

Babies in the main group had a body weight ranging from 920 grams to 3400 grams. And the control group body weight 4200 from 2280 grams grams of body weight created babies . 89(69%) of the total babies are boys and 41(31%) are girls.

The observed groups were collected, the sex of the babies, the study of the clinic of diseases, complications, and the observation of laboratory and instrumental examination were carried out.

The problem of perinatal damage of the central nervous system in newborns remains an urgent problem of neonatology, the solution of this problem will help to reduce the level of infant mortality and child disability.

Results: When the mothers' pregnancy anamnesis was collected, the main group of mothers were born with SMVI and various pathologies during pregnancy, according to which the risk of miscarriage in group I babies of the main group was 52 (86.7%) , in group II babies - and 28 (93.3%) were determined from the anamnesis of mothers. During the collection of anamnesis of pregnancy, it was found that various levels of anemia were observed in almost all mothers. It was detected in 58 (96.7%) mothers of group I babies , and in 29 (96.7%) mothers of group II babies . It was also found that mothers of the main group of babies had a history of difficult obstetrics in their previous pregnancies: 50 (83.3%) of the mothers of the first group of babies, and 24 (80%) of the mothers of the second group of babies . In addition, it was known during the anamnesis collection that mothers of the main group were diagnosed with acute toxicosis, small or large amount of vaginal discharge, turbidity,

premature discharge, pyelonephritis, severe and moderate preeclampsia. It's done. Among the above-mentioned indicators, only mild and moderate levels of anemia were detected in the mothers of the control group, 15 (75%) of the mothers of group III infants , 17 (85%) of mothers of infants of group IV , and high percentages were found in both groups. . Against the background of the risk of miscarriage, it was found that 2(10%) of the mothers of III-group babies , and 5(25%) of mothers of IV-group babies . Turbidity of water was found in 3(15%) mothers of infants of group III and in 4(20%) mothers of infants of group IV from the anamnesis survey data.

Pathological changes in all organ systems were detected during the adaptation period in the infants of the main group, whose mother had SMVI. In particular, problems of the central nervous system, respiratory system, urinary system, and pathological changes in the skin were more pronounced (Table 1). Respiratory disorder syndrome was detected in 10 (8.3%) infants of group I , and in 25 (83.3%) infants of group II. Prolonged jaundice was detected in 19 (63%) of the group of babies born before the term, and the increase of bilirubin in the clinic was observed to be high and prolonged despite medical treatment. Among the signs of MAT damage: convulsion syndrome was observed in 3(5%) of group I infants, and 7(23.3%) of group I infants . Extinction syndrome was found in 2 (3.3%) infants of group I , 5 (16.7%) of infants of group II . Anxiety syndrome was observed in 20 (33.3%) children of group I , and in 21 (70%) children of group II . Slow recall of reflexes in 13 (21.7%) children of group I , in children of group I It was found in 24 (80%) people. SMVI-specific petechial rash In group I babies , 3 (5 %) Group II was found in 3 (10%) of infants . In the control group, among the above-mentioned clinical indicators, prolonged jaundice was observed only in one of the babies of the I -II -group , and in the babies of the IV -group. 3 (15%) were found, jaundice quickly resolved after standard medical procedures.

Table 1. Clinical signs of the baby observed in the delivery room

No	Indicators	Primary group of infants (n= 90)		Control group (n=40)	
		Group I (n=60)	Group II (n=30)	Group III (n=20)	Group IV (n=20)
1	Shortness of breath, n (%)	10 (8.3%)	25 (83.3 %)	0(%)	2(10%)
2	Prolonged jaundice, n (%)	21(35%)	19(63%)	1 (5%)	3 (15%)
3	Seizure syndrome, n (%)	3(5%)	7(23.3%)	0(0%)	0(0%)
4	Extinction syndrome, n (%)	2 (3.3%)	5 (16.7%)	0(0%)	0(0%)
5	Anxiety, n (%)	20(33.3%)	21(70%)	1(5%)	2(10%)
6	Slow recall of reflexes, n (%)	13(21.7%)	24(80%)	0(5%)	2(10%)
7	Disturbances in the digestive system (stomach rest, vomiting, indigestion), n (%)	15(25%)	27(90%)	1(5%)	4(20%)
8	Hepatomegaly, n (%)	3(5%)	5(16.7%)	0(%)	0(%)
9	Petechial rash (SMVI specific), n (%)	3 (5 %)	3 (10%)	0(0%)	0(0%)
10	Infants with low birth weight for gestational age, n (%)	3 (5%)	5 (16.7%)	0(0%)	0(0%)
1 1	Congenital cataract, n (%)	0 (%)	1 (3.33%)	0(0%)	0(0%)

Babies were evaluated on the Apgar scale in the first minutes of life. According to it, compared to control group babies, it was found that the babies of the main group had lower scores (Table 2), and also the period of adaptation to life of the babies of this group was more difficult. The babies of the main group were born with an average of 3-4 points lower than the control group.

Table 2. Evaluation of infants on the APGAR scale

No	Indicators	Primary group of infants (n=90)		Control group (n=40)	
		Group I (n=60)	Group II (n=30)	Group III (n=20)	Group IV (n=20)

1	1-3 points, n (%)	8 (13.3%)	11(36.7%)	0 (%)	0 (%)
2	4-6 points, n (%)	44 (73.3 %)	16 (48%)	0 (%)	4 (20%)
3	7-10 points, n (%)	8 (13.3 %)	3 (10%)	20 (100%)	16 (80%)

The general condition of the groups of newborns after birth was evaluated . According to that, babies born to mothers with cytomegalovirus infection are group I babies 2 (3.33 %) and infants of group II 2 (6.67%) were found to be in critical condition in both groups. Babies born in severe condition are in group I babies of the main group It was found in 13 (21.67%) children, and in 10 (33.3%) children of the II group.

When we analyzed the results of the general group of infants according to gestational age and body weight, it was found that the main group of infants born to mothers with SMVI differed from the control group in terms of premature birth and low weight for gestational age . Also, compared to the group of premature babies in this group, it was found in the results of the tests that there were many pathological changes in the general condition of the birth of very low birth weight babies, and that they were fundamentally different from low birth weight babies born to mothers without SMVI. . The number of extremely low birth weight babies whose body weight was up to 1000 grams was 3 (10%) of the main group. No infants of this weight were identified in the control group. Babies with severe low body weight accounted for 10 (33.3%) of the premature babies of the main group, and 2 (10%) of the premature babies of the control group. Infants with late neonatal preterm birth weight were 17 (56.67%) in the preterm infants of the main group, and 18 (90%) in the preterm infants of the control group. It can be concluded that cytomegalovirus infection can affect the fetus at any time, and depending on the immune system of a pregnant woman, and the period of the first infection with SMVI, the fetus may be born prematurely, be born with pathological changes in its health. it was determined that

On the first day of laboratory tests, umbilical cord blood was drawn and a general blood analysis (Table 3) showed no significant change in the analysis of leukocytes between the main group I and II babies, leukocytosis was observed in both groups. According to it, the average of 15.58±4.95x in group I babies 10^9, and 17.60±6.1x 10^9/l in group II babies was determined. The same indicators 10^9were determined in the average amount of 11.70±3.19x /l in group III infants, and in the average amount of 9.75±1.97* in group IV infants . 10^9In general blood analysis, the reliability of differences between the group of preterm infants of the main group and the group of preterm infants of the control group was determined only when platelets were analyzed from their shaped elements P<0.001*. Hemoglobin, one of the indicators of anemia, was found to be low in hemoglobin among all groups of infants. Hemoglobin in group I babies was found to be 131.28±13.69g/l, and in group II it was 123.03±11.33g/l, in group III babies it was 126.45±12.87g/l, and in group IV It was determined that the average was 136.7±16.82g/l, and the reliability of the differences was determined to be P_1<0.003*, P_2<0.024*, P_3<0.003*. In our opinion, this was explained by the abundance of fetal hemoglobin in the neonatal period and their connection with metabolic processes. General blood tests did not reveal significant pathological changes in the remaining blood components.

Table 3. Observed infants' general blood analysis indicators on day 1 (M± m)

No	Indicators	Primary group of infants (n=90)		Control group (n=40		P_1, P_2, P_3
		Group I (n=60)	Group II (n=30)	Group III (n=20)	Group IV (n=20)	
1	Leukocytes 10^9/ l	15.58±4.95	17.60±6.1	11.70±3.19	9.75±1.97	0.167 0.002* <0.001*
2	Neutrophils %	52.02±13.57	58.97±7.70	53.50±13.57	53.7±14.63	<0.001* 0.628 0.377

3	Lymphocytes %	44.15±16.210	43.73±12.06	34.65±8.41	38.95±13.109	0.932 0.035* <0.001*
4	Monocytes %	7.51±3.10	6.74±2.86	6.66±2.77	28.8±8.96	0.186 0.371 0.704
5	Hemoglobin g/l	131.28±13.69	123.03±11.33	126.45±12.87	136.7±16.82	0.003* 0.024* 0.003*
6	Platelets 10^9g/l	226.37±30.91	217.13±24.51	225.6±43.21	258.8±31.38	0.128 0.925 <0.001*
7	Erythrocyte sedimentation rate mm/s	2.69±1.29	3.20±1.157	3.2±1.15	3.05±1.47	0.049* 0.095 0.760

Note : P_1Group I and II babies the reliability of the difference between ; P_2 Group I and III babies The reliability of the difference between ; P_3Reliability of indicator differences between infants of II and IV groups .

In the first day of life of the observed babies, together with the analysis of general blood taken from the umbilical cord, it was also analyzed by taking blood for biochemical blood analysis of waxy blood. According to him, the average ALT enzyme in group I babies of the main group is 43.7±17.60 Ed/l, AST is 76.43±38.15 Ed/l, and in group II babies, ALT is 54.7±19.85 Ed/l, AST o It was determined from the analysis results that the average is 81.67±31.25Ed/l. The same parameters of the control group babies, ALT average 32.35±11.63 Ed/l, AST average 47.25±11.06.63 Ed/l, ALT average 38.85±16.5 Ed/l in IV- infant group , AST was determined at an average value of 62.30±22.94 Ed/l.

C-reactive protein, an inflammatory marker of infection, was also examined in the infants' blood. The amount of C-reactive protein in the blood is normally 1-5mg/l. In babies, this indicator is 12 mg/l for a short period of time. According to the results of our examination, the average of group I babies of the main group was 29.18±21.05mg/l, and the average of group II babies was 33.47±17.47mg/l. In the control group, it was determined in an average amount of 6.4±2.62 mg/l in the I group of infants, and 7.75 ± 2.82 mg/l in the group of I V infants . C-reactive relative to full-term and preterm infants in the control group the protein was higher. The reliability of the differences was determined only between the two groups $P_2$and $P_3$was determined at a value of <0.001 when both groups were compared .

Table 4. Indicators of blood biochemical analysis of babies 1st day (M± m)

No	Indicators	Primary group of infants (n=90)		Control group (n=40)		P_1, P_2, P_3
		Group I (n=60)	Group II (n=30)	Group III (n=20)	Group IV (n=20)	
1	ALT, Ed/l	43.7±17.60	54.7±19.85	38.85±16.5	32.35±11.63	0.012* 0.3 0.142
2	AST, Ed/l	76.43±38.15	81.67±31.25	62.30±22.94	47.25±11.06	0.188 0.123 0.02*
3	The amount of total bilirubin, μmol/l	62.37±22.13	66.47±34.5	61.65±28.24	62.45±17.25	0.72 0.589 0.398
4	Directly bound bilirubin,	5.67±1.99	8.07±11.73	5.9±2.05	5.4±1.98	0.532

	μmol/l					0.676 0.398
5	Indirectly bound bilirubin, μmol/l	56.63±21.68	57.7±21.49	56.2±27.42	57±16.6	0.776 0.841 0.478
6	C-reactive protein mg/l	29.18 ± 21.05	33.47±17.47	6.4±2.62	7.75±2.82	0.106 <0.001* <0.001*

Note : P_1 Reliability of the difference between group I and II babies ; P_2 Reliability of the difference between group I and III babies ; P_3Reliability of indicator differences between infants of II and IV groups .

Radiological examination works in the radiological diagnostic department of SamDTU Multidisciplinary Clinic: Ultrasound brain neurosonography and dopplerometry were examined.

The results of the neurosonography analysis determined in the neonatal period are presented in Table 5. When analyzed in the main group of infants, hypoxic-ischemic changes in the periventricular zones in group I infants were 16 (26.7%) it was found in 16 (53.33 %) of II-group babies . Average ventriculomegaly GIE in 12 (20%) group I babies and 5 (16.7%) in group II babies, intracerebral hemorrhages (different types) in 2 (3.3%) group I babies, II It was found in 9 (30%) children of the - group. GIE changes in the basal and periventricular zones, the diagnosis of the expansion of the shiny uterus in 1 (1.7%) group I babies , and in 4 (13.3%) group I babies, BMIQQ, detection of throm in the ventricles of the brain in pseudocyst ventricles, with dilatation of the ventricles. It was found that the diagnosis was made with the detection of throm in the ventricles of the brain, expansion of the ventricles. 18 (30%) of the infants of group I of the main group born to mothers with SMVI had no brain pathology . Taking into account that 4 (13.3%) group II babies were born, it shows that the percentage of brain damage in premature babies is high. Also, in the main group, signs of brain immaturity were found in 9 (30%) of premature and very low birth weight babies. When neurosonographic findings were analyzed in control group infants born to healthy mothers From the above-mentioned cerebral pathologies, almost no changes were detected except for the sign of hypoxic-ischemic changes in the periventricular zones.'

Table 5. Results of analysis of brain neurosonography of infants

Indicators	**Primary group of infants (n=90)**		**Control group t (n=40)**	
	Group I **(n=60)**	Group II **(n=30)**	Group III **(n=20)**	Group IV **(n=20)**
Hypoxic-ischemic changes in periventricular zones, n(%)	16(26.7%)	16 (53.3 %)	2(10%)	6(30%)
Ventriculomegaly, n(%)	5(8.3%)	2(6.7%)	0(0%)	0(0%)
Mean ventriculomegaly GIE, n(%)	12(20%)	5(16.7%)	0(0%)	1(5%)
Intracerebral hemorrhages (various types), n(%), n(%)	2(3.3%)	9(30%)	0(0%)	0(0%)
in the basal and periventricular zones , expansion of the luminal sac, n(%)	1(1.7%)	4(13.3%)	0(0%)	0(0%%)
There is no displacement of the middle structures of the brain Pulsation of blood vessels visually. Increased echogenicity in periventricular tissues. Echo signs of brain tumor , n(%)	2(3.3%)	0(0%)	0(0%)	0(0%%)
BMIQQ, in pseudocystic ventricles, n(%)	2(3.3 %)	3 (10 %)	0(0%)	0(0)
Detection of throm in cerebral ventricles, with expansion of ventricles, n(%)	2(3.3)	1(3.3)	0(0)	0(0)
Without pathology, n(%)	18(30%)	4(13.3%)	20(100)	13(65)

Signs of brain immaturity	1 (1.66 %)	9(30%)	0(0%)	4(13.3)

Note: P_1– Reliability of difference between group I and group II, P_2-reliability of difference between group I and group III. P_3- Reliability of indicator differences between II-group and IV- group babies.

In our investigation, we examined brain dopplerometry analysis in infants in combination with infant brain neurosonography. In the results of our inspection, changes in the study of brain hemodynamics using dopplerometry in the newborns of the main and control groups were revealed (Table 6), according to which the index of resistance of the anterior cerebral artery (R-OBMA) in infants of group I was 0.783±0.094cm /sec., 0.833±0.066 cm/sec was found in group II- babies. It was found that the same indicator was 0.714±0.046cm/sec in group III infants, and 0.69±0.03cm/sec in group IV infants. Reliability of differences between groupsP_1 <0.008*, P_2 It was found that <0.03*, P_3 <0.001*. The resistance index of the right middle cerebral artery (ROBMA on the right) was 0.794±0.09cm/sec in infants of group I and 0.826±0.075cm/sec in infants of group II. In the analysis results of the control group, this indicator was determined as 0.71±0.04 cm/sec in III-group babies and 0.68±0.03 cm/sec in IV-group babies. Reliability of between-group differences between these indicatorsP_1 < 0.226,P_2 <0.001*, $P_3$was found to be <0.001*. The index of resistance of the middle brain was estimated at 0.796±0.09 in infants of group I and 0.81±0.07 in infants of group II when analyzing R(O'BMA) tests in the left artery. The results of this analysis were found to be 0.706±0.038 in group III of control group babies, and 0.691±0.023 cm/sec in group IV babies. The reliability of the differences between the groups was also proved in statistical evidence and P_1 was estimated at <0.699, P_2<0.001*, <0.001*. P_3Also, when analyzing the velocity of blood flow in the vein of Galen (V venous flow velocity cm/s) of the dopplerometry test, it was found that the velocity was partially decreased in the main group. 7.15±2.57 cm/sec in infants of group I of the main group . It was found to be 5.53±1.83 in infants of I -group . This indicator was 9.55±1.57 cm/sec in I II -group and I V -group of infants in the control group. It was determined from our inspection results that it is 9.95±1.05 cm/sec . Mean difference reliability was found to be <0.699, P_2<0.001*, P_3<0.001* in the group mean .P_1

Table 6. Comparative characteristics of cerebral hemodynamic parameters of the examined infants (M±m).

No	Indicators	Primary group of infants (n=90)		Control group (n=40		P_1, P_2, P_3
		Group I (n=60)	Group II (n=30)	Group III (n=20)	Group IV (n=20)	
1	R (OBMA) cm/sec	0.783±0.094	0.833±0.066	0.714±0.046	0.69±0.038	0.008* 0.03* <0.001*
2	R(O'BMA) is cm/sec from the right side	0.794±0.09	0.826±0.075	0.71±0.04	0.68±0.03	0.226 <0.001* <0.001*
34	R(O'BMA) left-sided cm/sec	0.796±0.09	0.81±0.07	0.706±0.038	0.691±0.023	0.699 <0.001* <0.001*
5	V venous flow velocity, cm/s	7.15±2.57	5.53±1.83	9.55±1.57	9.95±1.05	0.004* <0.001* <0.001*

Note : P_1Group I and II babies the reliability of the difference between ; P_2 Group I and III babies The reliability of the difference between ; P_3Reliability of indicator differences between infants of II and IV groups .

Conclusion: Studying the pathogenetic basis of early diagnosis of damage to the nervous system in newborns in the perinatal period, discovering new mechanisms (cerebral blood vessels) opens new opportunities for their early diagnosis, treatment and prevention. It was found that the resistance of the arterial blood vessels of the brain increased, and the velocity decreased in the venous blood vessel (vena Galena) in the neonatal period.

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