

M.S. Savvina, S.A. Evseeva, T.I. Nelunova, T. E. Burtseva  
M.P. Slobodchikova

## RISK FACTORS INFLUENCING THE PERSISTENCE OF PATENT DUCTUS ARTERIOSUS IN NEONATES WITH CHD IN THE REPUBLIC SAKHA (YAKUTIA)

DOI 10.25789/YMJ.2019.67.36

The authors present their research of factors, possibly influencing the duration of persistent patent ductus arteriosus (PDA) in the neonates with congenital heart defects (CHDs) in the Republic Sakha (Yakutia). Such factors as multiple pregnancy, operative delivery, gestational arterial hypertension, preeclampsia, fetoplacental insufficiency, anemia in pregnancy, threatened miscarriage, congenital heart defects in future mother, and ethnicity of a mother or a father are examined.

A retrospective clinical research work was based on the data of the Perinatal Centre of the Republican hospital No1, National Centre of medicine. A research work is based on clinical results of medical tests, taken from 162 medical records of the patients with a diagnosed "Congenital heart disease" (CHD).

According to the results of statistical analysis there were revealed most significant risk factors for long-term persistent arterial ducts among the neonate population of the Republic Sakha (Yakutia). They may be associated with: complicated course of pregnancy, i.e. gestational arterial hypertension with or without proteinuria, pregnancy edema associated with presence or absence of proteinuria, fetoplacental insufficiency, anemia of the current pregnancy and presence of CHD in the mother's past history.

**Keywords:** congenital heart defect, arterial duct, hemodynamically insignificant patent ductus arteriosus.

**Introduction.** The prevalence of the patent ductus arteriosus (PDA) in the newborns remains unknown as there are no distinct criteria from what period of gestation PDA is considered pathologic. Nominally it is supposed to close within the first two weeks after birth. Under such criteria the prevalence of the isolated pathology is 0.14-0.3 per 1,000 live-born children, 7% among all the CHDs and 3% among all the critical defects [7]. Persistence of the arterial duct considerably depends on the term of gestation besides that the data that some factors of the mother, such as intrauterine hypoxia, non-steroid anti-inflammatory medication

intake etc., are known. A number of several factors which can be associated with high risk of long-term persistence of PDA in neonates are not well studied in the territory of the Republic of Sakha (Yakutia).

**Objectives:** The factors that are possibly associated with the long-term persistence of PDA in neonates with CHDs are studied.

**Methods and materials:** A retrospective clinical research work was based on the data of the Perinatal Centre of the Republican hospital No1, National Centre of medicine. A research work is based on clinical results of medical tests, taken from 162 medical records of the patients with a diagnosed "Congenital heart disease" (CHD). The time distance of the medical records is registered two times, thus from 2001 to 2003 and from 2013 to 2015. The CHD is recorded according to Q20-Q28 (ICD-10, chapter XVII: Congenital malformations, deformations and chromosomal abnormalities). The delivery case reports (#010u) and patient's discharge statistic card (#066/u-02) were the initial documentations for analysis.

All the neonates had experienced ultrasound examination (Doppler echocardiography) of the heart to evaluate the anatomical structure and cardiovascular function. The selection is based on the cases with bypass through interatrial septum according to the results of ultrasound investigation. The functioning activity of the arterial duct was evaluated by colour Doppler test to define additional flow in the vessel projection, i.e. pulmonary trunk. According to the results of the ultrasound investigation, all the selection

of CHDs was divided into groups: the 1<sup>st</sup> group consists of the patients with non-revealed shunting according to the Doppler monitoring of the vessel with pulmonary artery projection, non-functioning arterial flow; the 2<sup>nd</sup> group consists of the patients with revealed systolic and diastolic disorders or systolic shunting, according to the Doppler monitoring of the vessel with pulmonary artery projection, functioning arterial flow; the 3<sup>rd</sup> group consists of all cases of CHD. The research was performed from 2001 to 2003 on the base of ATL-HDI-3000 Philips, from 2013 to 2015 on the base of EPIQ-7 Philips.

The age of the neonates included in the selective group was from 17 to 40 for mothers and from 17 to 48 for fathers. The period of gestation at the moment of birth of a child with CHD was from 25 to 41 weeks. The body weight at moment of the birth was from 564 gr to 4,500 gr. The height at the moment of the birth was from 30 cm to 58cm.

The family history of the both parents was retrospectively evaluated. Thus, the following factors were included: 1) the factors complicating pregnancy (gestational hypertension with or without proteinuria, edema with or without proteinuria for the current pregnancy, preeclampsia, fetoplacental insufficiency, anemia during the current pregnancy, multiple pregnancy, threatened miscarriage, operative delivery of the current pregnancy); 2) CHD in the mother's past history; 3) ethnicity of the parents (was registered by self-determination of the survey).

On data processing  $\chi^2$  criteria were used (comparing binary / nominal vari-

**SAVVINA Maya Semyonovna** – Ph.D., senior staff scientist of the laboratory of pediatric health level monitoring, Yakut science Centre of complex medical problems, Yakutsk, Russia, e-mail: maya\_savvina@mail.ru; **NELUNOVA Tuyara Ivanovna** – cardiologist of the Perinatal Center of the Republican hospital No1, postgraduate, St. Petersburg state pediatric medical university, St. Petersburg, Russia; **EVSEYEVA Sardana Anatolievna** – Ph.D., senior staff scientist of the laboratory of pediatric health level monitoring, Yakut science Centre of complex medical problems, Yakutsk, Russia; **BURTSEVA Tatiana Egorovna** – MD, professor of the department of pediatrics and pediatric surgery, Medical institute of the North-Eastern federal university, a head of the laboratory of the Yakut science Centre of complex medical problems, Yakutsk, Russia; **SLOBODCHIKOVA Maya Pavlovna** – a senior lecturer of the department of foreign languages with the course of Russian language, St. Petersburg state pediatric medical university, St. Petersburg, Russia.

ables) and the Mann-Whitney U test (comparing continuous variables). When  $p < 0.05$  the intergroup accuracy was considered significant. The initial data were accumulated in the database by means of Microsoft® Excel software, all the statistic operations were conducted by means of SPSS® Statistics software (IBM® USA).

**Results and discussion.** The statistical analysis of the repeated ultrasound investigations of one and the same child with CHD confirming the presence or absence of PDA was carried out. 162 cases were selected. A possible association of multiple pregnancy with the risk of long-term persistence of the ductus arteriosus during the medical reexaminations was analyzed (Table 1).

The following factors aggravating pregnancy were investigated, i.e. gestational arterial hypertension and edema with or without proteinuria, preeclampsia, fetoplacental insufficiency, anemia of the current pregnancy and threatened miscarriage, as well as operative delivery.

According to the research statistically unconfirmed results were obtained, i.e. the results were higher for multiple pregnancies among hemodynamically insignificant patent ductus arteriosus (HIS-PDA) ( $n=86$ ) – 5.8% than in groups with the hemodynamically significant patent ductus arteriosus (HS-PDA) ( $n=76$ ) – 1.3%. Multiple pregnancy as a predictor of long-term persistence of the patent ductus arteriosus among all the selections became statistically unsatisfactory.

The association of the gestational arterial hypertension with or without proteinuria of the current pregnancy with a risk of persistence of PDA ( $p=0.948$ ) was revealed, but the results are not statistically verified. In 34% of all cases of re-examination of the arterial duct ( $n=162$ ) the following factors were registered. The prevalence of the gestational arterial hypertension with or without proteinuria, and edema of the pregnancy with or without proteinuria in the structure of the arterial duct was equal in both groups: HIS-PDA– 33.7% ( $n=86$ ) and HS-PDA – 34.2% ( $n=76$ ).

According to the results, preeclampsia of the current pregnancy was registered in 72.8% of all cases of CHDs and was more significantly associated with the risk of long-term persistence of the ductus arteriosus. A part of preeclampsia in the groups of HIS-PDA ( $n=86$ ) was higher – 73.1%, (in a case of the patent ductus arteriosus ( $n=76$ ) – 65.8%). These results were statistically unverified ( $p=0.058$ ).

The results show an equal association of fetoplacental insufficiency with the risk of persistence arterial duct and closure of the

arterial duct ( $p=0.157$ ), the revealed data are not statistically confirmed. The fetoplacental insufficiency of the current pregnancy was registered in 36.4% of all cases born with CHDs ( $n=162$ ). A higher association of the fetoplacental insufficiency with a risk of persistence of PDA ( $p=0.157$ ) in comparison with closure of PDA are noticed, but not confirmed statistically.

Anemia in pregnancy was most common for the group of HIS-PDA ( $n=86$ ), in the group of the patent ductus arteriosus ( $n=76$ ), it composed 56.6% and 50.0% respectively. The revealed data were not statistically confirmed ( $p=0.402$ ), but they showed possible association of anemia with a risk of persistence of PDA, nevertheless a part of anemic turned consid-

erably higher in both groups and were of the same degree (Table 1).

Threatened miscarriage of the current pregnancy in the past history of the neonates as a possible predictor of a long-term persistence of the arterial duct was also studied. According to the common data, threatened miscarriage was revealed in 38.3% of all the selected groups of the arterial duct. The results of this research show that threatened miscarriage most commonly occurred in groups of HIS-PDA ( $n=86$ )-45.3% than in groups of PDA ( $n=76$ ) – 30.3%. The results are not statistically verified ( $p=0.049$ ) and show the association of the threatened miscarriage with a risk of persistence of PDA as well as closure of PDA.

Table 1

The proportion of factors aggravating the course of pregnancy in groups of newborns with HIS-PDA and PDA

Group	No factor	multiple pregnancy	p
1 n=86	94.2	5.8	0.130
2 n=76	98.7	1.3	0.130
Total n=162	96.3	3.7	0.130
	No factor	Gestational arterial hypertension with or without proteinuria	
1 n=86	66.3	33.7	0.948
2 n=76	65.8	34.2	0.948
Total n=162	66.0	34.0	0.948
	No factor	Preeclampsia	
1 n=86	20.9	73.1	0.058
2 n=76	34.2	65.8	0.058
Total n=162	27.2	72.8	0.058
	No factor	Fetoplacental insufficiency	
1 n=86	68.6	31.4	0.157
2 n=76	57.9	42.1	0.157
Total n=162	63.6	36.4	0.157
	No factor	Anemia	
1 n=86	50.0	50.0	0.402
2 n=76	43.4	56.6	0.402
Total n=162	46.9	53.1	0.402
	No factor	Threatened miscarriage	
1 n=86	54.7	45.3	0.049
2 n=76	63.7	30.3	0.049
Total n=162	61.7	38.3	0.049
	No factor	Mothers with CHD	
1 n=86	93.0	7.0	0.075
2 n=76	84.2	15.8	0.075
Total n=162	88.9	11.1	0.075
	No factor	Operative delivery	
1 n=86	53.5	46.5	0.821
2 n=76	55.3	44.7	0.821
Total n=162	54.3	45.7	0.821

Note. In the Tables 1-2 1st group - there were no signs of the functioning of the ductus arteriosus during re-examination (HIS-PDA); 2nd group - signs of the functioning of the arterial duct (PDA) were revealed.

Also the cases of CHD in the mother's past history of a CHD neonate as a possible predictor of long-term persistence of PDA are also studied. The research data show that mother's CHD was registered in 11.1% of all selected groups. Statistically unconfirmed data showed association of mother's CHD in PDA groups ( $p=0.075$ ). In PDA groups ( $n=76$ ) this factor far doubled than in groups of HIS-PDA ( $n=76$ ), it was 15.8% and 7.0% respectively.

The operative delivery of the current pregnancy as a factor of possible long-term persistence of the ductus arteriosus turned to be statistically unsatisfactory, it was common for HIS-PDA group of neonates – 46.5% (Table 1).

The ethnicity of the mothers and fathers in children with PDA and HIS-PDA was investigated (Table 2).

Among all the cases of reexamina-

tion in PDA group rather than in HIS-PDA group (16.1% and 8% respectively). In a group of HIS-PDA 4.7% corresponded to the peoples of Caucasus (1.3% in PDA group).

Among the fathers of the CHD neonates it was most common for Yakuts and Russian 73.51% and 17.3% respectively. There were 14.9% for Evenks, 2.5% for peoples of Caucasus and other nations (Ukrainians, Polishes, Germans, Tatars, Buryats, Kumyks and Khakasses) – 0.6% for each group. Statistically unconfirmed results show that the ethnicity of the father is associated with groups of arterial ducts ( $p=0.565$ ). The research revealed that PDA group was most common for Yakuts (75%). Russian and Evenks commonly occurred in the groups of HIS-PDA ( $n=86$ ) – 18.6% and 5.8%, and in a group PDA ( $n=76$ ) – 15.8% and 3.9%. Other nations (Evens, peoples of the Caucasus,

2. The association of a risk of persistent PDA and PDA closure with such factors as gestational hypertension with or without proteinuria, pregnancy edema associated with presence or absence of proteinuria, anemia in pregnancy and threatened miscarriage was statistically unconfirmed.

3. The association of fetoplacental insufficiency with risk of persistent PDA was unconfirmed statistically.

4. The association of mother's CHD in a group of PDA was also unconfirmed statistically.

According to the results of statistical analysis there were revealed most significant risk factors for long-term persistent arterial ducts among the neonate population of the Republic Sakha (Yakutia). They may be associated with complicated course of pregnancy, i.e. gestational arterial hypertension with or without proteinuria, pregnancy edema associated with presence or absence of proteinuria, fetoplacental insufficiency, anemia of the current pregnancy and presence of CHD in the mother's past history.

*The reported study was funded by RFBR according to the research project #18-05- 60035\_Arctica.*

**Table 2**

**Ethnicity of Parents of Newborns with HIS-PDA and PDA**

Groups of arterial duct	Mother ethnicity, %								P=
	1	2	3	4	5	6	7	8	
1 n=86	72.1	15.1	0.0	8.1	0.0	4.7	0.0	0.0	0.601
2 n=76	71.1	17.1	1.2	9.2	0.0	1.3	0.0	0.0	0.601
Total n=162	71.6	16.0	0.6	8.6	0.0	3.1	0.0	0.0	0.601
	Father ethnicity, %								P=
	1	2	3	4	5	6	7	8	
1 n=86	72.1	18.6	0.0	5.8	1.3	0.0	0.0	0.0	0.585
2 n=76	75.0	15.8	1.3	3.9	1.3	1.3	0.0	1.3	0.585
Total n=162	73.5	17.3	0.6	4.9	0.6	2.5	0.0	0.6	0.585

Note. 1 – Yakuts, 2 – Russians, 3 – Evens, 4 – Evenks, 5 – other indigenous small-numbered peoples of the North, Siberia and the Far East: Dolgans, Yukaghirs, Chukchis, 6 – peoples of the Caucasus, 7 – peoples of the Central Asia, 8 – others: Ukrainians, Polishes, Germans, Tatars, Buryats, Kumyks and Khakasses.

tion of the arterial ducts ( $n=162$ ), it was most common for the Yakut and Russian mothers 71.6% and 16.0% respectively, Evenks - 8.6%, peoples of the Caucasus – 3.1%. Statistically unconfirmed data ( $p=0.601$ ) of the distribution according to mothers' ethnicity were received when comparing the groups of arterial ducts. According to the results of the research there were Yakut mothers in both groups almost equally – 72.2% and 71.1% respectively. Evens were only in PDA group ( $n=76$ ), 1.2%. It was most common for Russian 17.1% and Evenks 9.2%

Ukrainians, Polishes, Germans, Tatars, Buryats, Kumyks and Khakasses) were present only in a group of PDA.

#### Conclusions:

1. Multiple pregnancy as a predictor of long-term persistence of arterial ducts on reexamination, according to current research, occurred statistically unreliable. Preeclampsia and operative delivery of the current pregnancy as factors of possible association with long-term persistence of PDA turned statistically unreliable, and most commonly occurred in groups of HIS-PDA.

#### References

1. Володин Н.Н. Протокол ведения недоношенных детей с гемодинамически значимым функционирующим артериальным протоком. Российский государственный медицинский университет Росздрава. 2009. [Volodin NN. Preterm infants with hemodynamically significant patent ductus arteriosus guidelines. Rossiiskii gosudarstvennii medicinskii universitet Roszdrava. 2009. (In Russ.).]
2. Гераськин А.В. Детская хирургия. Клинические разборы. ГЭОТАР – Медиа. 2011. [Geraskin AV. Pediatric surgery. Clinical examinations. Geotar-Media. 2011. (In Russ.).]
3. Детская хирургия: национальное руководство. ГЭОТАР – Медиа. 2009. [Pediatric surgery: national guideline. Geotar-Media. 2009. (In Russ.).]
4. Гриффин Б. Кардиология. Практика. 2008; 150-152. [Griffin B. Cardiology. Practica. 2008; 150-152. (In Russ.).]
5. Прахов А.В. Неонатальная кардиология. НГМА. 2008. [Prakhov AV. Neonatal cardiology. NGMA. 2008. (In Russ.).]
6. Руководство по перинатологии. Информ – Навигатор. 2015. [Perinatology guidelines. Inform-Navigator. 2015; 22. (In Russ.).]
7. Шарыкин А.С. Кардиология. Бином, 2009; 50-51. [Sharykin AS. Cardiology. Binom. 2009; 50-51. (In Russ.).]