ORIGINAL ARTICLE

ELECTROCARDIOGRAPHIC CHANGES IN NEWBORNS FROM MOTHERS WITH METABOLIC SYNDROME

DOI: 10.36740/WLek202106112

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ABSTRACT

The aim: Analysis of electrocardiographic parameters in newborns from mothers with metabolic syndrome.

Materials and methods: We conducted a prospective cohort trial of 125 newborns, which included the study of their anthropometric, clinical and laboratory indicators and, in particular, ECG parameters. The main group consisted of 40 children, born from mothers with diagnosed metabolic syndrome, the comparison group included 2 subgroups: 28 term newborn and 57 preterm, from mothers without metabolic syndrome.

Results: In newborns from mothers with metabolic syndrome on a fragmentary ECG we revealed abnormal depolarization, manifested by changes in the ventricular complex – QRS expansion ($p<0.001$), impaired conduction ($p = 0.004$), changes of T wave ($p<0.001$) and prolonged QT interval ($p<0.001$). There are such risk factors for QT prolongation in neonates: disease cardiovascular system and disorders of lipid metabolism in mother, asphyxia at birth and electrolyte disorders (hypernatremia OR 0.97), weight too high to gestational age at birth in newborn (OR 2.97), increased blood pressure in the neonatal period (OR 1.07), artificial feeding (OR 3.01).

Conclusions: Metabolic syndrome in women during pregnancy has a pronounced effect on the cardiovascular system of the newborn. The detected signs of cardiac dysfunction on the ECG can serve as early integrated indicators of metabolic syndrome and cardiovascular disease in children.

KEY WORDS: metabolic syndrome, ECG, newborns, prolonged QT-interval

Wiad Lek. 2021;74(6):1349-1354

INTRODUCTION

Cardiovascular diseases are the number one cause of death worldwide [1]. Metabolic syndrome is a combination of cardiovascular risk factors such as obesity, hyperglycemia, dyslipidemia and hypertension, and is associated with an increased risk of cardiovascular disease. A recent meta-analysis showed that individuals with metabolic syndrome had twice the risk of cardiovascular disease and 1.5 times the risk of death from other causes [2]. Obesity is a key component of the metabolic syndrome, which is becoming increasingly important due to its extremely high prevalence. [1].

Among the factors that negatively affect metabolism, lead to its disorders and obesity are genetic, prenatal, food, somatic, psychogenic and others. Not the last role is played by the phenomenon of food imprinting which defines processes of proliferation and differentiation of cells, formation of bodies and systems, their sizes, structure and a functional conditions, activity of enzyme systems, expression of genes encoding enzymes, receptor proteins, determining the nature and direction of metabolic processes, nutrition during the fetal period and the first years of life influences the taste preferences of a person throughout life. A high-calorie and high-fat diet during pregnancy contributes to hypertension and endothelial dysfunction in the unborn child in adulthood [3]. Insufficient or inadequate nutrition of a pregnant woman, infections, smoking, stress, endocrine disorders affect fetal development and cause growth retardation and low birth weight, on the one hand, and changes in metabolic or physiological profile with relevant diseases, on the other. Birth weight is not only a predictor of perinatal health, but also psycho-motor development, growth and formation of organs and systems in adulthood. Both low and overweight at birth are associated with an increased risk of obstetric and neonatal complications, as well as metabolic and cardiovascular disorders later in life [4, 5].

Pregnancy is accompanied by a special state of metabolism: insulin resistance, which appears in 2-3 trimesters of pregnancy, progresses to the level observed in people with type 2 diabetes. Insulin resistance and hyperinsulinemia may be the main basis of the metabolic syndrome of pregnancy – high blood pressure and diabetes. Moreover, the metabolic syndrome is also associated with endothelial dysfunction, oxidative stress, and attenuated inflammatory responses. How can metabolic changes in a pregnant woman affect the condition of the newborn? It turns out that obesity in adolescence is associated with maternal weight and concentration of insulin in amniotic fluid during pregnancy. Impaired glucose tolerance is diagnosed in 36% of children from mothers with diabetes, which is also

Table I. Analysis of basic electrocardiographic parameters in newborns from mothers with metabolic syndrome and in newborns of comparison groups

Main indicators	Main group[1] n=40	Comparison groups		p^{1-2} p^{1-3} p^{2-3}
		A (term neonates)[2] n=28	B (preterm neonates)[3] n=57	
HR min, per min	123.4±17.4	132.55±26.07	123.3±17.06	0.112 0.978 0.096
HR mean, per min	142.6±15.68	149.8±27.48	137.1±14.27	0.218 0.082 0.028
HR max, per min	165.6±17.7	162.66±27.06	152.7±16.59	0.617 0.043 0.082
RR min, s	0.368±0.041	0.37±0.07	0.387±0.054	0.893 0.052 0.265
RR max,s	0.494±0.06	0.47±0.09	0.51±0.09	0.224 0.296 0.059
RR mean,s	0.426±0.05	0.41±0.08	0.45±0.066	0.354 0.045 0.027
Alfa angle, degrees	163.4±8.5	142.7±5.01	131.6±22.39	<0.001 <0.001 <0.001
PQ, s	0.104±0.009	0.106±0.015	0.09±0.006	0.532 <0.001 <0.001
QRS, s	0.06±0.001	0.06±0.001	0.059±0.0018	1.000 <0.001 0.002
QT, s	0.266±0.016	0.26±0.026	0.254±0.022	0.284 0.003 0.299

associated with elevated amniotic insulin in utero. There are studies that confirm that maternal metabolic disorders during pregnancy are associated with poorer intellectual and psychomotor development, obesity and impaired glucose tolerance in the child [6]. Maternal conditions such as obesity, gestational diabetes, and preeclampsia may contribute to the development of intrauterine stress, which is responsible for the adverse effects of childbirth, such as low body weight or macrosomia; and through developmental programming, these maternal states can also increase susceptibility to metabolic diseases in offspring [7]. Although the basic biological and etiological mechanisms of these different hypotheses are not sufficiently clear, it is known that the susceptibility to adult disease lies in key moments of fetal and postpartum development, where there is a complex network of genetic, epigenetic, metabolic and environmental influences contributing to future disease risk [8].

Elevated insulin levels, hyperglycemia in pregnant women with metabolic syndrome impair the metabolic processes and development of the fetal myocardium [9]. Manifestations of the metabolic syndrome are associated with a higher prevalence of large and minor deviations on the ECG [10].

Early diagnosis of variational changes on the ECG is likely to identify newborns with metabolic disorders, including those with a high risk of cardiovascular disease.

THE AIM

Analysis of electrocardiographic parameters in newborns from mothers with metabolic syndrome.

MATERIALS AND METHODS

We conducted a prospective cohort trial of 125 newborns treated at the Perinatal Center of Poltava Regional Clinical Hospital, which included the study of their anthropometric, clinical and laboratory indicators and, in particular, ECG parameters. The main group consisted of 40 children, born from mothers with diagnosed metabolic syndrome, the comparison group included 2 subgroups: 28 term newborn

Table II. Associations between the rates of individual electrocardiographic changes in newborns and the presence of metabolic syndrome in the mother

Identified changes	Main group[1] n=40	Comparison groups		p^{1-2} p^{1-3} p^{2-3}
		A (term neonates)[2] n=28	B (preterm neonates)[3] n=57	
Sinus arrhythmia, n (%)	40 (100,0)	28 (100,0)	49 (85.96)	1.00 0.202 1.00
Deviation of the heart axis to the right, n (%)	40 (100,0)	28 (100)	49 (85.96)	1.00 0.202 1.00
Voltage reduction, n (%)	24 (60.0)	12 (42.86)	15 (26.32)	0.163 0.009 0.1237
QT elongation, n (%)	16 (40.0)	12 (42.86)	0	0.8137 <0.001 <0.001
Changes of T-wave, n (%)	24 (60.0)	9 (32.14)	0	0.024 <0.001 < 0.001
Changes in the T-wave in the chest leads, n (%)	32 (80.0)	22 (78.57)	8 (14.04)	0.886 <0.001 <0.001
Conductivity changes, n (%)	8 (20)	9 (32.14)	0	0.2551 0.004 <0.001

and 57 preterm, from otherwise healthy mothers (without metabolic syndrome).

Criteria for inclusion in the main group were the presence of metabolic syndrome in the mother during pregnancy (high blood pressure, hyperglycemia, body mass index (BMI) ≥30 kg/m^2), the absence of congenital malformations in the newborn. Parents of all newborns agreed to the study. All newborns underwent ECG recording in 12 standard leads for 3-7 days after birth.

Constant variables are presented as mean values (M) and standard errors (m), categorical variables as absolute numbers and percentages. Student's test was used to compare independent samples and a chi-square test to compare proportions. The obtained data are presented as an arithmetic mean (95% confidence interval). The level of differences between data groups was assessed using the confidence interval comparison method. The hypothesis of group difference was accepted in the absence of overlapping confidence intervals. Mann-Whitney U-test for nonparametric data was used to overlap the confidence intervals. The hypothesis of no group differences was confirmed at a coefficient of p> 0.05. All statistical analyzes were performed using the STATA version 11, licensed computer program package for Windows (StataCorp, Texas, USA).

By the decision of the Bioethics Commitee № 192 from 24.03.2021 the materials of scientific work meet the Rules of humane treatment of patients in accordance with the Tokyo Declaration of the World Medical Association, International Recommendations of the Helsinki Declaration of Human Rights, Council of Europe Convention on Human Rights and Biomedicine, Laws of Ukraine and the requirements of the Code of Ethics of the doctor in Ukraine. Materials of scientific work can be published in the open press.

RESULTS

During the analysis of the main ECG parameters it was found that children from mothers with metabolic syndrome had significantly higher rates of maximum heart rate compared with subgroup A (p = 0.043), the value of the alpha angle was significantly higher than in newborns from both subgroups (p = 0.0001), which indicates a sharper deviation of the axis of the heart to the right, increasing the bioelectrical activity of the right heart. The reason for this phenomenon may be a delay in the restructuring of the cardiovascular system, the persistence of fetal communications. There was also a lower minimum and average duration of the R-R interval compared with neonates of group B (p = 0.05), which is explained by the higher heart rate in neonates of the main group, ie the tendency to sinus tachycardia. Among the significant deviations in newborns with metabolic syndrome should be noted the longer duration of the PQ interval (p<0,001), the expansion of the QRS complex (p<0,001), which are manifestations of slowing of the excitation through the myocardium, as well as prolongation of the QT interval (p = 0,003). characterizes the processes of ventricular repolarization as a consequence of abnormal depolarization (Table I).

Table III. Risk factors for QT prolongation in newborns from mothers with metabolic syndrome

	Odds ratio	95% CI	p
Risk factors of mother			
Disorders of lipid metabolism in women	24,3	3,12-189,68	0,002
Gestational diabetes	0,27	0,05-1,23	0,091
Eating vegetables	4,38	1,68-11,43	0,003
Eating fast food	0,71	0,47-1,07	0,106
Cardiovascular disease	2,92	1,03-8,24	0,043
Gastrointestinal diseases	0,58	0,06-5,15	0,625
Hypertension	1,32	0,39-4,46	0,652
Preeclampsia	1,45	0,56-3,76	0,441
Threat of abortion	0,17	0,02-1,30	0,088
Polyhydramnios	1,89	0,54-6,59	0,313
Colpitis	0,81	0,21-3,09	0,769
Premature rupture of membranes	3,36	0,76-14,91	0,110
Risk factors of newborn			
Apgar 1 min	2,77	1,39-5,51	0,004
Apgar 5 min	2,31	1,21-4,43	0,011
Weight too high to GA	2,97	1,04-8,53	0,042
BMI	1,81	1,26-2,59	0,001
Increased blood pressure	1,066	1,02-1,111	0,002
Artificial feeding	3,01	1,57-5,76	0,001
Hypoxic encephalopathy	0,3	0,04-2,91	0,339
Increased hematocrit	0,95	0,92-0,99	0,019
Increased platelets level	0,99	0,98-0,99	0,048
Increased BE	1,25	0,99-1,57	0,052
Increased serum sodium level	0,97	0,96-0,99	0,004
Deacresed total protein level in serum	0,96	0,93-0,99	0,023
Increased serum urea	0,711	0,49-1,02	0,067
Increased serum creatinine level	0,99	0,97-1,01	0,627

The next step was to identify the associations of individual ECG phenomena in newborns with the presence of metabolic syndrome in the mother (Table II). After analyzing some pathological changes on the ECG in newborns from the study groups, we found that in children from mothers with metabolic syndrome significantly more often was a pronounced decrease in voltage ($p = 0.009$), which indicates the presence of metabolic disorders in the myocardium. Prolongation of the QT interval in children of the main group ($p<0.001$), as well as in adults with metabolic syndrome is the most characteristic indicator of violation of the functional reserve of the myocardium, due to the influence of metabolic disorders. Changes in the T wave ($p<0.001$) were characteristic of children from mothers with metabolic syndrome, which indicates a violation of the processes of ventricular myocardial repolarization. It should be noted that in newborns from the main group pathological changes of conduction were significantly more often ($p = 0.004$) as a reflection of electrophysiological processes impairment, which may be due to structural changes in the conduction system of the heart (ischemia, inflammation), autonomic, endocrine, electrolyte and metabolic disorders.

Measurement of the QT interval is of significant clinical importance, mainly because its prolongation may be associated with an increased risk of death, including sudden cardiac death, due to the development of fatal ventricular arrhythmias [11-15]. It is known that the prolongation of the QT interval can be caused by a number of reasons, including those that characterize lifestyle and nutrition, anthropometric indicators, biochemical abnormalities due to metabolic syndrome. In our study, maternal risk factors (anamnestic, somatic, obstetric, biochemical) and newborn risk factors (anthropometric, biochemical, nutritional, etc.) were analyzed. As a result of step-by-step logistic analysis, it was found that the reliable risk factors for QT prolongation in newborns are the following (Table III): the presence of cardiovascular disease (OR 2.92) and

lipid metabolism disorders in the mother (OR 24.3), low scores on the Apgar scale in the newborn at 1 and 5 minutes after birth (OR 2.77 and 2.31 respectively), high birth weight for gestational age (OR 2.97), increase in BMI (OR 1.81), increase in blood pressure in the newborn (OR 1.07), artificial feeding (OR 3.01), increase in hematocrit and platelets (OR 0.95) and 0.99), increase in basis excess (BE) as an indicator of increased metabolic acidosis (OR 1.25). Expectedly, that hypernatremia (OR 0.97) and decreased total protein (OR 0.96) were the reliable risk factors too.

Interestingly, the consumption of vegetables by women reduces the risk of repolarization impairment, namely the prolongation of the QT interval in the newborn (OR 4.38).

DISCUSSION

As a result of our study, a number of electrocardiographic changes in newborns from mothers with metabolic syndrome were revealed, that serves as a confirmation of the hypothesis of impaired differentiation and development of the cardiovascular system of the fetus due to metabolic disorders in pregnant women at different levels (molecular, cellular, organ). There are several options for the effect of metabolic syndrome on electrocardiographic parameters in older children and adults, while this issue has been little studied in newborns. The presence of metabolic syndrome in the mother was associated with increased heart rate in the newborn, slowing of the conduction of the excitation through the ventricular myocardium, manifested by dilation of the QRS complex, disruption of myocardial repolarization, which is realized by prolongation of QT interval, increased vascular rigidity [7, 8]. It is not clear how the metabolic syndrome leads to ECG abnormalities, there are hypotheses about the activity of the sympathetic nervous system, elevation of the diaphragm due to obesity and increased cardiac output, leading to left ventricular hypertrophy. Being overweight increases cardiac output and the risk of cardiomyopathy, and as a result, prolongs the PR interval. Hormones produced by adipose tissue affect the myocardial matrix, resulting in electrophysiological remodeling. There are also endovascular effects of obesity caused by the expression of paracrine hormone in adipose tissue, which can alter atrial function [4,6,16]. Analysis of risk factors for prolongation of the QT interval in the newborn showed that not only the indicators of the child's health affect the results of ECG studies, but also indicators of metabolic disorders in women during pregnancy.

CONCLUSIONS

Metabolic syndrome in women during pregnancy has a pronounced effect on the cardiovascular system of their newborns.

In newborns from mothers with metabolic syndrome on a fragmentary ECG we revealed: abnormal depolarization, manifested by changes in the ventricular complex – QRS expansion ($p<0,001$), impaired conduction of the excitation through the myocardium ($p = 0,004$). frequent changes of the T wave ($p<0.001$) and prolongation the QT interval ($p<0.001$).

Newborns with repolarization disorders, in the form of QT prolongation, which is considered as a predictor of threatening ventricular arrhythmias, need an in-depth examination to analyze the duration of QT correction and detect maximum values during long-term ECG monitoring.

The step-by-step logistic analysis revealed reliable risk factors for QT prolongation in newborns: in addition to cardiovascular disease and lipid metabolism disorders in mother, asphyxia at birth and electrolyte disorders in newborn (hypernatremia OR 0.97), big weight to gestational age at birth (OR 2.97), increase in blood pressure in the neonatal period (OR 1.07), artificial feeding (OR 3.01), while the vegetable diet of women reduces the risk of repolarization disorders in newborns (OR 4.38).

The identified signs of cardiac dysfunction on the ECG can serve as early integrated indicators of metabolic syndrome and cardiovascular diseases in children, and therefore require further study and follow-up to develop a personalized approach to treatment tactics.

REFERENCES

1. Elffers T.W., de Mutsert R., Lamb H.J. et al. Association of metabolic syndrome and electrocardiographic markers of subclinical cardiovascular disease. Diabetol Metab Syndr.2017;40 (9). https://doi.org/10.1186/s13098-017-0238-9.
2. Alvarez M.V., Aparicio-Martinez P., Fonseca Pozo F.J. et al. Sustainable approach to the metabolic syndrome in children and its economic burden. Int. J. Environ. Res. Public Health. 2020;17:1891.
3. Gaillard R., Steegers E.A., Duijts L. Childhood cardiometabolic outcomes of maternal obesity during pregnancy: the Generation R Study. Hypertension. 2014;63(4):683-91. DOI: 10.1161/HYPERTENSIONAHA.113.02671.
4. Oostvogels A.J., Stronks K., Roseboom T.J. et al. Maternal prepregnancy BMI, offspring's early postnatal growth, and metabolic profile at age 5-6 years: the ABCD Study. J Clin Endocrinol Metab. 2014;99(10):3845-54. https://pubmed.ncbi.nlm.nih.gov/24955609/ DOI: 10.1210/jc.2014-1561.
5. Belmer S.W. Chastyie voprosy pishchevogo programirovaniia. Fetalnoe programirovanie. [Particular issues of food programming: fetal programming]. Questions of children's nutrition. 2016;14(1):26-31.(in Russian).
6. Silverman B.L., Rizzo T.A., Cho N.H. et al. Long-term effects of the intrauterine environment. The Northwestern University Diabetes in Pregnancy Center. Diabetes Care. 1998;21(2):142-9.
7. Kajantie E., Eriksson J.G., Osmond C. et al. Pre-eclampsia is associated with increased risk of stroke in the adult offspring: the Helsinki birth cohort study. Stroke. 2009;40:1176–1180.
8. Ryckman K.K., Borowski K.S., Parikh N.I. et al. Pregnancy Complications and the Risk of Metabolic Syndrome for the Offspring. Curr Cardiovasc Risk Rep. 2013;7(3):217-223. doi:10.1007/s12170-013-0308-y.
9. Vick G.W., Fisher D.J. Cardiac Metabolism in the Fetus and Neonate. In: Cowett R.M. Principles of Perinatal—Neonatal Metabolism. New York:Springer, 1998. https://doi.org/10.1007/978-1-4612-1642-1_27 .
10. Ebong I.A., Bertoni A.G., Soliman E.Z. et al. Electrocardiographic abnormalities associated with the metabolic syndrome and its components: the multi-ethnic study of atherosclerosis. Metabolic syndrome and related disorders. 2012;10(2):92–97. https://doi.org/10.1089/met.2011.0090 .

11. Al-Khatib S.M., LaPointe N.M.K., Kramer J.M. What clinicians should know about the QT interval. JAMA. 2003;289(4):2120–7.
12. Algra A., Tijssen J.G., Roelandt J.R. et al. QTc prolongation measured by standard 12-lead electrocar-diography is an independent risk factor for sudden death due to cardiac arrest. Circulation.1991;83:1888–94.
13. van Noord C., Eijgelsheim M., Stricker B.H.Ch. Drug- and non-drug-associated QT interval prolongation. British Journal of Clinical Pharmacology.2010;70(1):16–23.
14. Liew R. Electrocardiogram-Based Predictors of Sudden Cardiac Death in Patients With Coronary Artery Disease. Clin. Cardiol. 2011;34(8):466–73.
15. Zhang Y., Post W.S., Blasco-Colmenares E. et al. Electrocardiographic QT interval and mortality: a metaanalysis. Epidemiology. 2011;22(5):660–70.
16. Znamenska T.K., Vorobiova O.V., Holota T.V. et al. Differential diagnostics of inherited metabolic disorders in newborns. Wiadomości Lekarskie. 2020;72(6):1211-121.

This article was written in the frames of Scientific research work «To develop clinical and laboratory criteria, methods for predicting and preventing metabolic disorders in young children» 0120U102856.

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Conflict of interest:
The Authors declare no conflict of interest.

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Received: 19.11.2020
Accepted: 14.04.2021

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article