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# Comparison of glucose and lipid values in cord blood of newborns with small, normal and large birth weight according to gestational age

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**Abstract**

**Aim:** Fetal growth is a complex process influenced by environmental and genetic factors. Environmental factors such as glucose, lipids and amino acids play a role in growth of the fetus. Glucose, insulin and lipid levels in the cord blood can change the birth weight according to the gestational age of the newborn. The aim of the study is to examine the relationship between glucose, insulin and lipid levels in cord blood of newborns with small (SGA), normal (AGA) and large (LGA) birth weight according to gestational age.

**Materials and Methods:** 358 term newborns born in our hospital between January 2019 and January 2020 were included in the study. By looking at the weight percentile of the newborns, those with birth weight below the 10th percentile were considered as SGA newborns, those with birth weight of 10-90 percentiles as AGA newborns, and those with birth weight above the 90th percentile was considered as LGA newborns. Insulin, glucose, LDL cholesterol, HDL cholesterol, VLDL cholesterol, total cholesterol, and triglyceride levels of umbilical cord blood were studied after delivery.

**Results:** Of 358 newborns included in the study, 27 (7.5%) were SGA, 312 (87.2%) were AGA, and 19 (5.3%) were LGA. The mean insulin, glucose, cholesterol and triglyceride values of the newborns in all three groups were compared. Cord blood glucose value was found lower as significantly in newborns with SGA. There was not significant difference between cord blood insulin, cholesterol and triglyceride levels of SGA, AGA and LGA newborns.

**Conclusion:** In our study, significant correlation was found between birth weight and cord blood glucose and cholesterol levels.



## Introduction

Fetal growth and development are affected by many factors. It is known that there are permanent changes in physiology and fetüs metabolism in order to adapt to the limited nutrient supply during the intrauterine period [1,2]. When insulin in fetal plasma is reduced, lipoprotein lipase activation is reduced, which inhibits lipolysis of lipoproteins. Insulin and lipid metabolism play an important role in intrauterine growth. Correlation of cord blood lipid profile in neonates with anthropometric measures and their predictive role for cardiometabolic diseases in adulthood are still not investigated [2]. Various factors are reported to have a strong effect on fetal lipid metabolism during pregnancy [3,4].

Growth retardation in the intrauterine period may change the metabolism in childhood and adulthood [5]. Newborns with small birth weight for gestational age (SGA) have a risk of insulin resistance, hyperlipidemia, cardiovascular diseases and diabetes mellitus in adulthood [6,7]. Similarly, newborns with a large birth weight according to gestational age (LGA) are prone to develop obesity, insulin resistance, and cardiovascular diseases at later ages [8,9]. It is important to know the possible risk factors of SGA and LGA. It is known that there is a positive relationship between glucose, insulin, C peptide and lipid levels, which are the main components of the metabolic balance in mother and the birth weight of newborn [10-12]. Metabolic markers in the cord blood may show intrauterine situation and first metabolic state of fetus and potentially next metabolic dysfunction. Evidence regarding relationship between birth weight and fetal metabolism is limited [13]. The relation between cord blood lipid levels in newborns with low and high birth weight for gestational

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age is not well understood [11,12,14]. Understanding the metabolic profile in SGA and LGA newborns can provide new information about the metabolic pathways of neonates and help reveal effective intervention strategies to prevent metabolic illnesses that may develop in later years [13]. The primary output of the study is to compare the glucose, insulin and lipid levels in cord blood of newborns with different birth weights according to gestational age and the end point of the study to examine the relationship between birth weight and cord lipid and glucose levels.

## Materials and Methods

Newborns were included the study who were born between January 2019 and January 2020 in our hospital. Between January 2019 and January 2020, 740 newborns were born term. Of these newborns, 28 were SGA, 52 were LGA, and 660 were AGA newborns. A total of 358 newborns (27 SGA, 312 AGA, 19 LGA) out of 740 newborns were included. The sample size was formed in the GPower 3.1 program, with at least 20 newborns from each of the three groups, assuming a medium effect size, with a 5% margin of error, 95% confidence interval, and 80% power. The corrected randomization method was used in the distribution of the individuals included in the study into groups. The study was approved by Medical Sciences Ethics Committee (12.01.2022 / 20.478.486-1155) and the study was conducted with the principles of the Helsinki Declaration. Informed consent was obtained. Multiple pregnancies, prematures (gestational age <38 weeks), stillbirths, maternal pre-pregnancy diabetes, gestational diabetes, hypertension, infants with premature rupture of membranes and with major congenital anomalies were excluded. The number of pregnancies, number of births, maternal age, height, prepregnancy weight, gaine weight during pregnancy, education and income levels of the mothers were recorded in detail. Body mass index (BMI) ($kg/m^2$) was calculated according to the pre-pregnancy body weight and height measurements of the mothers. In the World Health Organization BMI classification, if the mother's prepregnancy BMI: <18.5 $kg/m^2$ is below normal, BMI: 18.5-24.9 $kg/m^2$ is normal weight, if BMI: 25-29.9 $kg/m^2$ is overweight, and BMI is: ≥30 $kg/m^2$ was considered obese. After birth, newborns were examined and weight, height and head circumference measurements were made. Mode of delivery, Apgar scores, and gender were recorded. By looking at the weight percentile of the newborns, those with birth weight below the 10th percentile were evaluated as SGA newborns, those with a birth weight of 10-90 percentiles as normal-birth-weight (AGA) newborns, and those with a birth weight above the 90th percentile were evaluated as LGA newborns. Simple random sampling method was used in the study. Insulin, glucose, LDL cholesterol, HDL cholesterol, VLDL cholesterol, total cholesterol and triglyceride levels were studied taken from the umbilical cord blood samples after delivery.

### *Statistical analysis*

Statistical evaluation of the data was carried out using the "SPSS (Statistical Package for Social Sciences) 25.0 for Windows" program. The conformity of the numerical variables to the normal distribution was checked with the shapiro -wilk or kolmogorov -smirnov test. Variables conforming to normal distribution were expressed as mean ± standard deviation, and variables not conforming to normal distribution were expressed as median (min, max). Categorical variables were given as numbers and percentages. Intergroup analyzes of categorical variables were performed using the chi-square test by creating cross tables. Comparisons of two groups in numerical variables were made by t-test for normally distributed variables and by Mann Whitney U test for non-normally distributed variables. One Way ANOVA was used for comparisons of three groups. Logistic regression, nominal regression, and Cohen's kappa coefficient methods were also used to evaluate the data. Spearman correlation test was used to determine the relationship between insulin, glucose, LDL cholesterol, HDL cholesterol, VLDL cholesterol, total cholesterol, triglyceride levels in cord blood and birth weight. $p < 0.05$ was evaluated as statistical significance.

## Results

Between January 2019 and January 2020, 740 term newborns were born in our hospital. A total of 358 term newborns out of 740 newborns were included. When the demographic features of the newborns were examined, the average gestational age was 38.44 ± 0.81 (38-41) weeks, the average birth weight was 3202.76 ± 469.14 g (1860-4800), and the mean birth length was 47.62 ± 2.10 cm ( 40-54), mean head circumference was 34.40 ± 1.55 cm (30.5-38.5). Of the newborns, 165 (46.1%) were girls and 193 (53.9%) were boys. Of 358 newborns included in the study, 27 (7.5%) were SGA, 312 (87.2%) were AGA, and 19 (5.3%) were LGA. When the demographic characteristics of newborns with SGA, AGA, and LGA were examined, a significant correlation was found between birth week, birth weight, birth length, birth head circumference, birth week according to ultrasonography, ponderal index, and intrauterine growth restriction (Table 1).

Considering the antenatal history of newborns with SGA, AGA, and LGA, maternal age was found to be similar in three groups. There was not significant difference between three groups in terms of pre-pregnancy weight, gained weight during pregnancy, weight at the end of pregnancy, height, education level and income level of the mothers. There was significant difference between the three groups according to the body mass index (BMI) of the mothers and the age of the fathers. Among the three groups, mothers in the SGA group were found to have a higher rate of normal and subnormal weight compared to BMI before pregnancy. It was observed that the mothers in LGA group gained higher weight significantly during pregnancy than the mothers in the AGA and SGA groups (Table 2).

When lipid and glucose profiles in the cord blood of newborns with SGA, AGA, and LGA were examined, the glucose level in the cord blood was found lower as significantly in the group with SGA. There was not significant difference between three groups in terms of insulin, HOMA, LDL cholesterol, HDL cholesterol, VLDL cholesterol, total cholesterol and triglyceride values. When LGA and AGA groups were compared, cord blood total cholesterol and triglyceride values were found lower as significantly in newborns with LGA compared to newborns with AGA.

**Table 1.** Comparison of demographic features of newborns with SGA, AGA, and LGA.

| | SGA (n=27) | AGA (n=312) | LGA (n=19) | p |
|---|---|---|---|---|
| Gestational age (weeks) | 38.14 ± 0,45 (38-40) | 38.43 ± 0.81 (38-41) | 39.10 ± 0.87 (38-41) | <0.001<br>*0.006<br>**0.004<br>***<0.001 |
| Birth weight (g) | 2291.11 ± 143.24 (1860-2500) | 3222.88 ± 345.73 (2510-3970) | 4167.89 ± 182.71 (4000-4800) | <0.001<br>*<0.001<br>**<0.001<br>***<0.001 |
| Birth length (cm) | 44.79 ± 1.94 (40-48) | 47.75 ± 1.93 (42-54) | 47.87 ± 1.41 (45-50) | <0.001<br>*<0.001<br>**<0.001<br>***<0.001 |
| Birth head circumference (cm) | 32.44 ± 1.23 (31-36.5) | 34.45 ± 1.43 (30.5-38.5) | 36.28 ± 0.90 (35-38) | 0,018<br>*<0.001<br>**<0.001<br>***<0.001 |
| Gender (n,%)<br>-Girl<br>-Boy | <br>13 (48,1)<br>14 (51,9) | <br>141 (45,1)<br>171 (54,9) | <br>11(57,8)<br>8 (42,2) | 0.545 |
| Ponderal index (g/cm$^3$) | 2.56 ± 0.33 (2.10-3.40) | 3.05 ± 0.65 (2.10-3.60) | 3.43 ± 0.27 (2.92-3.90) | 0.153<br>*<0.001<br>**0,001<br>***<0.001 |
| Type of birth (n,%)<br>-NspD<br>-C/S | <br>0 (0)<br>27 (100) | <br>16 (5,1)<br>296 (94,9) | <br>1 (5,2)<br>18 ( 94,8) | 0.483 |
| Gestational age according to US (weeks) | 34.14 ± 2.08 (31-40) | 37.84 ± 1.32 (33-41) | 38.94 ± 1.17 (36-41) | <0.001<br>*<0.001<br>**0,001<br>***<0.001 |
| Intrauterine growth restriction (IUGR) (n,%) | 14 (51,8) | 27 (8,6) | 0 (0) | <0.001<br>*<0.001<br>**<0.001<br>***<0.001 |
| 1st min Apgar score (mean) | 7 (6-9) | 8 (6-10) | 8 (7-8) | 0.628 |
| 5th min Apgar score (mean) | 8 (8-10) | 9 (8-10) | 9 (8-10) | 0.980 |

*: SGA-AGA p value, **: LGA-AGA p value, ***: SGA-LGA p value.

When LGA and SGA groups were compared, cord blood LDL cholesterol value was found lower as significantly in newborns with LGA than in newborns with SGA (Table 3).

When the relation between anthropometric features at birth and glucose and lipid values in the cord blood was examined, a positive relationship was determined between birth weight and head circumference and the glucose level in cord blood, and a negative relationship was determined between birth weight and total cholesterol and LDL cholesterol levels in the cord blood. A negative correlation was also found between the weight gained by the mother before

**Table 2.** Comparison of antenatal features of newborns with SGA, AGA, LGA.

| | SGA (n=27) | AGA (n=312) | LGA (n=19) | p |
|---|---|---|---|---|
| Maternal age (years) | 28. 25 ± 7.07 (19-44) | 29.97 ± 5.68 (18-44) | 29.84 ± 5.52 (21-40) | 0.337 |
| Number of maternal pregnancies (n) | 3 (1-6) | 3 (1-10) | 3 (1-6) | 0.499 |
| Number of maternal births (n) | 2 (0-6) | 2 (0-10) | 2 (1-6) | 0.438 |
| Pre-pregnancy weight (kg) | 72.59 ± 17.43 (40-113) | 72.15 ± 15.38 (40-131) | 77.73 ± 15.77 (56-104) | 0.317 |
| Weight at the end of pregnancy (kg) | 83.66 ± 18.92 (56-128) | 82.06 ± 17.11 (47-138) | 92.0 ± 17.46 (65-124) | 0.370<br>**0.025 |
| Weight gained during pregnancy (kg) | 11.37 ± 4.08 (4-27) | 11.48 ± 4.54 (7-27) | 14.26 ± 3.84 (9-27) | 0.261<br>**0.013<br>***0.019 |
| Mother's height (cm) | 162.65 ± 6.52 (150-175) | 161.89 ± 5.75 (145-178) | 159.73 ± 6.94 (150-174) | 0.186 |
| Maternal body mass index (kg/cm$^2$) | 28.24 ± 6,90 (17.50-47) | 30.37 ± 6.23 (15.60-54.11) | 30.94 ± 6.23 (22.50-45.55) | 0.218 |
| Weight by body mass index (n,%) | | | | |
| -Under normal weight | 2 (%7) | 1 (%0.3) | 0 (%0) | |
| -Normal weight | 7 (%26) | 64 (%20.6) | 6 (%32) | 0.008 |
| -Over-weight | 8 (%30) | 95 (%30.4) | 5 (%26) | |
| -Obese | 10 (%37) | 152 (%48.7) | 8 (%42) | |
| Mother education status (n,%) | | | | |
| -Illiterate | 3 (11) | 25 (8) | 0 (0) | 0.183 |
| -Primary education | 16 (59) | 185 (59) | 15 (79) | |
| -High school | 5 (19) | 41 (13) | 4 (21) | **0.041 |
| -University | 3 (11) | 61 (20) | 0 (0) | |
| Father age (years) | 30.55 ± 5.95 (20-45) | 33.31 ± 5.69 (21-48) | 34.05 ± 5.69 (26-46) | 0.045<br>*0.028 |
| Family income level (TL) | 2996. 29 ± 1809.26 (1500-10000) | 2922.98 ± 1623.20 (500-10000) | 2217.89 ± 866.94 (500-4000) | 0.169<br>**0.003 |

*: SGA-AGA p value, **: LGA-AGA p value, ***: SGA-LGA p value.

pregnancy and cord blood cholesterol and HDL cholesterol (Table 4 and table 5).

## Discussion

Metabolic markers such as glucose and lipid profile in cord blood may show intrauterine status or initial metabolic state in fetus and potentially be associated with next metabolic disturbance [13]. A significant portion of newborns with low birth weight for gestational age (SGA) encountered growth restriction in the intrauterine period, and it has been shown that insulin production is decreased in these newborns [15]. Newborns with a large birth weight (LGA) for gestational age, also cause fat accumulation with increased food supply in the intrauterine period and the resulting increased insulin secretion [16]. When both SGA and LGA newborns are compared with AGA newborns according to gestational age, it has been shown that the insulin concentration is not optimal depending on the intrauterine environment and the risk of cardiometabolic complications such obesity, diabetes and cardiovascular diseases increases in the later years of life [13,17,18,19]. It is known that many factors have an effect on fetal glucose and lipid metabolism during pregnancy [3,4]. The relation between birth weight and cord blood lipid levels is not fully understood [11,12,14]. Understanding the metabolic profile in newborns with different birth weights according to the gestational week could provide new information about the metabolic mechanism of neonates and could help reveal effective intervention strategies to prevent metabolic illnesses that may develop in later ages [13].

In our study, glucose levels in the cord blood of newborns with SGA were found lower significantly than those of LGA and AGA newborns. There was not significant difference between insulin values. A positive correlation was determined between the glucose level in the cord blood and birth weight and head circumference. Most of the cord blood glucose is freely transported by mother, and for this reason, it could have an important role in measuring the glucose level and also insulin secretion in fetus [16]. It is known insulin secretion plays a important role in the fetal growth. High insulin levels increases the glucose uptake in adipose and muscle tissue, and also blocks glycogenolysis and gluconeogenesis in liver, stimulates synthesis of glycogen [20]. In many studies, it's known newborns with SGA and LGA are in the risk of hypoglycemia [21-23].

Evidence regarding the relationship between birth weight and fetal metabolism is limited and controversial. It was found cord blood insulin level was associated indepen-

**Table 3.** Comparison of insulin, glucose, lipid values in cord blood of newborns with SGA, AGA, and LGA.

| | SGA (n=27) | AGA (n=312) | LGA (n=19) | p |
|---|---|---|---|---|
| Glucose (mg/dl) | 40.44 ± 19.10 (10-77) | 54.07 ± 20.45 (10-134) | 52.63 ± 11.88 (17-64) | 0.003<br>*0.001<br>***0.011 |
| Insulin (mIU/ml) | 10.65 ± 24.37 (0.2-129) | 9.73 ± 26.69 (0.2-148) | 9.04 ± 10.37 (0.6-49.1) | 0.989 |
| HOMO | 1.57 ± 4.67 (0.03-24.58) | 1.76 ± 5.59 (0.04-39.84) | 1.21 ± 1.40 (0.04-6.42) | 0.964 |
| Cholesterol (mg/dl) | 68.07 ± 25.30 (13-131) | 64.33 ± 21.53 (13-154) | 56.78 ± 13.93 (29-80) | 0.209<br>**0.037 |
| LDL Cholesterol (mg/dl) | 35.48 ± 16.92 (3-93) | 28.91 ± 17.24 (3-102) | 26.15 ± 11.58 (6-54) | 0.893<br>***0.032 |
| HDL Cholesterol (mg/dl) | 31.44 ± 11.92 (12-58) | 29.41 ± 8.11 (12-59) | 28.26 ± 6.18 (17-38) | 0.388 |
| VLDL Cholesterol (mg/dl) | 4.51 ± 2.06 (2-9) | 6.02 ± 4.60 (2-35) | 5.0 ± 1.97 (2-8) | 0.157<br>*0.003 |
| Triglyceride (mg/dl) | 25.96 ± 19.14 (8-107) | 30.32 ± 22.79 (8-173) | 24.10 ± 10.17 (8-40) | 0.327<br>**0.027 |

*: SGA-AGA p value, **: LGA-AGA p value, ***: SGA-LGA p value.

**Table 4.** The relationship between glucose, insulin, HOMA values in cord blood and birth anthropometric measurements, pre-pregnancy weight and weight gained during pregnancy.

| | Glucose (mg/dl) | | Insulin (mIU/ml) | | HOMA | |
|---|---|---|---|---|---|---|
| | r | p | r | p | r | p |
| Birth weight (g) | 0.143 | 0.007 | 0.069 | 1.96 | 0.076 | 0.149 |
| Birth lenght (cm) | 0.047 | 0.371 | 0.047 | 0.380 | 0.052 | 0.331 |
| Birth head circumference (cm) | 0.157 | 0.003 | -0.010 | 0.845 | 0.016 | 0.758 |
| Pre-pregnancy weight (kg) | 0.044 | 0.410 | 0.098 | 0.068 | 0.094 | 0.074 |
| Weight gained during pregnancy (kg) | -0.071 | 0.181 | 0.044 | 0.403 | 0.020 | 0.705 |

**Table 5.** The relationship between lipid values in cord blood and birth anthropometric measurements, pre-pregnancy weight and weight gained during pregnancy.

| | Cholesterol (mg/dl) | | LDL Cholesterol (mg/dl) | | HDL Cholesterol (mg/dl) | | VLDL Cholesterol (mg/dl) | | Triglyceride (mg/dl) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | r | p | r | p |
| Birth weight (g) | -0.161 | 0.002 | -0.159 | 0.003 | -0.090 | 0.091 | -0.045 | 0.395 | -0.70 | 0.189 |
| Birth length (cm) | -0.058 | 0.276 | -0.023 | 0.662 | -0.096 | 0.055 | 0.007 | 0.888 | -0.001 | 0.983 |
| Birth head circumference (cm) | -0.063 | 0.236 | -0.99 | 0.60 | 0.004 | 0.939 | 0.055 | 0.299 | 0.039 | 0.461 |
| Pre-pregnancy weight (kg) | -0.151 | 0.004 | -0.097 | 0.068 | -0.211 | <0.001 | 0.047 | 0.378 | 0.039 | 0.458 |
| Weight gained during pregnancy (kg) | -0.097 | 0.068 | -0.102 | 0.054 | 0.00 | 0.997 | -0.074 | 0.160 | -0.075 | 0.159 |

dently with increased birth weight in newborns of mothers with type 1 diabetes, however this relationship was not found in newborns of mothers without type 1 diabetes [24]. On the other hand, a positive correlation was determined between the birth weight of term newborns of mothers without diabetes and cord blood insulin levels in a study [25].

In our study, there was not significant difference between the SGA, AGA and LGA groups in terms of cholesterol and triglyceride (TG) values. When LGA and AGA groups were compared, cholesterol and TG values were found to be significantly lower in newborns with LGA. When LGA and SGA were compared, LDL cholesterol value was found lower as significantly in newborns with LGA. Negative correlation was determined between the level of cholesterol and LDL cholesterol in cord blood and birth weight. Adipose tissue plays a important role in metabolism, buffering the daily flow of fatty acids and storing more energy in the form of TG. Ectopic fatty acid accumulation occurs in nonadipose tissues such as muscle and liver when TG accumulation exceeds the buffer capacity. The intrauterine environment can play an central role in the development of adipose tissue [26].

The results of the studies show differences between cord blood lipid values and birth weight. In a study, there was not relation between birth weight and cord blood lipids, but in another study, there was a relation between birth weight and cord blood lipid profile in newborns born with SGA and LGA [11,12]. High TG levels were observed in newborns born with SGA in the studies [25,27]. In the study of Aletayeb et al., cholesterol, LDL-cholesterol and TG levels were found to be high in newborns with both SGA and LGA [28]. It was determined that HDL and LDL cholesterol values were low in newborns with LGA [11], and there was no relationship between birth weight and cord blood lipid profile [12,29]. It was shown that the TG value in the cord blood of newborns with SGA was higher significantly, and the cholesterol, LDL and HDL cholesterol values were significantly lower [13].

In our study, when the pre-pregnancy weights of the mothers were evaluated according to BMI, it was seen that the mothers of SGA newborns were more normal and below normal weight than the newborns of AGA and LGA mothers. It was found that mothers of newborns with LGA gained higher weight significantly during pregnancy than mothers of newborns with both SGA and AGA. It is known that maternal weight gain before and during pregnancy has a critical effect on fetal growth. Maternal weight disorders before and during pregnancy can affect the fetal growth and maturation, and their effects to cord blood lipid changes are controversial [30,31]. In our study, the weight gained during pregnancy was determined higher as significantly in newborns with LGA than newborns with SGA and AGA; however, no significant correlation was found between weight gained during pregnancy and cord glucose and lipid values. A negative correlation was found between the mother's pre-pregnancy weight and the cholesterol and HDL cholesterol levels in the cord blood.

It is thought that the fact that the mother is obese according to the BMI before pregnancy affects the cord lipid values only when it is associated with fetal macrosomia. Macrosomic newborns of obese mothers have high TG and low HDL cholesterol [32]. Cord blood lipid values were determined higher in newborns born to overweight mothers, and lower cord blood lipid values in newborns born to low-weight mothers [11].

In a study, it was shown that cord blood glucose was lower in newborns of overweight mothers before pregnancy, especially in newborns with LGA [13]. It was shown that significant correlation between prepregnancy BMI and cord blood TG values [11]. In a study, it was shown that prepregnancy BMI is independent marker of neonatal hypoglycemia in infants of gestational diabetic mothers [33]. In another study, it was shown that prepregnancy obesity and excessive weight gain during pregnancy increase the risk of neonatal hypoglycemia in infants of gestational diabetic mothers [34].

## Conclusion

As a result, cord blood glucose value was found to be significantly lower in newborns with small birth weight according to gestational age, and cord blood triglyceride and cholesterol values were found to be significantly lower in newborns with large birth weight according to gestational age. Cord blood glucose value, which is positively correlated with birth weight, and cord blood cholesterol value, which is negatively correlated with birth weight, may be indicators of future metabolic dysfunction in the newborn. Future studies are needed to explain the differences in lipid profiles of term newborns with different birth weights.

*Ethics approval*

The study protocol was reviewed and approved by Medical Sciences Ethics Committee (12.01.2022 / 20.478.486-1155).

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