

Correlation of serum resistin level and other metabolic hormones and immune function in neonatal umbilical cord blood

Na Wang, MD^{a,*}, Gaowa Eerdun, MD^a, Yan Dong, MD^a, Ling Hao, MD^a, Tiezhi Li, MD^b

Abstract

The present study was conducted with an attempt to explore the correlation of serum resistin level and other metabolic hormones and immune function in neonatal umbilical cord blood.

The levels of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, thyrotropin, thyroid hormone (T3, T4), IgM, IgA, IgG, CD4, and CD8 were measured in 180 full-term newborns delivered in hospital from October 2018 to November 2019. The delivery mode, weight, height, and gender at birth were recorded.

The levels of resistin, insulin, and growth hormone in umbilical cord blood of newborns delivered vaginally were significantly higher than those born by cesarean section ($P < .05$), while the levels of adiponectin, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 were comparable between the 2 groups ($P > .05$). The levels of resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 in cord blood of male and female newborns were comparable ($P > .05$). The newborns with birth weight ≥ 3501 g reported comparable results in the levels of resistin and growth hormone compared with those with birth weight of 3000 to 3500 g ($P > .05$), but were significantly higher than those with birth weight ≤ 2999 g ($P < 0.05$). In addition, the levels of adiponectin, insulin, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 were comparable among the 3 groups ($P > .05$). Based on Pearson correlation analysis, neonatal umbilical cord blood resistin was positively correlated with adiponectin, leptin, growth hormone, T3, and T4 ($r = 0.281, 0.287, 0.321, 0.276, 0.269, P < .05$). However, there was no significant correlation between neonatal umbilical cord blood resistin and insulin, TST, IgM, IgA, IgG, CD4, and CD8.

The level of serum resistin in neonatal umbilical cord blood was associated with the delivery mode and birth weight, and positively correlated with adiponectin, leptin, growth hormone, T3, and T4. However, no correlation was observed between serum resistin in neonatal umbilical cord blood and insulin, TST, IgM, IgA, IgG, CD4, and CD8.

Abbreviation: T3, T4 = thyroid hormone.

Keywords: immune function, metabolic hormone, neonatal, serum resistin, umbilical cord blood

Editor: Khaled Saad.

This study was approved by the Ethics Committee of The First Hospital of Hebei Medical University and agreed by the guardian and an informed consent form was signed.

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

No funding was received for this study.

The authors have no conflicts of interest to disclose.

^a Department of Pediatrics, The First Hospital of Hebei Medical University,

^b Department of Thoracic Surgery, The Second Hospital of Hebei Medical University, Shijiazhuang, China.

* Correspondence: Na Wang, Department of Thoracic Surgery, The Second Hospital of Hebei Medical University, No. 89 Donggang Road, Yuhua District, Shijiazhuang, Hebei 050031, China (e-mail: 1083181114@qq.com).

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How to cite this article: Wang N, Eerdun G, Dong Y, Hao L, Li T. Correlation of serum resistin level and other metabolic hormones and immune function in neonatal umbilical cord blood. *Medicine* 2021;100:11(e25195).

Received: 31 March 2020 / Received in final form: 18 October 2020 / Accepted: 18 February 2021

<http://dx.doi.org/10.1097/MD.00000000000025195>

1. Introduction

Umbilical cord blood is the earliest blood and has no adverse effect on neonatal blood samples, which is not only of great significance to the guidance of diagnosis and treatment of newborns, but also can achieve the purpose of examination. It is considered one of the most useful samples for early diagnosis instead of early peripheral blood examination.^[1,2] The level of resistin in umbilical cord blood of newborns is different. Resistin is a new type of lipogenic hormone, which is secreted by white adipose tissue in the body and participates in regulating the balance of energy metabolism and has positive correlation with several inflammation factors.^[3,4] Resistin was first reported by Steppan et al in 2001, which contains cysteine peptide hormones, and its main target cells include vascular endothelium, fat, skeletal muscle, and liver cells. Resistin participates in the formation of atherosclerosis and mediates vascular inflammatory response by regulating the role of target cells, and has an effect on lipid metabolism and glucose, thus regulating energy metabolism. It can prevent islet β -cell proliferation, has a negative effect of insulin on promoting cell proliferation. Resistin is also able to release norepinephrine and inhibit hypothalamic dopamine to regulate appetite. Adiponectin, which mainly is produced from the secretion of adipocytes, is a sensitivity factor for the regulation of blood glucose metabolism and insulin. Adiponectin can accelerate the proliferation and differentiation of preadipocytes into adipocytes and act on energy metabolism in the body.^[5]

Leptin is an important hormone of fat metabolism in the body, which can promote the relationship between neuroendocrine system and adipose tissue.^[6] Growth hormone is a peptide hormone, which is able to promote the synthesis of proteins and other tissues in the body. Thyroid hormones can be produced by newborns, which are the main indicators to reflect the degree of thyroid development and function. Thyroid hormones are regarded as important factors for newborns not only to predict the growth and development, but also to reflect the intelligence level of newborns.^[7] Currently basic research has confirmed that with the increase of fetal age, the immune system of the fetus has been gradually improved, and humoral immunity has been formed since the second month of pregnancy and the uterus tends to strengthen contraction during term delivery. But the changes of the immune function and indicators of newborns remain largely unknown. In addition, resistin is mainly distributed in trophoblast cells and can be involved in the regulation of insulin sensitivity during pregnancy; hence, it is highly associated with the regulation of energy metabolism. Given that newborns are affected by maternal antibodies, along with their undeveloped immune system and function without being exposed to external antigenic substances such as food proteins and pathogens in the air, there is special pathogen susceptibility, course of disease, and treatment of newborns. During literature review, limited studies exist regarding the correlation of delivery mode, gender, birth weight with the levels of resistin, adiponectin, insulin, growth hormone, leptin, thyrotropin, thyroid hormone (T3, T4), IgM, IgA, IgG, CD4, and CD8 in umbilical cord blood of newborns. Therefore, the current study was performed in an attempt to explore the correlation of neonatal umbilical cord blood serum resistin levels with other metabolic hormones and immune function.

2. Materials and methods

2.1. Participants

A total of 180 full-term newborns delivered in hospital were enrolled from October 2018 to November 2019. The participants included 102 males and 78 females, the gestational age was 37.68 to 42.72 weeks, with an average gestational age of (39.61 ± 1.08) weeks; the birth weight was 2500 to 4100g, with an average weight of (3301.08 ± 28.92) g. The delivery mode included cesarean section ($n=79$) and spontaneous vaginal delivery ($n=101$). Inclusion criteria: the clinical data were complete; all cases were full-term delivery and singletons; this study was approved by the hospital ethics committee and agreed by the guardian and an informed consent form was signed. Exclusion criteria were incomplete clinical data, less than full-term delivery, twins or triplets, congenital anomalies, congenital heart disease, neonatal asphyxia, severe anemia; neonatal infection; pathological jaundice. This study was approved by the Ethics Committee of The First Hospital of Hebei Medical University and agreed by the guardian and an informed consent form was signed.

3. Method

After the delivery of the fetus and before the delivery of the placenta, 12 mL of umbilical cord artery blood was collected and injected into a clean test tube. After coagulation, it was centrifuged at 3000 rpm/min for 15 minutes and stored in a refrigerator at -80°C . The gestational age, delivery mode, gender, and weight of the newborn were recorded. All specimens

were tested in the same batch. The concentration changes of resistin, adiponectin, insulin, and leptin were detected by enzyme-linked immunosorbent assay kit purchased from Wuhan Doctor Germany Bio-engineering Co, Ltd with SM600 automatic microplate reader. Thyrotropin and thyroid hormone (T3, T4) were detected by electrochemiluminescence immunoassay kit purchased from Roche in Germany with UniCel DxI 800 automatic immunoanalyzer from Beckman company in the United States. Growth hormone was detected by radioimmunoassay kit purchased from Tianjin Jiuding Medical Bioengineering Co, Ltd. Moreover, IgM, IgA, and IgG were detected by IMM AGE double-path immune turbidimetric analyzer from Beckman Coulter Co, Ltd, and the kit used for the detection was purchased from Roche in Germany. The levels of CD4 and CD8 are determined by IMMAGE double-path immune turbidimetric analyzer produced by Beckmann, and the kit was purchased from Roche in Germany. The abovementioned indexes were detected in accordance with the instructions of the kit by 2 laboratory technician of over 8-year experience to ensure the accuracy of the data.

3.1. Statistical analysis

All the data in this study were analyzed by SPSS19.0 software. The measurement data were expressed by $(\bar{x} \pm s)$, and t test was used for comparison between the 2 groups. Analysis of variance was used for comparison between groups, pairwise comparison with LSD- t test, and Pearson correlation analysis was used to analyze the correlation. A $P < .05$ represented significant difference.

4. Results

4.1. Comparison of levels of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 in newborns with different delivery modes

The levels of resistin, insulin, and growth hormone in cord blood of newborns delivered naturally were significantly higher than those of newborns born by cesarean section ($P < .05$), while the levels of adiponectin, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 were comparable between the 2 groups ($P > .05$), as shown in Figure 1.

4.2. Comparison of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 levels in newborns of different gender

The levels of resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 in cord blood of male and female newborns were comparable ($P > .05$), as shown in Figure 2.

4.3. Comparison of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 levels in newborns of different weights

The levels of resistin and growth hormone in newborns with birth weight ≥ 3501 g were comparable compared with newborns with

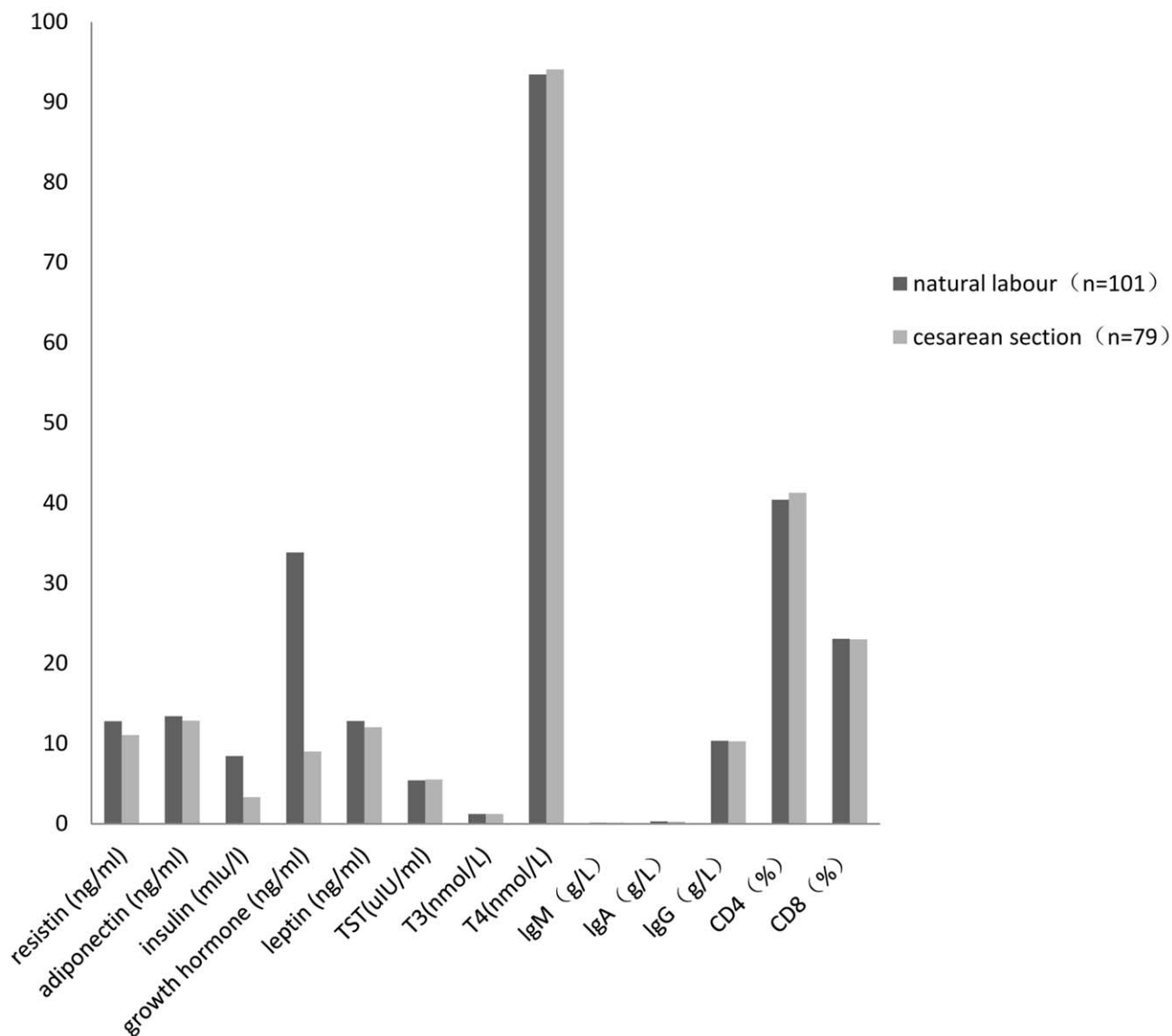


Figure 1. Comparison of levels of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 in newborns with different delivery modes.

birth weight of 3000 to 3500 g ($P > .05$), but were significantly higher than those with birth weight ≤ 2999 g ($P < .05$). The levels of adiponectin, insulin, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 were comparable among the 3 groups ($P > .05$), as shown in Figure 3.

4.4. Correlation of resistin and adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 in neonatal cord blood

Based on Pearson correlation analysis, the level of resistin in neonatal umbilical cord blood was positively correlated with adiponectin, leptin, growth hormone, T3, and T4 ($r=0.281, 0.287, 0.321, 0.276, 0.269, P < .05$). However, there was no significant correlation of resistin and insulin, TST, IgM, IgA, IgG, CD4, and CD8 ($P > .05$).

5. Discussion

The purpose of this study was to investigate the effects of neonatal resistin, related hormones, and immune function on infants with different delivery modes, gender, and body weight. Based on the results, the levels of resistin, insulin, and growth hormone in cord blood of newborns delivered naturally were significantly higher than those of newborns born by cesarean section ($P < .05$), while adiponectin, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 levels were comparable between groups ($P > .05$). The reason may attribute to the adaptive regulation of the fetus who are constantly squeezed by external forces during natural delivery, producing a large number of pro-inflammatory cytokines, enhancing the activity of inflammatory cells to promote the acute inflammatory response mediated by inflammatory mediators and lead to inflammatory waterfall effect. By contrast, the stress response of cesarean section is significantly

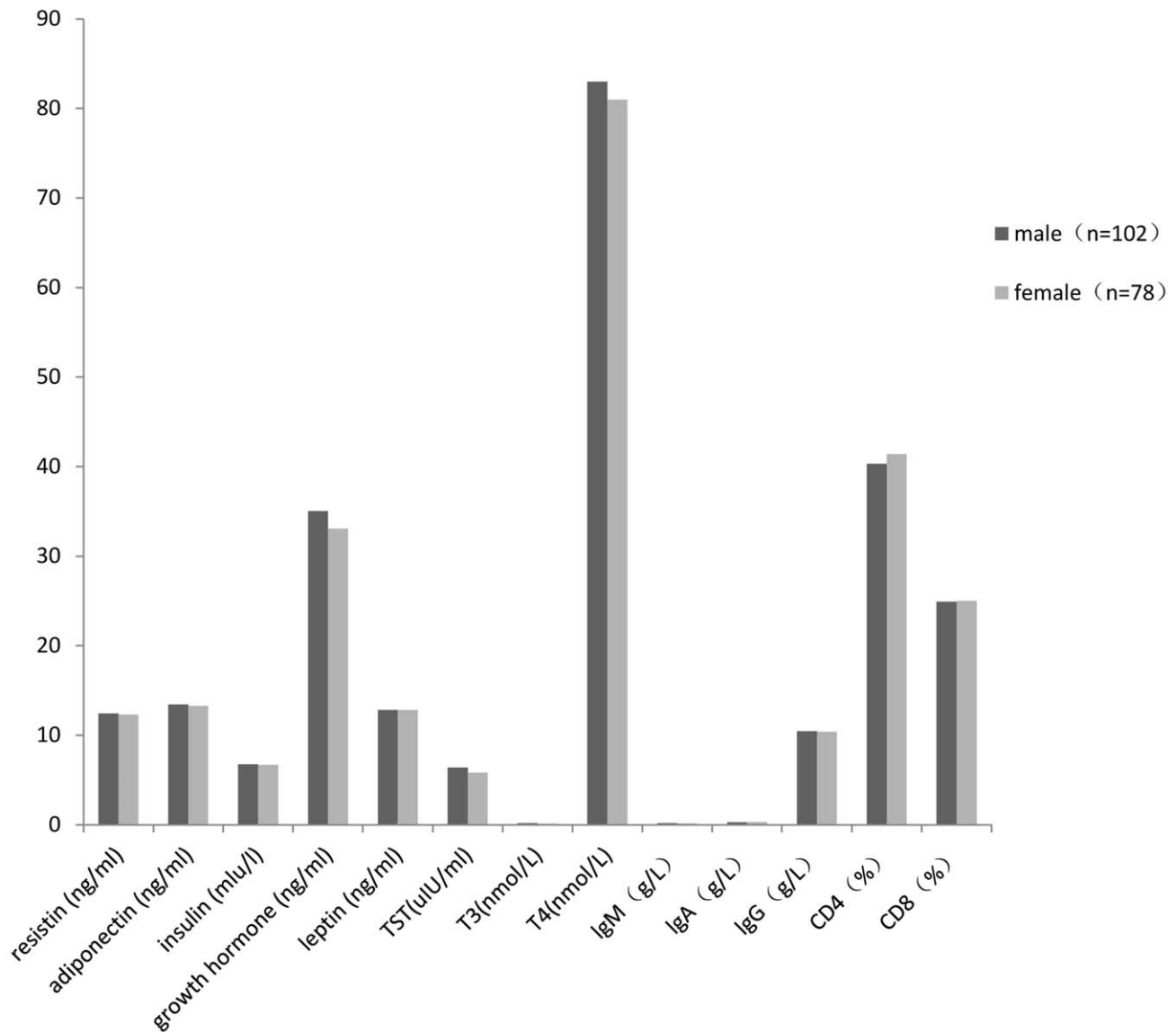


Figure 2. Comparison of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 levels in newborns of different gender.

lower than that of natural delivery; hence, the secretion of resistin tends to be less.

In the present study, the levels of resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 in umbilical cord blood of newborns of different gender were compared. There was no significant difference between male and female, which was consistent with the result of Yang and Kim^[8] and Hellstrom et al,^[9] suggesting that leptin had no significant change in different gender. Similar to the results of Yalinbas et al,^[10] it has been suggested that there was no significant change in the levels of resistin, adiponectin, leptin, IgM, IgA, IgG, CD4, and CD8 in different gender, indicating that gender has no effect on the levels of these factors in umbilical cord blood of newborns. Based on our study, the levels of above factors in umbilical cord blood of newborns with different birth weights were compared. The levels of resistin and growth hormone in newborns with birth weight ≥ 3501 g were

comparable compared to newborns with birth weight of 3000 to 3500 g ($P > .05$), but were significantly higher than those with birth weight ≤ 2999 g ($P < .05$). The levels of adiponectin, insulin, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 were comparable among the 3 groups ($P > .05$), which were similar to Thorsen and Pipper.^[11] It was suggested that the levels of serum resistin and growth hormone in newborns with normal body weight were higher than those with low birth weight, which fully confirmed that resistin and growth hormone could reflect the growth of newborns.

Based on the correlation analysis of Pearson conducted by our study, neonatal cord blood resistin was positively correlated with adiponectin, leptin, growth hormone, T3, and T4, but not with insulin, TST, IgM, IgA, IgG, CD4, and CD8 ($P > .05$). In the course of the study, it was found that resistin could inhibit adipocyte differentiation, negatively regulate adipocyte differentiation, and produce feedback regulation. Resistin was positively

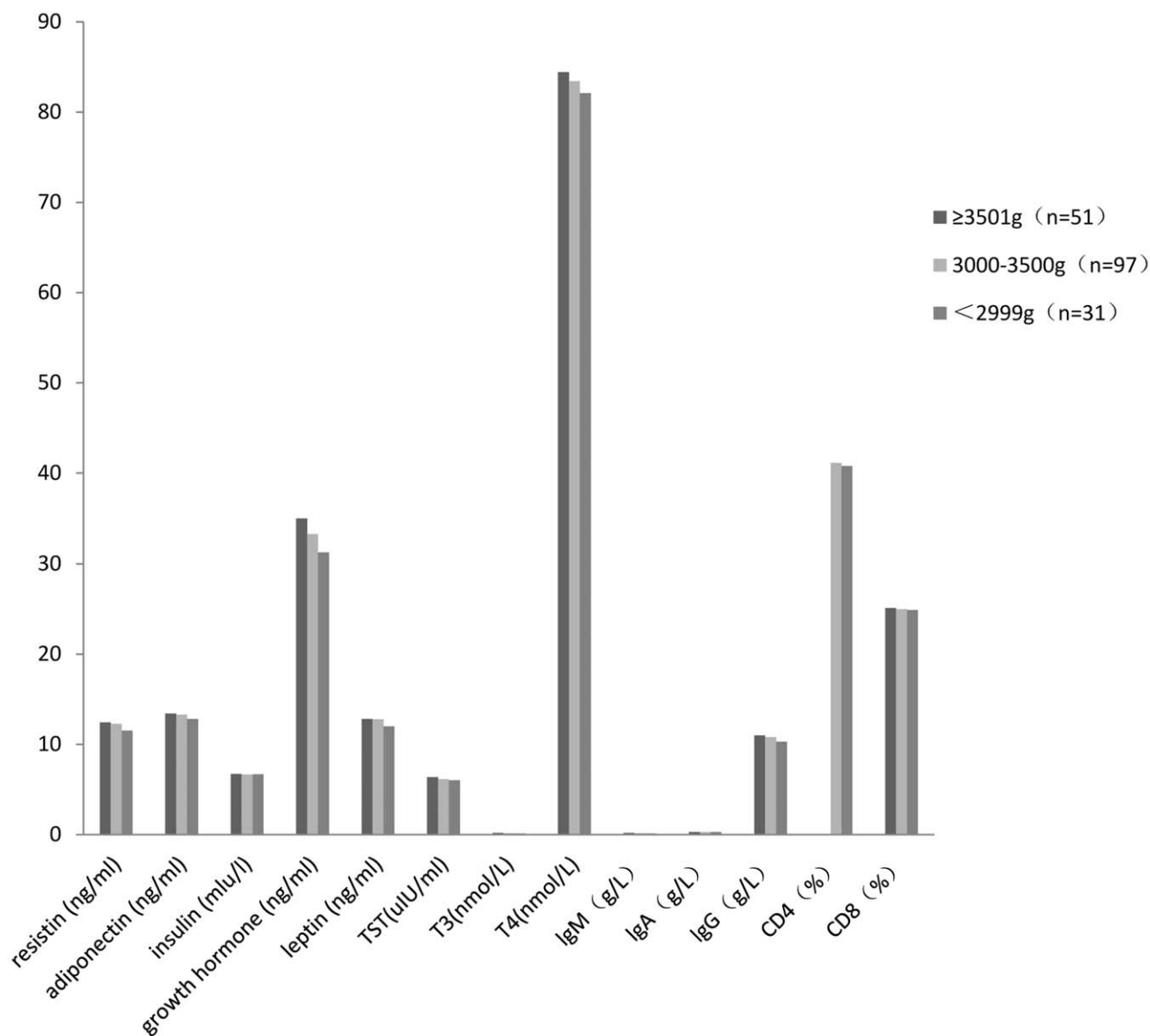


Figure 3. Comparison of umbilical cord blood resistin, adiponectin, insulin, growth hormone, leptin, TST, T3, T4, IgM, IgA, IgG, CD4, and CD8 levels in newborns of different weights.

correlated with nutritional status and hormone levels in adipose tissue, which can reflect the nutritional status of human and animals to some extent.^[3,12] According to related animal experiments, the expression of resistin protein was found in pituitary and arcuate nucleus of rats by immunohistochemical method, and pituitary could regulate the expression of resistin in the process of resistin expression. Song et al^[13] confirmed that the expression level of resistin was low at birth and increased significantly 20 days after birth. Resistin plays an important regulatory role in fetal growth and development, mainly by regulating fat distribution and energy consumption; thus it is positively correlated with adiponectin and leptin, which can affect the normal development of newborns and play a crucial part in the process.^[14,15] Farid et al^[4] found that resistin level had reverse correlation with fetal weight in term neonates. Wang et al^[16] found that adiponectin and resistin play an important role

in controlling body weight and may be related to the occurrence of fetal macrosomia and fetal growth restriction. Our study exerted the first effort to explore neonatal umbilical cord blood resistin, adiponectin, leptin, growth hormone, T3, and T4 as indicators to determine the growth and development of newborns, which provided important clinical value and significance for fetal growth and development.

There are also some limitations in our research. First, the sample size of this research is still limited. In future research, we will expand the sample size to verify our conclusions of this study. Second, the factors evaluated in this study remain limited. The level of serum resistin may be related to other variables, such as cytokines related to growth and development. Future research still needs to explore more variables. In addition, whether the level of serum resistin can be a predictor of neonatal growth and development remains unknown, and whether more

developmental indicators are related to its level needs to be explored.

6. Conclusion

In conclusion, the level of serum resistin in neonatal umbilical cord blood was associated with the delivery mode and birth weight, and positively correlated with adiponectin, leptin, growth hormone, T3, and T4. However, no evident association was found between resistin and insulin, TST, IgM, IgA, IgG, CD4, and CD8.

Author contributions

NW and GE contributed to the conception and design of the study; YD and LH performed the experiments, TL collected and analyzed data; NW wrote the manuscript; All authors reviewed and approved the final version of the manuscript.

Investigation: Na Wang, Tiezhi Li.

Methodology: Na Wang, Gaowa Eerdun, Yan Dong, Ling Hao.

Supervision: Gaowa Eerdun.

Writing – original draft: Na Wang, Yan Dong, Ling Hao, Tiezhi Li.

Writing – review & editing: Na Wang.

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