

Research Article

Prediction of the Immunodeficiencies in the Restriction of the Fetal Growth

Adrian Ruiz Lopez^{1,*} , Vicente Jose Hernandez Moreno² 

¹Basic Sciences, Faculty of Medicine University of Medical Sciences of Villa Clara, Institute of Medical Sciences, Santa Clara, Cuba

²Biomedical Sciences Unit, Faculty of Medicine University of Medical Sciences of Villa Clara, Institute of Medical Sciences, Santa Clara, Cuba

Abstract

Introduction: Birth weight has historically been used as an indicator to assess fetal growth, and newborns below the 10th percentile for a given gestational age have generally been associated with poor outcomes. Current knowledge about the functional capacity of the immune system in the first weeks of life highlights the importance of infections as one of the most important causes of morbidity and mortality in newborns. **Objective:** To identify risk factors for the onset of immunodeficiency in births with restriction of the fetal growth at the Mariana Grajales Gynecological-Obstetric Hospital in the municipality of Santa Clara, Villa Clara province, from January 2016 to December 2023. **Material and Methods:** A descriptive, cross-sectional, and retrospective study was carried out in births with restriction of the fetal growth at the Gynecological-Obstetric Hospital of the municipality of Santa Clara, Villa Clara province, from January 2016 to December 2023. The universe was made up of 44 patients. **Results:** The main risk factor was a history of admission, which represented 56% of the total, followed by not breastfeeding, which in turn represented 40% of the total cases analyzed. **Conclusions:** It is important to understand the risk factors for the development of immunodeficiency, as well as the warning signs, in order to understand the mechanism of its onset and prevent conditions from leading to the underlying cause.

Keywords

Restriction of the Fetal Growth, Risk Factor, Immunodeficiency

1. Introduction

The weight when sprouting has used historically as indirect indicator to evaluate the fetal growth, and the newborns for under the 10 percentile with regard to the "weigh waited" to a gestational certain age been associated generally with bad results [1]. Given the population heterogeneity as for the weight when sprouting, exists a clear difference between the newborns that reach your trajectory of foreseen growth, but

are inherent small for the gestational age (PEG), and the newborns that not reach your trajectory of growth and are small (10 percentile), which usually it is due to a placental insufficiency and it knows one another collectively as restriction of the restriction of the fetal growth (FGR) [2]. The restriction of the fetal growth (FGR) is a complex problem for obstetricians, neonatologists and pediatricians, and constitutes

*Corresponding author: adrian1312@nauta.cu (Adrian Ruiz Lopez)

Received: 8 July 2025; **Accepted:** 18 July 2025; **Published:** 7 August 2025



Copyright: © The Author(s), 2025. Published by Science Publishing Group. This is an **Open Access** article, distributed under the terms of the Creative Commons Attribution 4.0 License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited.

a factor of risk for the appearance of non-transferable illnesses (IT) in later stages of the included life the pediatric ages. According to the calculations estimated, in the world it occurs 30 from birth millions of childrens with FGR, of them/it 75% in Asia, 20% in Africa and 5% in Latin America [3]. In Cuba, in 2021, of the total of the paid attention alive inflamed boils in the services of neonatolog á, 6.7% had a smaller weight that the tenth percentile [4], by keeping in mind the nutritional valuation [5]. All chases of the immunological system of the newborn (adaptive: cellular and humoral, and innate: phagocyte, receiving toll type and other, complement) are immature, besides having scarce immunological memory, which is translated in a special susceptibility to gram germs negative, B, staphylococcus, pseudomona, listeria, toxoplasma and funguses streptococcus in this period. Numerous non-immunological factors contribute to the susceptibility of the newborn to infections: cutaneous barrier fragile mucous membrane, get ready respiratory immature, micro non-established digestive biota, the pathology of any type (prematuridades, bronchopulmonary dysplasia, infect congenital, congenital cardiopathy, trisomies, malformations in general) and associates problems nutritional and metabolic, instrumental interventionism, and secondary immunosuppression to medicines or to nosocomial infections [6]. The immunodeficiencies are illnesses for quantitative alteration and/or functional of the different mechanisms implied contradiction in the immunological answer, that originates an augmented predisposition to infecting, and also to autoinmunes, inflammatory processes, of immune anomalous, allergic or oncological regulation [7]. The neonatal mortality, it is a fundamental indicator of health and well-being; for which the sanitary authorities award you a special attention. The current knowledges on the functional capacitance of the immunological system in the first weeks of life are limited; even so, results evident the place they occupy the infections as one of the more important causes of morbidity and mortality in newborns [8, 9]. The breast-feeding constitutes a fundamental element in the feeding of the childrens, indispensable in an exclusive way in the firsts six monthes; your start-up in the first hour is suggested of life, that it is to giving birth claim and avoid the use of infantile formulae because this lactation constitutes a nutritious food with equilibrium between consistency, vitaminize, mineral, nutrients and the other main elements [10]. Along the first years of life the child is in a period of transitory immunodeficiency in which is susceptible to infecting that, in occasions can cause you the death. This condition of transitory immunodeficiency, can mix up, and more still if disavow the own characteristics of this stage. The infancy of the human being is the period of vulnerability major, it is a stage of ripeness and of development of the vital organs and of the system of immunological defense that will permit combat square clinical futures. It understands, then, that the neonatal nutrition is fundamental for your biological development. In effect, the breast milk possesses great importance as source of factors that favors the development of

the immune system, capable of it prevents multiple frequent illnesses in the first monthes, thanks to the combination of the diverse bioactive components presents in it [11]. Studies carried out in Cuba give to know that, 49% of the milk-fed babies you are provided exclusive breast-feeding until the sixth month of life, 77% of the newborns receives it in the first hour of life and 90% in the first day of inflamed boil. The bigger prevalence is registered in the eastern region of the country with 58.7% [12]. The umbilical cord has converted in an element of interest for the regenerative medicine in the last years, because constitutes an important source of stem cells and hematopoietic progenitors, besides that represents the being union the foetus and the mother during the embarasment, it takes part in in the fetal nutrition and permits resist the intra-uterine pressures and the fetal tractions [13]. It has demonstrated that the umbilical cord of the so much newborns to term as term pre, contains a certain number of progenitresses cells immature and committed, result of the fetal hematopoiesis, that it is the physiologic process for which is produced the ripeness of the types of cells that compose the blood. Your correct functioning permits the formation of responsible cells of the transport of oxygen, of the blood coagulation and the immunity. The bleeds of the umbilical cord is a source of diverse cellular types, among them the mononuclear cells, those who it is included: the monoblastoses, the lymphoblasts, the lymphocytes, the monocytes, and the precursors of erythrocytes, proeritroblastoses and erythroblasts [14]. Allude to young that suffer infections with a frequency it appears are bigger that those of other childrens of your same age. In the developed countries, between 18% and 25% of the childrens they have respiratory infections of high pathes of encore in the firsts 4 years of life, as consequence of the exposition to pathogens, generally virus, with those who your immune system has not had previous contact. It has estimated that the annual stocking during this time of the life is of six to eight infections of respiratory high pathes, but it can reach until 10-12 infections a year, when the child or your brothers attend post of guard or there is environmental factors, as the tobaccoism in the parents. The succession of thesings to infect, by keeping in mind that your duration is of about 8 days, it makes room for the printing that the child is continuously sick, which generates preoccupation and anxiety in your parents [15].

2. Materials and Methods

Carried out a descriptive study, transversal and retrospective, in birthes with restriction of the fetal growth, at the Mariana Grajales Gynecological-Obstetric Hospital in the municipality of Santa Clara, Villa Clara province in period of January of the 2016 to December of the 2023. The universe remained agreed for 44 patients. The sample was constituted for 25 patient elects for sample random.

The selected variables went: Number of newborns with restriction of the fetal growth, newborns with the condition of

FGR that it received or not exclusive breast-feeding until the six months, newborns with FGR and antecedents of hospitable revenues, newborns with FGR and fallen normal school, premature or late of the umbilical cord and from birth with

condition of FGR those who had immunodeficiency. The data's were gathered of the clinical records of the newborns, at the Mariana Grajales Gynecological-Obstetric Hospital in the municipality of Santa Clara, Villa Clara province.

3. Results

Table 1. Distribution of newborns with FGR according to exclusive breast-feeding, antecedents of hospitable, fallen revenues of the umbilical cord and immunodeficiency in the period understand of January of the 2016 to December of the 2023.

Characteristitics of FGR newborn	Immunodeficiency No %	Immunocompetent No %
Exclusive breast feeding	6	3
	24	12
Not exclusive breast feeding	10	6
	40	24
Hospitable revenues	14	3
	56	12
Not hospitable revenues	2	6
	8	24
Fall of the umbilical cord <5 days and >10 days	8	3
	32	12
Fall of the umbilical cord between 5 and 10 days	8	6
	32	24

Source: Clinical record of the newborns.

$\chi^2 = 3.841$, gl = 1 P = 0.0432.

In the [Table 1](#) observes a predominance between the newborns that had hospitable revenues and the appearance of immunodeficiency, by representing these 56% of the affected, followed sample of the patients that not had not exclusive breast-feeding until the 6 monthes, representing a 40% of the

sample. The performance of the result of the statistical proof of ch ísquared to the evaluate the variables, resulted significant for the report between the not breast-feeding and the occurrence of immunodeficiency because p is smaller than 0.05.

Table 2. Validity of the points of best cut for the development of immunodeficiency according to exclusive breast-feeding, antecedents of hospitable and fallen revenues of the umbilical cord in the understood period of January of the 2016 to December of the 2023.

Indicators of immunodeficiency	Sensibility (%) (IC 95%)	Specificity (%) (IC 95%)	Reason of verisimilitude (+) (IC 95%)	Reason of verisimilitude (-) (IC 95%)
Exclusive breast feeding	37.5	66.7	1.126	0.937
Hospitable revenues	87.5	66.7	2.628	0.187
Fall of the umbilical cord <5 days and >10 days	50	66.7	1.502	0.749

Source: Own manufacture.

In the [table 2](#) show the indicators of immunodeficiency and your points of best cut for the prediction of this alteration. It

observes that the antecedents of hospitable revenues, expresses the better values as a whole of all used measures. The other indicators, to weigh that exhibit value to consider, the

Fall of the express umbilical cord a sensibility of a 50%, and a specificity of 66.7%.

Table 3. Predictive capacitance of the variable exclusive breast-feeding, antecedents of hospitable and fallen revenues of the umbilical cord, for the development of immunodeficiency the understood period of January of the 2016 to December of the 2023.

Indicators of immunodeficiency	Area of ROC below the curve	Confidential interval (95%)	
		Limit lower	Superior limit
Exclusive breast feeding	0.4632	0.2146	0.7119
Hospitable revenues	0.6618	0.4392	0.8843
Fall of the umbilical cord <5 days and >10 days	0.4459	0.1895	0.6899

Source: Own manufacture.

In the Table 3 observes the predictive capacitance of the variable exclusive breast-feeding, antecedents of hospitable and fallen revenues of the umbilical cord, for the development of immunodeficiency. The hospitable revenues predict 66.1%

(area below the curved ROC=0.661). In order of descending frequency, follows you the not exclusive breast-feeding (0.463) of area below the curved ROC.

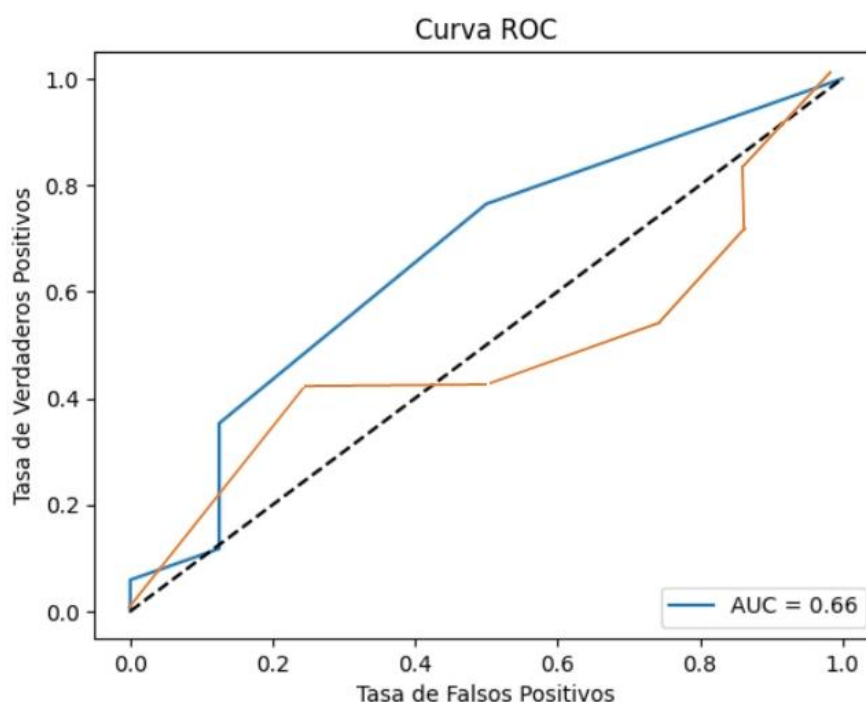


Figure 1. Area below the curved ROC of the predictors of immunodeficiency: Hospitable revenues and the not exclusive breast-feeding the understood period of January of the 2016 to December of the 2023.

The Figure 1 shows the curve of classification for the diagnosis of immunodeficiency, of the indicating hospitable revenues and not exclusive breast-feeding until the six months, in which a predominance in the sketched line for the hospitable revenues is observed (0.661 and 0.463) respectively.

4. Discussion

In the study carried out have a predominance as for the existent report between the antecedents of entrance of the new-

borns with FGR and the appearance in the same of immunodeficiency, by representing this 56% of the total, followed of the not exclusive breast-feeding until the six months of age that represents a 40% of the total of the analyzed sample. According to studies carried out for Huwyler C, Lin SY et al to the [16], point out also the existent report between the multiple revenues and the immunodeficiency secures that the immunodeficiencies are the paradigm of the illnesses that frequents with infecting appellants and they must be suspicious as long as existing one of the signs of mentioned alarm by Jeffrey Modell Foundation [16]. Authors as Bohy M, Poowuttikul P et al [17] it depose that the main immunodeficiencies in these stages of the life are caused for deficiencies of B cells, as the agamma or congenital hypogammaglobulinaemias, the variable immunodeficiency people and the specific deficiency of antibodies, characterize for pulmonary infections appellants and multiple revenues for these causes. As for the exclusive breast-feeding the study kept report with authors as Rodríguez Avilés DA, good mud-runner MK brook et al to the [11] whom explains the report between the breast-feeding and the ripeness of the immune system of the newborn as of your high content in immunoglobulins, proteins and fatty in general, with regard to the compromise luck and ripens, which facilitates in the male infant the necessary protection. According to roast lightly P, bring bad luck met to the [18] the prevalence of feeding exclusively to the chest during the six first months went of 39% in countries in the process of development. In Spain the percentage of fed childrens total or partially with breast milk to the six months it went 38.8%, according to statistics of the 2021, date related with the study. Of similar trained late or premature the Fall of the umbilical cord it forms part of the existence of immunodeficiency in the newborn, by associating this to deficit of leucocyte adhesion, syndromes of hyper IgE, defect of marking with signals of the receiving toll type (mutations in IRAK 4 and Myd88). If relate these factors of risk to the condition of a FGR newborn with specific characteristics as the diminution of the innate immunity since are accustomed to present a smaller production of inflammatory profit citosinases, as the TNF- α and the IL-6, in answer to infectious stimuluses [19]. This suggests a decreased function of the cells of the immune innate system, as the neutrophils and the macrophags, the reduction of the adaptive immunity for the answer of the t lymphocytes and B that also is committed in the newborns with FGR, as well as an alteration in the proportion of subpoblaciones of t lymphocytes, as the helper t lymphocytes (Th1 and Th2) and the regulating t lymphocytes [20]. Diminution of the transference of maternal antibodies, although the placenta carries out the transference, the efficiency of this process sees affected in the FGR, which reduces still more the immunoprotección of the newborn, the oxidative stress it damages the cells of the immune system and alter your function, the alteration of the micro intestinal biota for disbiosis (alteration of the equilibrium of the micro intestinal biota). The

fetal programming, by altering the fetal programming of the immune system, which it means that the genes they regulate the development and the function of the immune system activate or deactivate in an incorrect way and the epigenetic modifications, where the FGR it can induce epigenetic modifications, as the methylation of the DNA, that they can alter the expression of related genes with the immune function [21].

5. Conclusions

It is important to know the factors of risk for the appearance of an immunodeficiency, as well as the signs of alarm and the special situations as the FGR that in combination with certain variables can gestate the necessary media fulfilled this condition in a male infant in any stage of the life and thus to understand the mechanism of appearance and prevent the conditions in order that do not take to the cause.

Abbreviations

TNF- α	Factor of Tumorous Necrosis Alpha
IL-6	Interleukina
DNA	Deoxyribonucleic Acid
Th	Owner of Answer

Author Contributions

Adrian Ruiz Lopez: Conceptualisation, Formal analysis, Acquisition of financing, Investigation

Vicente Jose Hernandez Moreno: Methodology, Data cure validity, Resources, Validity, Supervision

Conflicts of Interest

The authors declare no conflicts of interest.

References

- [1] Melamed N, Baschat A, Yinon Y, et al. Iniciativa de la FIGO (Federación Internacional de Ginecología y Obstetricia) sobre crecimiento fetal: recomendaciones prácticas para la detección, el diagnóstico y el tratamiento de la restricción del crecimiento fetal. *Int J Gynaecol Obstet* 2021; 152 (Supl. 1): 3-57. <https://doi.org/10.1002/ijgo.13522>
- [2] Lees CC, Stampalija T, Baschat A, et al. Guía de práctica de la ISUOG: diagnóstico y manejo del feto pequeño para la edad gestacional y restricción del crecimiento fetal. *Ultrasound Obstet Gynecol* 2020; 56(2): 298-312. <https://doi.org/10.1002/uog.22134>
- [3] Kesavan K, Devaskar SU. Intrauterine growth restriction: postnatal monitoring and outcomes. *Pediatr Clin North Am.* 2019; 66(2): 403-23. <https://doi.org/10.1016/j.pcl.2018.12.009>

- [4] Ministerio de Salud Pública. Dirección Nacional de Estadísticas. Registro de morbilidad continúa, Servicios cerrados de Neonatología. La Habana: Oficina Nacional de Estadísticas del MINSAP; 2021.
- [5] Turner S, Williams M. Customized growth charts: rationale, validation and clinical benefits. *Am J Obstet Gynecol*. 2018; 218(2 Suppl): S609–S618.
<https://doi.org/10.1016/j.ajog.2017.12.011>
- [6] Lewis DB, Tu W. The physiologic immunodeficiency of immaturity. En: Stiehm RE, Ochs HD, Winkelstein JA. *Immunologic disorders in infants and children*. Philadelphia: Elsevier Saunders, 2004. p. 687-760.
- [7] Al-Herz W, Bousfiha A, Casanova JL, Chatila T, Conley ME, Cunningham-Rundles CH et al. Primary immunodeficiency diseases: an update on the classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency. *Front Immunol*. 2014; 5: 162.
- [8] Laboratorios Saval. Lactancia materna refuerza inmunidad de neonatos. Chile: Laboratorios; 2021 [20/11/2021].
- [9] Andegiorgish AK, Andemariam M, Temesghen S, Ogbai L, Ogbe Z, Zeng L. Neonatal mortality and associated factors in the specialized neonatal care unit Asmara, Eritrea. *BMC Public Health*. 2020; 20(1): 10.
<https://doi.org/10.1186/s12889-019-8118-x>
- [10] Jiménez Acosta SM. Alimentación y nutrición en edades pediátricas durante la COVID- 19. *Rev Cubana Pediatr*. 2020 [acceso 20/11/2021]; 92(1): 15.
- [11] Rodríguez Avilés DA, Barrera Rivera MK, Tibanquiza Arreaga LP, Montenegro Villavicencio AF. Beneficios inmunológicos de la leche materna. *RECIAMUC*. 2020; 4(1); 93-104.
<https://doi.org/10.26820/reciamuc/4>
- [12] Tamayo-Velázquez O, Góñez-Tejeda J, Dieguez-Guach R, Iparraguirre-Tamayo A, PérezAbreu M. Intervención educativa sobre los beneficios inmunológicos de la lactancia materna para los lactantes. *Rev Cubana de Medicina General Integral*. 2022 [citado 11/09/2023]; 38(2).
- [13] Quezada L, Leon C C, Fernandez S, Nicolau E. Celula Madre: una revolución en la medicina regenerativa. *MediSan*. 2017; 21(5): 574-81. 2017 [citado 09/02/21].
- [14] Martínez-Murillo CI. El banco de células madre hematopoyéticas de cordón umbilical para trasplante. *Gac Méd Méx*; 139 (Supl 3): S93-S95. [citado 09/02/21].
- [15] Gluckman E. History of cord blood transplantation. *Bone Marrow Transplant*; 44(10): 621-6. PMID: 19802032. [citado 09/02/21].
- [16] Huwylar C, Lin SY, Liang J. Primary Immunodeficiency and Rhinosinusitis. *Immunol Allergy Clin North Am*. 2020; 40: 233-49. Disponible en:
<https://doi.org/10.1016/j.iac.2019.12.003>
- [17] Bohy M, Poowuttikul P, Secord E. Humoral Immune Deficiencies of Childhood. *Immunol Allergy Clin North Am*. 2021; 41: 527-33. Disponible en:
<https://doi.org/10.1016/j.iac.2021.07.004>
- [18] Torre P, Salas M, Silva CI. Desafíos para la promoción de la salud: el caso del mercado de las fórmulas infantiles en México. *Glob Health Promot*. 2020; 27(2): 175–83.
<https://doi.org/10.1177/1757975918823011>
- [19] Jablonska J, et al. The impact of intrauterine growth restriction on the development of neonatal immune system. *Front Immunol*. 2022; 13: 957781.
<https://doi.org/10.3389/fimmu.2022.957781>
- [20] Li W, et al. Gut microbiota dysbiosis contributes to impaired intestinal immune development in intrauterine growth restriction piglets. *Front Immunol*. 2021; 12: 765432.
<https://doi.org/10.3389/fimmu.2021.765432>
- [21] Wu Y, et al. Maternal gut microbiota and its metabolites in offspring health: A review. *Aging Dis*. 2022; 13(3): 901-918.
<https://doi.org/10.14336/AD.2021.1104>