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Original Article

Factors associated with gastrointestinal disorders in the first year of late and moderate premature infants

Fatores associados a agravos gastrointestinais no primeiro ano de prematuros tardios e moderados

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ABSTRACT

Objective: to analyze the factors associated with the development of gastrointestinal disorders in the first year of life of late and moderate premature infants. **Methods:** longitudinal study, which followed infants born late and moderate, during the first year of life, via telephone, to develop gastrointestinal disorders, in the maternal perception. Data collected using the Likert scale, in the assessment of acute condition, and analyzed under comparison of frequency and odds ratios (p<5% and 95% Confidence Interval) between variables. **Results:** the most frequent gastrointestinal injuries in the assessment of the first months of life were colic and vomiting, which reduced the intensity, the closer to the infant's first year of life, followed by the diarrheal condition that maintained constant intensity throughout the first year. **Conclusion:** the study has implications for the identification of risk factors, in view of the vulnerability of the premature population, still little described in the literature.

Descriptors: Vomiting; Colic; Diarrhea; Infant, Premature, Diseases; Risk Factors.

RESUMO

Objetivo: analisar os fatores associados ao desenvolvimento de agravos gastrointestinais, no primeiro ano de vida de prematuros tardios e moderados. **Métodos**: estudo longitudinal, que acompanhou lactentes nascidos tardios e moderados, durante o primeiro ano de vida, via telefone, para desenvolvimento de agravos gastrointestinais, na percepção materna. Dados coletados por meio de escala likert, na avaliação da condição aguda, e analisados sob comparação de frequência e *odds ratio* (p<5% e Intervalo de Confiança 95%) entre as variáveis. **Resultados**: os agravos gastrointestinais mais frequentes na avaliação dos primeiros meses de vida foram a cólica e o vômito, que reduziram a intensidade, quanto mais perto do primeiro ano de vida do lactente, seguidos do agravo diarreia que manteve intensidade constante ao longo do primeiro ano. **Conclusão**: o estudo traz implicação para identificação dos fatores de risco, tendo em vista a vulnerabilidade da população de prematuros, ainda pouco descrita na literatura.

Descritores: Vômito; Cólica; Diarreia; Doenças do Prematuro; Fatores de Risco.

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Introduction

The World Health Organization classifies a newborn with a gestational age of 32 to 36 weeks and six days as premature and moderate[1]. These preterm infants should be considered at high risk, because prematurity makes them physiologically and hemodynamically unstable, with risk for congenital disorders, metabolic changes and perinatal asphyxia, requiring special care[2].

The high rate of prematurity in Brazil is prevalent among late preterm infants, in most cases, it occurs spontaneously, however, iatrogenic cesarean rates are still experienced, which intensify the numbers of prematurity, which currently revolve around 11.0% in the general population, 88.0% of these are considered premature with more than 32 weeks of gestational age[3].

It is recognized that late and moderate premature infants have immaturity in the systems of physiological regulation. When considering this characteristic, aspects of gastrointestinal immaturity stand out, in which manifestation such as vomiting, reflux, diarrhea and colic may be more frequent. By the seventh week of gestation, the stomach is anatomically mature, but the rhythmic contractions will occur from approximately four days of life of the newborn. In premature infants, this emptying is slower and may be one more reason for greater colic intensity, also justified by the transient immaturity of intestinal functions, such as enterohepatic functions and bile acid homeostasis, gastrointestinal motility and colon microbiota[4].

The gastrointestinal repercussions in preterm infants are not only established in the neonatal period, since in the childhood of these preterm infants, gastrointestinal disorders are very prevalent, sometimes functional and sometimes structural. The functional ones do not present abnormalities and/or anatomical deformations. In the structural ones, they manifest themselves in a decisive way. However, several factors may be associated with the clinical picture[5]. Food allergies, such as eosinophilic esophagitis, celiac disease, metabolic disorders, food intolerances are conditions that can be related to digestive conditions, and short and transient periods are even more challenging[6-7]. Gastroesophageal reflux disease, on the other hand, considered the most common esophageal disease in the neonatal period, still presents aspects and definitions that are not adequately known, especially in late preterm and term infants[8-9].

There is a high number of infants who have gastrointestinal signs and symptoms. A portion of these infants exposes more than one symptom and these manifestations are frequently the reason for changes in the infant's diet, especially changes in the types of infant formulas, which can have an impact on aspects of child growth and development and risk factors for future diseases[10].

Therefore, discussing the occurrence of these diseases and associated factors in a population considered "almost full term", in health care services, moderate and late preterm is extremely relevant, in view of the epidemiological rise of these babies and manifestations of immature biological functions. Thus, the recognition of factors allows early identification and guidance of services, in order to minimize the problems. Thus, this study had the guiding question: what are the neonatal and socioeconomic factors associated with the intensity of gastrointestinal disorders of late and moderate premature infants in the first year of life? To answer the study question, the objective was to analyze the factors associated with the development of gastrointestinal disorders, in the first year of life of late and moderate premature infants.

Methods

Open longitudinal study, from the project database entitled Health conditions of moderate and late preterm infants in the first year of life, developed in the municipality of Santa Maria, RS, Brazil.

The selection of participants was carried out during a year of data collection (May/2017 to May/2018), with the objective of reducing seasonali-

ty bias (region of the study with climatic conditions in which extreme temperatures - winter and summer - could interfere in the health problems), in an Obstetric Center of a reference hospital for high-risk pregnancies in the central region of Rio Grande do Sul, Brazil. After the selection of participants, there was an active search for these in the services of Joint Accommodation (Tocogynecological Unit) and Therapy Unit Neonatal Intensive Care. The monitoring and data collection took place through telephone contact of the researchers, in the first month of life. The data collection team, which followed all stages, was composed of a responsible researcher and research assistants, graduates in the health field.

The study participants were 151 premature newborns, who were born with gestational age, in the period from 32 to 36 weeks and six days. The group was classified into late preterm infants, those born at 34 to 36 weeks and six days of gestational age; and moderate premature infants who had 32 to 33 and six days. For the initial selection of participants, gestational age was considered to be that presented in the hospital's birth record book and in the patient's medical record, determined by the Capurro method, immediate post-neonatal.

As selection criteria, the study included newborns considered moderate or late premature, born in the institution where the study was conducted, and residing in Santa Maria, Rio Grande do Sul, Brazil, at the time of hospital discharge. A proper form was used, properly tested, whose neonatal and socioeconomic variables were collected during hospitalization. Neonatal variables were: gestational age (moderate and late), birth weight (SGA=Small for Gestational Age, AGA=Adequate for Gestational Age, LGA=Large for Gestational Age), need for admission to the Neonatal Intensive Care Unit) or accommodation set and type of power. As for the socioeconomic class, the groups were allocated to classes of types A-B, C and D-E.

The follow-up contact was made in the third, sixth and 12th month of life, for the feasibility of the study; and to reduce transportation expenses, over the phone. The evaluation months were defined according to the frequency established by the evaluation instrument, on a quarterly basis. The instrument is characterized as a Likert type, in which health conditions (colic, vomiting and diarrhea) are assessed and classified according to the scores. Vomiting and diarrhea were assessed in the third and 12th month assessments; colic condition was assessed in the 3rd and 6th months of life. Answers ranged from never = 0, almost never = 1, almost always = 2 and always = 3[11]. The instrument was translated, adapted and validated for Portuguese in 2010. Understanding that acute conditions have repercussions, especially for caregivers, who define the severity of the injury and how much this situation may have on the child's health and demand health services.

As for the analysis of variables associated with the frequency of acute conditions, the frequency comparison tests were applied (using the Chi-Square test), using the statistical software Statistical Package for the Social Sciences for Windows, version 20.0. A statistically significant association was established with the outcome, with variables whose p-value was less than or equal to 5% ($p \leq 0.05$). In the analysis of Odds Ratio (OR) (odds ratio) of the variables vomiting and colic, comparisons of the responses Never and Always and 95% Confidence Interval (CI) were adopted. In the OR analysis of the diarrhea variable, the responses Never and Almost Always were used for calculation and 95% CI, since the response Always had a low frequency (n=1).

The study followed the ethical recommendations and was approved by the Consolidated Opinion of the Research Ethics Committee of the Universidade Federal de Santa Maria, nº 1,511,201/2016, and Presentation Certificate for Ethical Appreciation nº 53898916,9,0000,5346.

Results

119 children participated in the study in the third month, who were evaluated for vomiting, colic

and diarrhea [21.2% loss (1 loss due to death; 31 due to no response by telephone contact)]; in the sixth month evaluation, 108 children were evaluated only for the colic condition [loss of 28.5% (there were five more losses due to lack of response by telephone contact; six due to withdrawal from participating in the study)]; and, in the last evaluation, at 12 months of age, regarding the vomiting and diarrhea problems, 105 children participated, with a loss of 30.0% of the initial population (plus three losses due to dropping out of the study).

Table 1 shows the intensity of the vomiting condition and the comparison of the variables with the intensity, in the third and 12th months of life.

Table 1 – Distribution of the intensity of the vomiting condition, in the third and 12th months of life of late and moderate premature infants. Santa Maria, RS, Brazil, 2019

Neonatal and socioeconomic variables	Never	Always	p*	*Odds Ratio*	CI† 95%
	n(%)	n(%)			
Third month	57(47.1)	5(5.0)			
Moderate	7(38.9)	1(5.6)			
Late	50(49.5)	5(5.0)	0.531	0.71	0.07-7.14
Small for gestational age	11(45.8)	1(4.2)			
Adequate for gestational age	42(47.2)	5(5.6)	0.499		
Large for gestational age	4(66.7)	-			
Egress from intensive care	21(43.8)	2(4.2)	0.412	1.2	0.202-7.12
Joint accommodation	36(50.7)	4(5.6)			
Breastfeeding	53(49.5)	5(4.7)	0.480	2.6	0.246-27.97
Did not receive breastfeeding	4(33.3)	1(8.3)			
A-B	12(57.1)	-	0.201		
C, D-E	44(34.1)	6(4.6)		1.13	1.026-1.259
12th month	74(70.5)	1(1.0)			
Moderate	12(70.6)	-	0.559	1.01	0.98-1.05
Late	62(70.5)	1(1.1)			
Small for gestational age	16(72.7)	-			
Adequate for gestational age	54(70.1)	1(1.3)	0.917		
Large for gestational age	4(66.7)	-			
Egress from intensive care	29(69.0)	-	0.258	1.02	0.97-1.06
Joint accommodation	45(71.4)	1(1.6)			
Exclusive breastfeeding	70(72.2)	1(1.0)	0.231	0.98	0.95-1.01
Did not receive breastfeeding	4(50.0)	-			
A-B	15(75.0)	-	0.615	1.01	0.98-1.05
C-D-E	59(69.4)	1(1.6)			

*Chi-square test; †CI: Confidence Interval

In the analysis of neonatal and socioeconomic variables, there was no significant difference between the intensity of vomiting in the third and 12th months of life. It is noteworthy that, in the third month, 8.3% of babies who did not receive breastfeeding always presented vomiting, compared to 4.7% of those who were exclusively breastfed. Still, socioeconomic classes C, D-E showed a higher frequency of intensity, always, when compared to other classes, 13.0% more likely to develop vomiting in the third month of life. In Table 2, the worsening diarrhea stands out, in comparison with the variables.

Table 2 – Distribution of the intensity of the diarrhea problem, in the third and 12th months of life of moderate and late premature infants. Santa Maria, RS, Brazil, 2019

Neonatal and socioeconomic variables	Never	Often	p*	*Odds Ratio*	CI† 95%
	n(%)	n(%)			
Third month	86(72.3)	8(6.7)			
Moderate	14(77.8)	0	0.629		
Late	72(71.3)	8(7.9)		1.11	1.03-1.19
Small for gestational age	15(62.5)	1(4.2)			
Adequate for gestational age	65(73.0)	7(7.9)	0.241		
Large for gestational age	6(100.0)	0			
Egress from intensive care	31(64.6)	2(4.2)	0.105	0.61	0.13-2.88
Joint accommodation	55(77.5)	6(8.5)			
Breastfeeding	80(74.8)	7(6.5)	0.012		
Did not receive breastfeeding	6(50.0)	1(8.3)		0.56	0.08-3.95
A-B	13(59.1)	2(9.1)	0.314		
C, D-E	73(56.6)	6(27.2)		1.9	0.42-8.5
12th month	76(72.1)	4(3.8)			
Moderate	12(70.6)	0	0.597		
Late	64(72.7)	4(4.5)		1.06	1.01-1.13
Small for gestational age	16(72.7)	0			
Adequate for gestational age	55(70.5)	4(5.2)	0.441		
Large for gestational age	6(100.0)	0			
Egress from intensive care	31(73.8)	1(2.4)	0.809	0.49	0.05-4.49
Joint accommodation	45(71.4)	3(4.8)			
Breastfeeding	71(73.2)	4(4.3)	0.578		
Did not receive breastfeeding	5(62.5)	0			
A-B	15(75.0)	0	0.043		
C, D-E	61(47.3)	4 (3.1)		1.07	1.01-1.36

*Chi-square test; †CI: Confidence Interval

In the analysis of neonatal and socioeconomic variables, a difference was noticed in the prevalence of the intensity of diarrhea almost always, in the third and 12th months of life. Babies born late had a higher risk of developing diarrhea in the third and 12th months of life. It is emphasized that, in the third month, 74.8% of babies who received exclusive breastfeeding, never had diarrhea, compared to 50.0% of those who were breastfeeding. Still, socioeconomic classes C, D-E indicated a higher frequency of intensity, always, and a greater risk of developing diarrhea at the end of the first year of life. In Table 3, the colic condition stands out, in comparison with the variables.

Table 3 – Distribution of the intensity of the colic condition, in the third and sixth months of life of moderate and late premature infants. Santa Maria, RS, Brazil, 2019

Neonatal and socioeconomic variables	Never	Always	p*	*Odds Ratio*	CI† 95%
	n(%)	n(%)			
Third month	49(41.2)	14(11.8)			
Moderate	7(38.9)	2(11.1)	0.930	1.000	0.26-3.74
Late	42(41.6)	12(11.9)			
Small for gestational age	10(41.7)	12(13.5)			
Adequate for gestational age	35(39.3)	0	0.609		
Large for gestational age	4(66.7)	0			
Egress from intensive care	15(31.3)	5(10.4)	0.208	1.19	0.46-3.1
Joint accommodation	34(47.9)	9(12.7)			
Breastfeeding	44(41.1)	12(11.2)	0.655		
Did not receive breastfeeding	5(41.7)	2(16.7)		0.75	0.21-2.68
A-B	11(52.4)	1(4.8)	0.488		
C, D-E	38(29.5)	13(10.1)		0.33	0.05-2.26
Sixth month	70(64.8)	1(0.9)			
Moderate	11(61.1)	1(5.6)	0.147	0.92	0.77-1.09
Late	59(65.6)	0			
Small for gestational age	16(76.20)	0			
Adequate for gestational age	50(61.7)	1(1.2)	0.870		
Large for gestational age	4(66.7)	0			
Egress from intensive care	28(63.6)	1(2.3)	0.672		
Joint accommodation	42(65.6)	0			
Breastfeeding	63(63.6)	0	0.003		
Did not receive breastfeeding	7(77.8)	0		1.14	0.88-1.48
A-B	17(85.0)	0	0.160		
C, D-E	53(41.1)	1(4.0)		1.01	0.98-1.05

*Chi-square test; †CI: Confidence Interval

In the analysis of neonatal and socioeconomic variables, there was no significant difference between the intensity of colic in the third month of life. In the third month, 16.7% of babies who did not receive breastfeeding always had colic, compared to 11.2% of those who were exclusively breastfed. However, in the sixth month of life, there was a significant difference between the intensity of colic. It is evident that, in the sixth month, 63.6% of babies who received exclusive breastfeeding, never had colic, compared to 77.8% of those who were breastfeeding. However, there was no significant difference between the intensity of colic in the third month of life of small babies for gestational age, which always presented 13.5% of intensity, compared to babies suitable for gestational age and large for gestational age who did not present the grievance in the period.

Under the analysis of the three conditions, it is highlighted that colic was more frequent in the third month, when compared to the sixth month. The other diseases, vomiting and diarrhea, presented similar percentages, in the two evaluated periods (3rd and 12th month of life), which may represent a tendency of these complications throughout the first year of life, in terms of intensity.

Discussion

The limitations of this study are considered to be the collection of clinical findings, through the maternal perception or main caregiver, however, it is understood that the repercussion of the injury is experienced by the family/caregiver and this is the one who must consider how intense the injury affects the family and child context. The perception of this will guide the demand for services and formation of the health care network. Another weakness, like the other longitudinal studies, refers to the loss of follow-up, due to withdrawal or absence of contact.

However, this study addresses relevant aspects about the health conditions of an increasingly prevalent and physiologically immature population. The

identification of the prevalence and risk factors allows the organization of childcare and follow-up services, in the perspective of diseases, since gastrointestinal disorders, vomiting, colic and diarrhea are the main clinical manifestations in the first year of life. These signs may be associated with normal digestive physiology or the specific development of this system, in the first year of life. When relating the premature newborn to the immaturity of the digestive system and food, it is possible that these children have negative repercussions, such as vomiting[10].

In this study, for the population of late and moderate preterm infants, vomiting was the most prevalent in the third month of life, when compared to the end of the first year of life. A study shows that vomiting in the first months of life is associated with gastroesophageal reflux and that, in most cases; it is physiological and more frequent in early life[12]. It is a common condition in childhood, it has a prevalence of approximately 30.0% of full-term infants, in the first year of life, and it becomes more frequent in the population of premature babies[9-10]. Thus, it can be inferred that vomiting in preterm children follows patterns of the population of other preterm infants, whose prevalence is higher when compared to the preterm ones.

Vomiting due to gastroesophageal reflux usually improves with age, less than 5.0% of children with vomiting or regurgitation in childhood continue to show symptoms after 12 months of age. This is due to the combination of growth in the length of the esophagus, a more upright posture, increased tone of the lower esophageal sphincter and a more solid diet[13].

The main factors associated with vomiting include the high volume of milk ingested, posture and functional immaturity of the lower esophageal sphincter, the latter being strongly related to prematurity. It appears that late and moderate premature births are more vulnerable to vomiting, due to the biological factor, early hospital discharge and other clinical repercussions of prematurity[9]. A study with premature newborns highlights a prevalence of 2.0 to 6.0% in the premature population and considers risk, factors such as low weight, gestational age less than 34 weeks and longer than 30 days of hospitalization[14].

Vomiting can also compromise the child's growth and development, being pointed out as a cause of stress for parents and caregivers. When these children are still in the hospital, care to prevent and treat the causes of vomiting is carried out by professionals and directed to food. However, at the time of discharge, this care is performed by family members and can also be quite appropriate, in preventing aspirations and asphyxiation[15].

Diarrhea, because it is not associated with conditions of physiological immaturity, either, with processes of physiological adaptation, maintained frequent intensity throughout the evaluations of the third and 12th months of life in this study. It is considered to be more intense in the first months of life, when compared to the others. The illness of children under one year of age, due to diarrhea, may be related to the biological point of view, aggravated by factors such as prematurity, low birth weight and congenital malformation[16].

Infants who were not on exclusive breastfeeding had a higher intensity of diarrhea in the assessment of the third month (p=0.012), as well as those classified in classes C, D-E had a higher intensity of the disease at the end of the first year of life (p=0.043). This finding corroborates a study conducted in the interior of Ceará, Brazil, which revealed that the lower the family income, the lower the maternal self-efficacy to prevent diarrhea, especially for infants under one year of age and the greater risk of this disease[17].

Breastfeeding is a key intervention in protecting against acute diarrhea. Children under six months of age who were exclusively breastfeeding had fewer episodes of diarrhea, as this confirms the measure, because due to the introduction of other foods in the babies' diet and a decrease in exclusive breastfeeding, there was an increase in episodes of infant diarrhea[16].

Still, as the most frequent problem in the first

months of life, colic may be related to physiological immaturity, especially in the most intense cases of late and moderate premature infants. Guiding parents that colic can be a natural phenomenon of the child's gastrointestinal development, helps them to overcome in fears and anguishes, with a view to reducing anxiety in the face of crying[18].

As for the factors associated with the intensity of colic, in the third and sixth months of life, it is noteworthy that diet was considered a predisposing factor. Regarding the factors associated with colic, a study states that there is no difference between sex or type of diet, as it differs from that presented by this study. This disparity may be associated with the population difference between studies, not considering prematurity as a bias. However, the evidence highlights that maintaining breastfeeding allows control of this manifestation[10].

Behavioral action strategies between parents and children can help to cope with these symptoms, and colic can be viewed differently, in the perception of each family. The social support offered to the mother can be an important factor in reducing episodes of colic. In another study, it was found that babies of mothers who received affective support had fewer symptoms of colic[19].

Conclusion

For late and moderate preterm infants, vomiting and colic disorders are more intense in the first three months of life, and diarrhea remains constant throughout the first year of life. No neonatal and socioeconomic factors associated with the development of vomiting were identified. However, for diarrhea and colic disorders, it is noteworthy that preterm infants who are not exclusively breastfeeding, present greater intensity of colic and diarrhea. It is also more frequent, at the end of the first year of life, the development of diarrhea, in those belonging to socioeconomic classes C, D-E.

Collaborations

Jantsch LB collaborated in the conception and design, analysis and interpretation of data, writing of the article, relevant critical review of the intellectual content and final approval of the version to be published. Barzotto VS and Silva EB contributed to the analysis and interpretation of data, writing of the article, relevant critical review of the intellectual content and final approval of the version to be published.

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