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Season of birth and neonatal jaundice

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Abstract

Neonatal jaundice (NJ) is a multifactorial condition specific to the neonatal age. Clinical experience shows that seasons of the year influence the frequency and severity of NJ.

Objective: To investigate the influence of annual seasons on the frequency and severity of NJ.

Material and methods: The study was conducted at the Neonatology Department of University Hospital "Medica Ruse" with 566 full-term newborns. The follow-up of NJ was carried out with transcutaneous bilirubinometry. The newborns are residents of Ruse region, Republic of Bulgaria.

Results: We found a significant difference in bilirubin (BR) levels depending on the season of birth during the early neonatal period. Summer-borns had the highest average levels, followed by spring-borns, and autumn-borns had the lowest. Born in the spring had significantly high levels of BR at the end of neonatal period. Climatic factors average and maximum monthly temperature, average monthly rainfall and monthly sunshine duration had a significant influence on the levels of bilirubin on Day 4 ($p=0.014$), Day 5 ($p=0.016$) and Day 14 ($p=0.004$). Prolonged NJ is most commonly observed in summer-borns ($p<0.001$).

Conclusion: Birth season along with meteorological factors affects the frequency of pathological neonatal jaundice.

Keywords: Newborn; Jaundice; Season of birth; Bilirubin; Meteorological factors

1. Introduction

Neonatal jaundice (NJ) is a yellow coloration of the skin, mucous membranes, and sclera of the newborn (NB) because of increased levels of total bilirubin (BR) [1, 2]. NJ affects at least 60% of full-term and 80% of preterm NBs [3]. The level of total BR considered pathological for term NBs at values above 5 mg/dL (85.5 μmol/L) on the first day, 10 mg/dL (171 μmol/L) on the second day, above 12-13 mg/dL (205.2-222.3 μmol /L) on the third and every subsequent day [4].

The classification of NJ can be carried out according to several criteria: the time of appearance, the pathogenesis (the place of violation in the exchange of BR), the type of elevated BR. Although hyperbilirubinemia (HB) is usually a benign physiological condition, very high levels of BR can occur in certain pathological conditions and can cause damage to the central nervous system [5, 6]. The severity of NJ varies and may be related to race, gender, diet, eating habits, hormones, and genetic factors. Seasons of the year may influence the frequency and severity of neonatal HB [7, 8, 9].

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Purpose

To investigate the influence of annual seasons on the frequency and severity of NJ in full-term newborns.

2. Material and methods

This study was conducted from January 2017 to November 2020 in Neonatology Department at the University Hospital "Medica Ruse". It includes 566 full-term newborns. The criteria for inclusion and exclusion of the patients are presented in Table 1. The selection process of the patients is reflected in Figure 1.

Table 1 Criteria for the selection of participants in the study

Inclusion criteria
• Gestational age at birth ≥37 weeks and birth weight ≥2500 g • Follow-up of NB to the 30th postnatal day or to involution of neonatal icterus
Exclusion criteria
• Need for surgical treatment during the follow-up period • Death during the neonatal period • Congenital chromosomal diseases and inborn errors of metabolism • Gestational age at birth <37 weeks and/or birth weight <2500 g • Incomplete patient follow-up period data

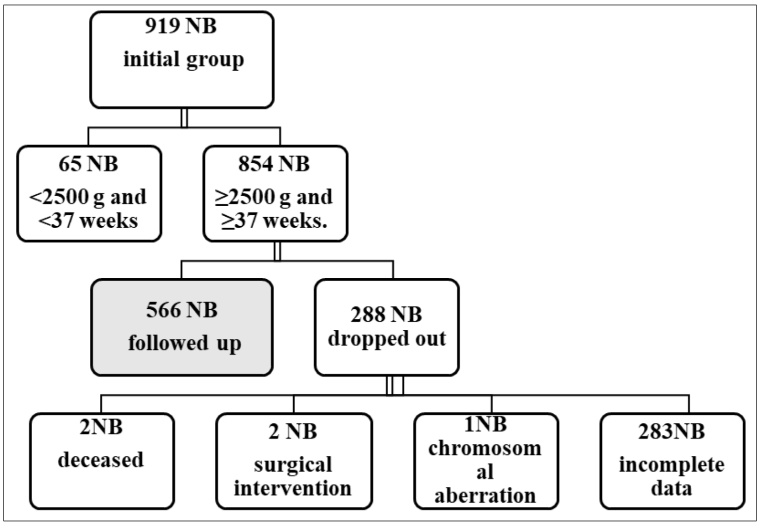

Figure 1 Presentation of the process of selection of patients

The children included in the present observation are residents of Ruse and Ruse region, at the following geographical coordinates: 3° 51' 00" N/ 25° 58' 00" E. The average altitude of the region is 45 m. The average daily air temperature for the period 2017-2020 is lowest in January (-0.08^{0}C) and highest in August (23.38^{0}C). For the same period, the fluctuations of the average highest daily temperatures are between 21.5 and 44.7^{0}C. The average duration of sunshine is greatest in August – 10.5 hours, and the shortest in December – 2.8 hours. The amount of rainfall is highest in May-June – 71.9 L/m^2, and lowest in August – 29.7 L/m^2 [10].

BR was measured transcutaneously in μmol/L on the forehead of NB with bilirubinometer KJ-8000, avoiding areas of bruising or congenital skin changes. The average of three measurements was recorded. The first measurement was performed about 12 hours after birth, then daily repeated until NB was discharged. Two more measurements followed - on the Day 12-14 and on the Day 28-30. To assess the need for therapy in case of diagnosed NJ we used a nomogram for the treatment of hyperbilirubinemia by phototherapy of the American Academy of Pediatrics, as there is no accepted one for Bulgaria [4]. The study was approved by the Ethics Committee of University Hospital "Medica Ruse".

The data were entered and processed with SPSS 23.0 statistical package and Excel for Windows. For a significance level at which the null hypothesis is rejected, $p < 0.05$ was chosen. The following methods were applied: descriptive analysis of quantitative and qualitative data; statistical tests to establish statistically significant difference – t-test, t-test for independent samples; variance analysis; correlation analysis to determine the strength of the relationship between two variables; linear regression analysis; graphical analysis.

3. Results

Randomized in the study were 566 newborn children, of which 274 (48.4%) were girls and 292 (51.6%) were boys. Average weight of the observed group was 3316.3±385.5 g. The average gestational age was 38.8±1.1 weeks. There were no significant differences in birth weight, gestational age, mechanism of birth, Apgar score on the 1st minute in distribution of children according to birth season (Table 2).

Tracking the dynamics of BR is reflected in Figure 2. The average values of BR from the 2nd to the 5th postnatal days are respectively: 135.5±40.5 μmol/L, 154.4±38.8 μmol/L, 157.2±32.6 μmol/L, 147.3±31.1 μmol/L for the whole group. Pathological NJ occurs on the second postnatal day in 15.5% of children with a tendency to decrease in the following days - 10% on the third, 4.1% on the fourth and 2.3% on the fifth postnatal day.

Table 2 Characteristics of the study population

	Total	**Winter**	**Spring**	**Summer**	**Autumn**	**p**
N	**566**	**123**	**171**	**151**	**121**	**NS**
Weight (g)	3316.3±385.5	3206.8±317.7	3346.4±356.4	3304.1±385.1	3368.0±450.1	NS
Gestational age (weeks)	38.8±1.1	38.8±1.1	38.7±1.1	38.8±1.1	38.7±1.1	NS
Gender ♀:♂(%)	48.8/51.6	53.0/47.0	40.9/59.1	51.8/48.2	50.4%/49.6	NS
Mechanism of birth (%)*	43.5 / 56.5	56.6 / 43.4	42.7 / 57.3	38.7 / 61.3	43.0 / 56.0	NS
Apgar on the 1st min	8.3±1.5	8.1±1.5	8.3±1.5	8.5±1.4	8.3±1.4	NS

*Vaginal delivery / Caesarean section

As of Day 14, the average level of BR was 125.3±49.5 μmol/L and 12% of the whole group had HB with an average value of BR 194.0±28.0 μmol/L. As of Day 28, the average level of BR was 77.6±45.6 μmol/L of which 82 children or 14.5% of the whole group had HB ~~and~~ with an average value of BR 137.3±30.9 μmol/L.

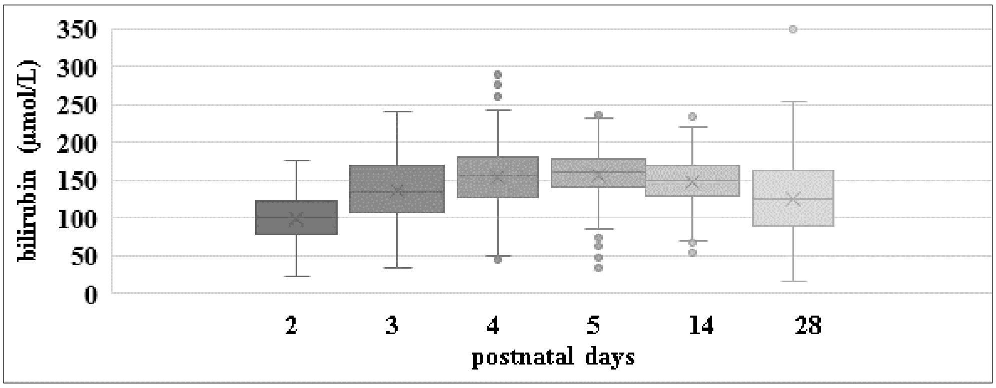

Figure 2 Mean levels of transcutaneous bilirubin by postnatal days in μmol/L

We compared the levels of BR, distributed according to the sex of the observed children, for the entire neonatal period and found no significant difference (Figure 3).

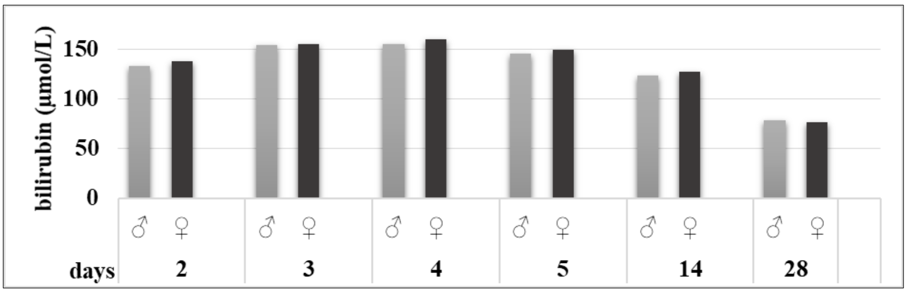

Figure 3 Transcutaneous bilirubin levels by sex from Day 2 to Day 28 (µmol/L)

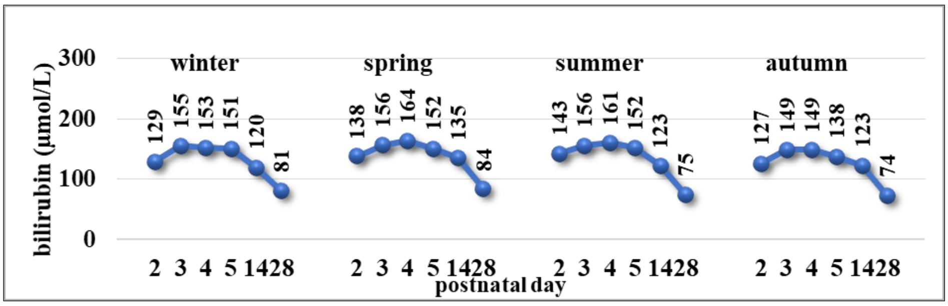

Figure 4 Mean levels of total bilirubin in newborns in the observed population according to birth season

The measured average BR levels by postnatal days of the children depending on the season of birth are presented in Figure 4. Comparing average BR levels, we found a significant difference depending on the birth season for the period from the 2nd to the 5th postnatal day (Table 3). Children born in summer have the highest average levels of BR, followed by those in spring. The lowest values are those born in the autumn. By the 14th and 28th day, the highest levels are those born in the spring, and for the 28th day this difference is significant (Figure 4).

In the observed group of 566, NBs 82 children (14.5%) were found with Prolonged NJ (PrNJ). The largest number of them were born in summer – 37%, followed by those in autumn – 23%, winter – 22% and the smallest number in spring – 19% (p<0.001) (Figure 5).

Table 3 Difference (p) in bilirubin levels in the observed population according to season of birth for 2nd to 5th postnatal day (T-test)

Season	Winter	Spring	Summer	Autumn
Winter		Day 4 / p=0.044	Day 2 / p=0.023	Day 5 / p=0.040
Spring	Day 4 /p=0.044			Day 1 / p=0.004 Day 4 / p=0.001 Day 5 / p=0.018
Summer	Day 2 / p=0.023			Day 2 / p=0.003 Day 4 / p=0.012 Day 5 / p=0.009
Autumn	Day 5 / p=0.040	Day 1 / p=0.004 Day 4 / p=0.001 Day 5 / p=0.018	Day 2 / p=0.003 Day 4 / p=0.012 Day 5 / p=0.009	

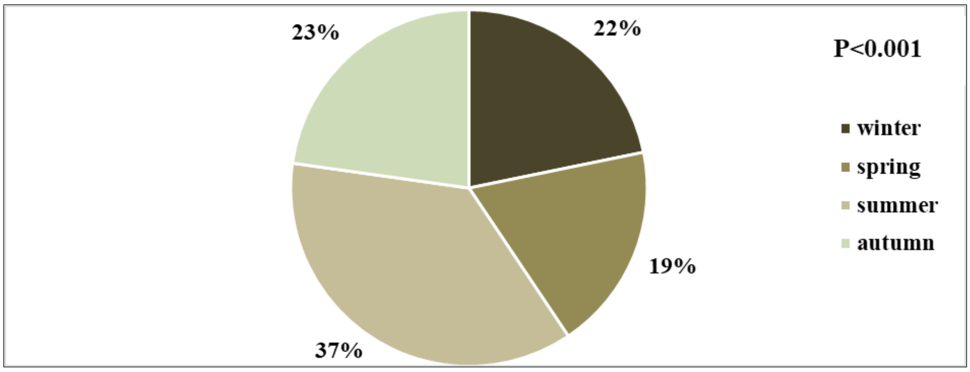

Figure 5 Distribution of newborns with prolonged neonatal jaundice according to season of birth

By Day 28, a statistically significant difference was reported between the average levels of the BR of those born in summer (155.4±31.8 µmol/L) and autumn (134.4±19.9 µmol/L) (p=0.018). In the duration of appearance of PrNJ according to the season of birth, a statistically significant difference was also found: the longest is the icterus of those born in summer (64.7±15.2 days) and there is a statistically significant difference with those born in winter (53.8±11.1 days, p=0.018) and autumn (55.0±10.5 days, p=0.008) (Figure 6).

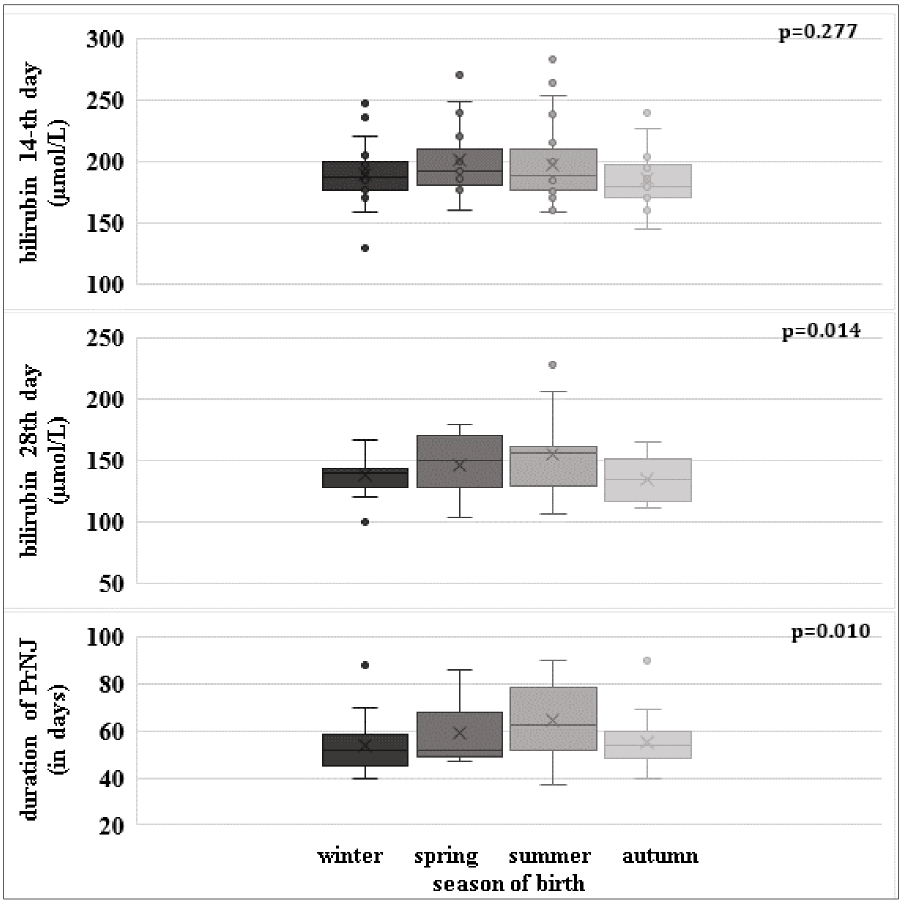

Figure 6 Transcutaneous bilirubin (µmol/L) levels at Day 14 and 28 and duration of prolonged neonatal jaundice (PrNJ), distributed according to the season of birth at 92 newborns with PrNJ

In 34% of those born in summer, jaundice was pathological (measured transcutaneous levels of BR requiring phototherapy), while in the other seasons the frequence of pathological jaundice was lower, the lowest in winter (for spring - 26%, for autumn - 22%, and for winter - 18%) (Figure 7).

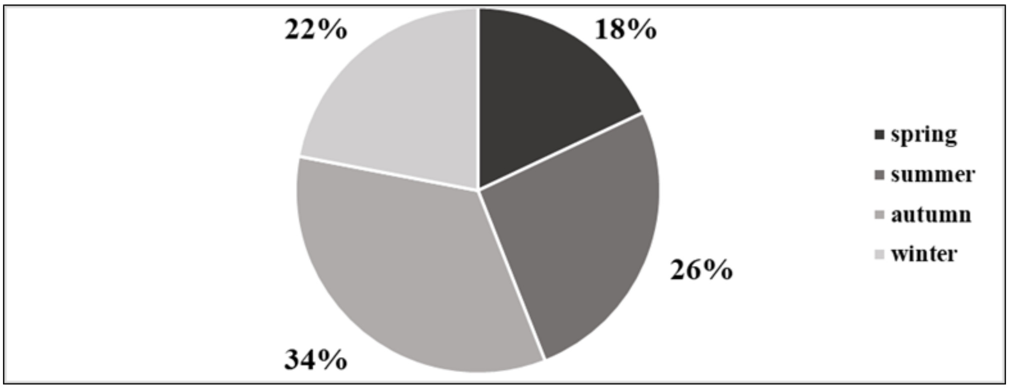

Figure 7 Frequency of pathological neonatal jaundice according to season of birth

A stepwise analysis was conducted by multiple linear regression to assess the impact of the independent variables average monthly temperature (in ^{0}C), maximum monthly temperature (in ^{0}C), average rainfall for a month (in L/m^2) and monthly sunshine duration (in hours) on BR levels by postnatal days (Table 4). A significant influence of their combination on the values of BR were found on Day 4 (p=0.014), Day 5 (p=0.016) and Day 14 (p=0.004). An independent role is played by the monthly average temperature on the values of BR for Day 4 (p=0.052), Day 5 (p=0.005) and Day 14 (p=0.002). For Day 4, 5 and 14, a positive linear relationship between these two factors was found, while for Day 28 it was inverse. A similar regularity was found between maximum monthly temperature and BR levels for the same days.

Duration of sunshine also has an individual influence for the levels of BR (on Day 4 – p=0.037 and Day 5 – p=0.002) (Tab. 4). A positive linear relationship was observed on Day 4, Day 5, and Day 14 between the levels of BR and sunshine continuity. On Day 28 this linear dependence changes its course in reverse.

The amount of rainfall plays a significant independent role on the value of BR (on Day 5 – p=0.018, Day 14 – p=0.034). A straight linear relationship is observed on Day 28 and Day 14, while it is reversed on Day 4.

Table 4 Multiple linear regression between bilirubin levels on Day 4, Day 5, Day 14 and month of birth, average monthly temperature, maximum monthly temperature, mean rainfall per month, monthly sunshine (from https://www.stringmeteo.com)

Day 4	**F**	**p**	**R^2**	**p**
total	2.882	**0.014**	0.039	
month of birth				0.513
average monthly temperature				**0.052**
maximum monthly temperature				0.589
rainfall for a month				0.149
duration of sunshine				**0.037**
Day 5	**F**	**p**	**R^2**	**p**
total	2.87	**0.016**	0.064	
month of birth				0.27
average monthly temperature				**0.005**
maximum monthly temperature				0.139
rainfall for a month				**0.018**
duration of sunshine				**0.002**
Day 14	**F**	**p**	**R^2**	**p**

total	3.502	**0.004**	0.048	
month of birth				0.581
average monthly temperature				**0.002**
maximum monthly temperature				0.437
rainfall for a month				**0.034**
duration of sunshine				0.198

4. Discussion

In our study, we found a significant difference in BR levels in newborns depending on the birth season for the period from the 2nd to the 5th postnatal day. Children born in the summer have the highest average levels of BR. The difference in bilirubinemia according to the season of birth during the early neonatal period affects the frequency of pathological NJ – It is the highest in the summer and the lowest in the winter. This reflects on the hospital stay, which is the longest during the summer months. We found no difference in bilirubinemia levels according to the gender.

According to a study in Japan by Kuniyoshi Y et al [11] between provinces with different sunshine durations, there are regional differences in the cost of medical care for neonatal hyperbilirubinemia, and the short duration of sunshine may be a prognostic factor in the development of neonatal hyperbilirubinemia.

With increasing average daily temperature and maximum daily temperature, as well as lengthening of sunshine, BR levels increase during the early neonatal period, but at the end of first month of life these climatic factors have the opposite effect.

Increased rainfall leads to an increase in the levels of BR during the late neonatal period. This indicator is not subject to control, unlike the others – temperature and sunshine. For the time of rains, the sun exposure and, accordingly, the exposure of NB to sunlight is reduced. The peak rainfall amounts for the geographical region of observation are in the spring, probably therefore by day 28 significant are higher levels of BR in those born in spring.

The first study discussing seasonal variations and frequency of neonatal hyperbilirubinemia was performed in 1969 by Milby et al [12]. Based on the first-day-measured BR levels, the frequency of neonatal unconjugated hyperbilirubinemia was found to be significantly higher in the fourth quarter of each year. However, the climatic information is not given, the observations are conducted in California area.

Over the past 50 years, several research results have been published with the aim of establishing the possible influence of the birth season on neonatal BR levels. The results are contradictory. Anttolainen et al [13] compared the rearing conditions of premature infants in Finland and found a significantly lower mean value of BR on the fifth postnatal day in children born in the bright half of the year compared to those born in the dark half of the year. In another study, Mohsen Hojat et al [14] in Iran found no influence of the birth season on the levels of BR in the first week.

Sunlight can prevent hyperbilirubinemia, as the sun emits blue-green light in the spectrum required for the most efficient conversion of BR into its water-soluble excretion isomers [8]. It is likely that the shorter sunshine in winter leads to a decrease in the radiation of BR during this season. On the other hand, often the room temperature in winter is higher to avoid cooling of the NB. This can cause dehydration and lead to an increase in the level of BR in NB [14, 8]. In addition, dehydration – both in winter and in summer, can stimulate more frequent feeding of the NB. This, in turn, can further compromise BR emission, due to certain substances in breast milk that suppress its exchange [9, 15]. It should also be considered the fact that during the warm sunny months, parents avoid NBs being outside due to the extreme heat, so do not benefit from natural phototherapy. Children are less clothed and this allows better observation of skin color [16].

In our study, we reported an influence of climatic factors during the early neonatal period, when children were raised in a controlled environment – a patient room. High levels of unconjugated BR protect against oxidative stress. Since NB is very sensitive to oxidative damage, it is possible that seasonal fluctuations in the level of BR during the first few days of life will affect further development and susceptibility to pathological manifestations. So, the increase in serum BR level during the first 24 hours of life has been shown to depend on the season of birth (more stress in summer) [17].

5. Conclusion

For the first time in Bulgaria, an attempt was made to assess the impact of the birth season on the manifestation of the NJ. Our observations suggest that the birth season along with meteorological factors affects the frequency of pathological NJ. The present study focuses only on climatic factors, and the NJ is a multifactorial condition. Several pre-, intra- and postnatal factors influence the metabolism of BR. In this sense, more thorough and larger-scale studies on the interaction of the internal environment of NB and the environment are needed to predict the evolution of NJ and prevent associated severe neurological consequences.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflict of interest to declare.

Statement of ethical approval

The study was approved by the ethics committee at the University Hospital Medica Ruse and Medical University of Pleven.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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