

## Climatic factors and prolonged neonatal jaundice

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### Abstract

Prolonged neonatal jaundice (PrNJ) in full-term newborns (NB) is defined if it persists beyond the 14th day after birth. Clinical experience shows that seasons of the year influence the frequency and severity of neonatal jaundice (NJ).

**Objective:** To establish the role of climatic factors on PrNJ expression in term neonates.

**Material and methods:** The study was conducted at the Neonatology Department of University Hospital "Medica Ruse" with 92 full-term newborns who were with PrNJ. The follow-up of NJ was carried out with transcutaneous bilirubinometry. The NBs are residents of Ruse region, Republic of Bulgaria.

**Results:** We found that air temperature directly affects the levels of bilirubin (BR) for the entire neonatal period and the duration of PrNJ. The amount of rainfall during the first two weeks after birth directly correlated with bilirubinemia at end of neonatal period and the duration of PrNJ. A higher level of atmospheric pressure during the early neonatal period was associated with lower BR levels at the same and a shorter duration of PrNJ. The degree of cloudiness after postnatal day 14 is inversely related to the levels of BR and the duration of the PrNJ. Sunshine during the first two weeks affects the levels of BR on the end of neonatal period and the prolongation of PrNJ.

**Conclusion:** According to our data climatic factors: air temperature, amount of rainfall, atmospheric pressure, degree of cloudiness, duration of sunshine affect the degree of manifestation and duration of PrNJ.

**Keywords:** Newborn; Prolonged jaundice; Season of birth; Climatic factors

### 1. Introduction

Prolonged neonatal jaundice (PrNJ) in full-term newborns (NB) is defined if it persists beyond the 14th day after birth [1; 2]. The upper limit value of transcutaneous bilirubin (BR) is  $\geq 85.5 \mu\text{mol/L}$  ( $\geq 5 \text{ mg/dL}$ ) after day 28 of birth [3]. The majority of children with PrNJ have benign unconjugated hyperbilirubinemia (HB) [4]. Its duration may be associated with breastfeeding or with some pathological conditions such as hemolysis (due to Rh or ABO incompatibility or G6PD deficiency), congenital hypothyroidism, urinary tract infection [1, 5]. The frequency of PrNJ ranges from 2 to 15% [6], although there have also been reports of a higher incidence in the Asian population – 32% [7]. The prognosis of PrNJ is good in more than 90% of the cases, depending on timely diagnosis and underlying pathology [8]. Almost all children with PrNJ recover without complications by the age of 8 weeks [9]. Clinical experience proves that annual seasons influence the occurrence and severity of neonatal HB. However, there is no consensus on the influence of the season of birth on the risk of developing NJ [10, 11, 12, 13, 14]. And whether climatic factors influence the prolongation of jaundice is not known.

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## Objective

To establish the role of climatic factors on PrNJ expression in term neonates.

## 2. Material and methods

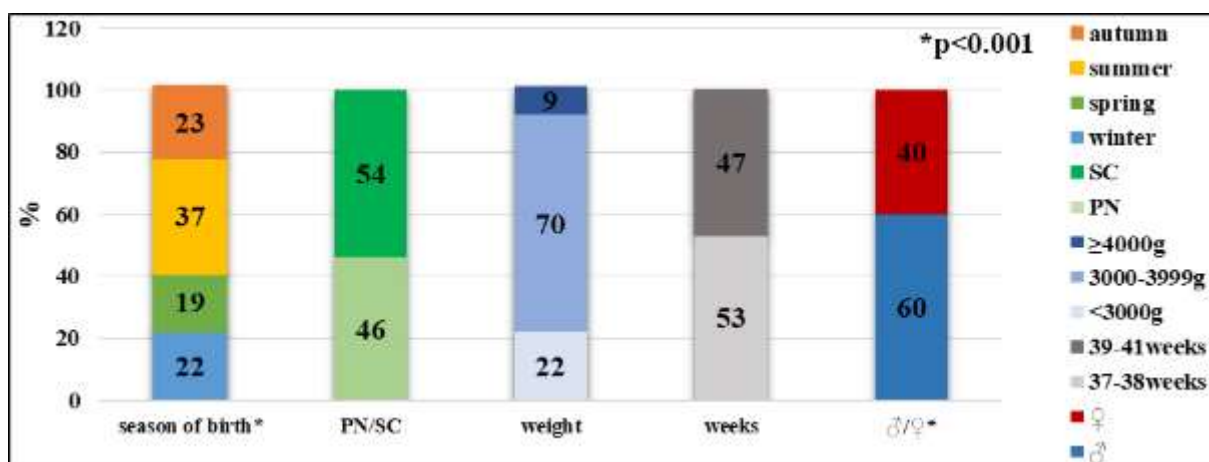
This study was conducted from January 2017 to November 2020 in Neonatology Department at the University Hospital "Medica Ruse". During this period, 92NBs were treated with PrNJ (14.5%) of the total follow-up of 566 full-term infants until complete involution of NJ. This study included NBs with gestational age at birth  $\geq 37$  weeks and birth weight  $\geq 2500$  g. Follow-up of NJ is until the 30th postnatal day or until its final involution. Bilirubinemia monitoring was performed using a KJ-8000 transcutaneous bilirubinometer. The BR was measured in  $\mu\text{mol/L}$  on the forehead of NB. The first measurement was performed about 12 hours after birth, then repeated daily until discharge. Two further measurements of BR- between day 12 and day 14 and day 28 and day 30 followed. If tanscutaneous BR levels were found above the reference values for the respective day, these were confirmed by examination of serum BR levels with fractions. When NJ persisted, follow-up was continued until physiological BR values were reached. To assess the need for therapy in established NJ we used a nomogram for the treatment of HB by phototherapy of the American Academy of Pediatrics, as there is no accepted one for Bulgaria (15).

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.

The children included in the present observation are residents of Ruse and Ruse region, at the following geographical coordinates:  $3^{\circ} 51' 00'' \text{ N} / 25^{\circ} 58' 00'' \text{ E}$ . The average altitude of the region is 45 m. The average daily air temperature for the period 2017-2020 is lowest in January ( $-0.08^{\circ}\text{C}$ ) and highest in August ( $23.38^{\circ}\text{C}$ ). For the same period, the fluctuations of the average highest daily temperatures are between  $21.5$  and  $44.7^{\circ}\text{C}$ . 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 –  $71.9 \text{ L/m}^2$ , and lowest in August –  $29.7 \text{ L/m}^2$  (16).

## 3. Results

92 full-term newborns with PrNJ born from January 2017 to October 2020 who had indirect HB were covered. Gender distribution shows that 60% are boys, 40% are girls. The average gestational age is  $38.5 \pm 1.0$  weeks, with  $\leq 38$  weeks being 53% and  $\geq 39$  weeks being 47%. The average weight is  $3374.4 \pm 401.1$  g, predominant children weighing 3000-3999 g – 70%. A larger proportion of children were born by surgery – 54% (22% of those born by surgery are born in an emergency)(Figure 1).



**Figure 1** Characteristics of the group of 92 newborns with PrNJ (in %).

Mean BR levels from Day 1 to Day 5, on Day 14 and Day 28 were, respectively:  $101.6 \pm 24.1 \mu\text{mol/L}$ ;  $150.6 \pm 36.9 \mu\text{mol/L}$ ;  $170.4 \pm 31.8 \mu\text{mol/L}$ ;  $171.4 \pm 20.8 \mu\text{mol/L}$ ;  $160.8 \pm 27.5 \mu\text{mol/L}$ ;  $194.0 \pm 27.4 \mu\text{mol/L}$ ;  $145.1 \pm 26.3 \mu\text{mol/L}$ .

Distribution of NB according to season of birth shows the largest share of those born in summer – 37%, followed by autumn – 23%, winter – 22% and smallest in spring – 19% (  $p < 0.001$ ). Compared mean levels of BR at Day 28 show a significant difference according to season of birth, with the highest mean levels of BR being those born in summer ( $p = 0.014$ ). By Day 28, a levels of the BR of NB born in summer is  $155.4 \pm 31.8 \mu\text{mol/L}$  and in autumn is a lowest level of BR -  $134.4 \pm 19.9 \mu\text{mol/L}$  ( $p = 0.018$ ). The longest is the icterus of those born in summer ( $64.7 \pm 15.2$  days) and there is a statistically significant difference with those born in winter ( $53.8 \pm 11.1$  days,  $p = 0.018$ ) and autumn ( $55.0 \pm 10.5$  days,  $p = 0.008$ ).

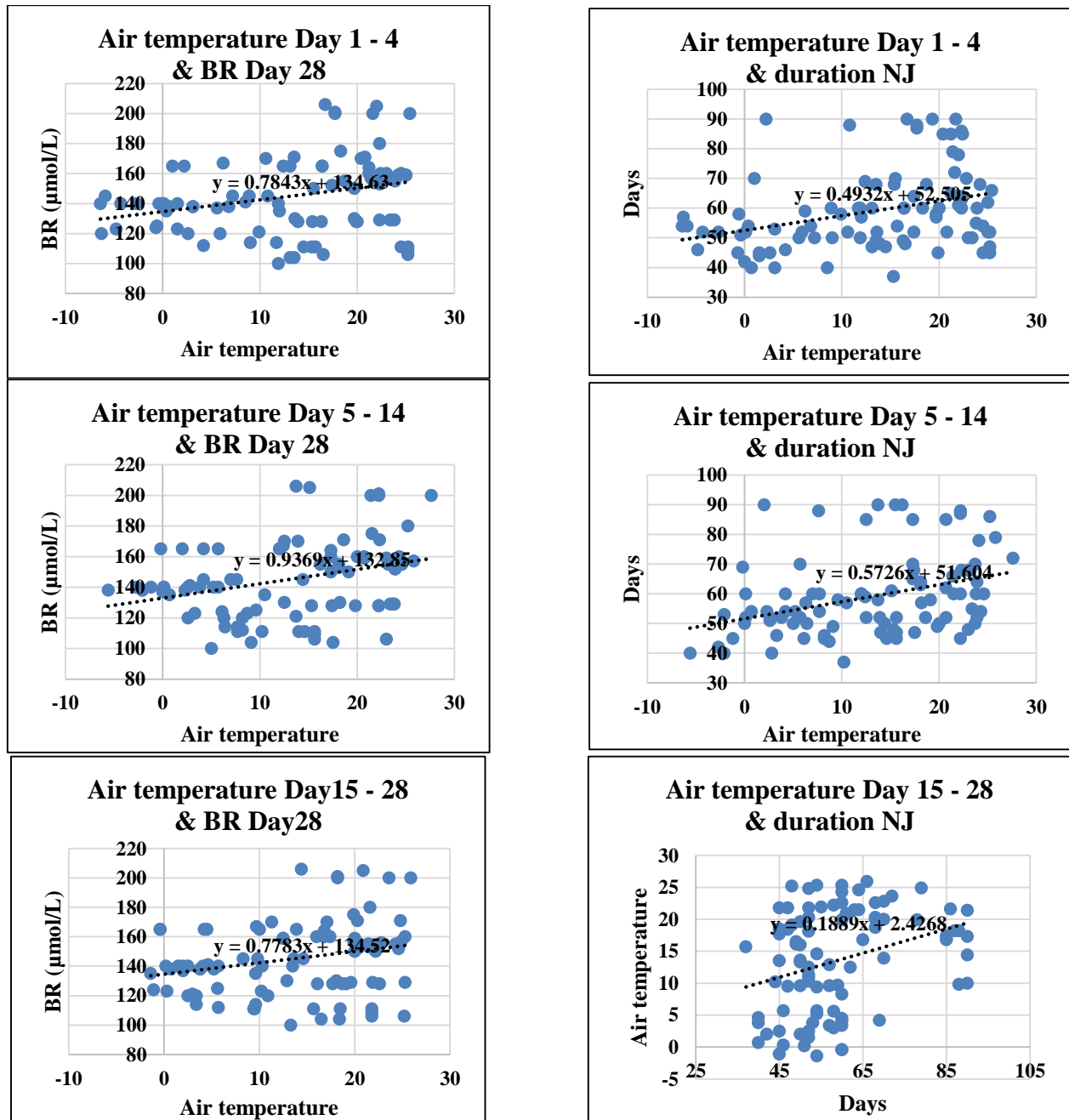
Table 1 presents a correlation between transcutaneous levels of BR on Day 14 and Day 28 and mean values of temperature, rainfall, atmospheric pressure, cloudiness, sunshine for periods Day 1 - 4, Day 5 - 14 and Day 15 - 28.

**Table 1** Correlation between transcutaneous bilirubin levels on Day 14 and Day 28 and mean values of air temperature, rainfall, atmospheric pressure, cloudiness, sunshine until Day 4, between Day 4 - 14, between Day 15 - 28 (\*r – Pearson Coefficient; \*\* $p < 0.05$ )

Indicator		Bilirubin( $\mu\text{mol/L}$ )		
		Day 14	Day 28	Duration of NJ
Temperature of air( $^{\circ}\text{C}$ )	Day 1-4	NS	$r = 0.274^*$ $p = 0.008^{**}$	$r = 0.335$ $p = 0.001$
	Day 5-14	$r = 0.263$ $p = 0.012$	$r = 0.303$ $p = 0.003$	$r = 0.360$ $p < 0.001$
	Day 15-28		$r = 0.238$ $p = 0.022$	$r = 0.317$ $p = 0.002$
Rainfall ( $\text{L/m}^2$ )	Day 1-4	$r = 0.261$ $p = 0.012$	$r = 0.272$ $p = 0.009$	$r = 0.327$ $p = 0.001$
	Day 5-14	$r = 0.252$ $p = 0.014$	NS	NS
	Day 15-28	NS	NS	NS
Atmospheric Pressure (hPa)	Day 1-4	NS	$r = -0.250$ $p = 0.016$	$r = -0.247$ $p = 0.017$
	Day 5-14	NS	NS	$r = -0.226$ $p = 0.030$
	Day 15-28	NS	NS	NS
Cloudiness	Day 1-4	NS	NS	NS
	Day 5-14	NS	NS	NS
	Day 15-28	NS	$r = -0.266$ $p = 0.012$	$r = -0.212$ $p = 0.047$
Sunshine (hour)	Day 1-4	NS	NS	$r = 0.212$ $p = 0.043$
	Day 5-14	NS	$r = 0.209$ $p = 0.046$	$r = 0.222$ $p = 0.033$
	Day 15-28	NS	NS	NS

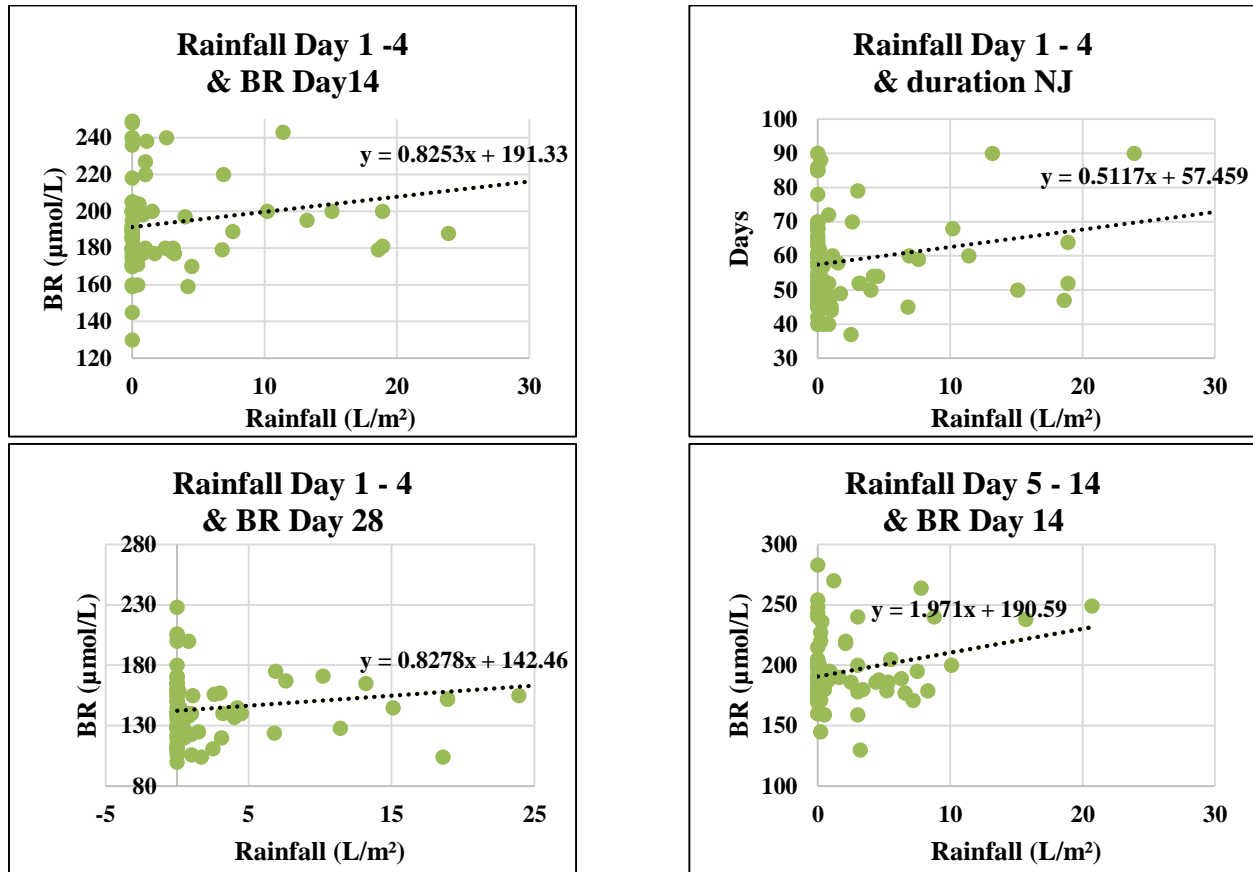
We found a positive correlation between the mean air temperature for period Day 1 - 4 and the BR at Day 28 ( $r = 0.274$ ;  $p = 0.008$ ) and a moderately strong relation with and the duration of the NJ ( $r = 0.335$ ;  $p = 0.001$ ). The air temperature between Day 5 - 14 also positively correlated with the measured BR on Day 14 ( $r = 0.263$ ;  $p = 0.012$ ), BR on Day 28 ( $r = 0.303$ ;  $p = 0.003$ ) and duration of HB ( $r = 0.360$ ;  $p < 0.001$ ). Air temperature between Day 15 - 28 also affects the

level of BR on Day 28 ( $r=0.238$ ;  $p=0.022$ ), for the duration of NJ this influence is moderately strong ( $r=0.317$ ;  $p=0.002$ ) (Figure 2).



**Figure 2** Relationship between temperature changes and bilirubin levels on Day 28 and duration of PrNJ

The amount of rainfall for Day 1 - 4 had a direct relation with the level of BR on Day 14 ( $r=0.261$ ;  $p=0.012$ ) and moderately correlated with the level of BR on Day 28 ( $r=0.272$ ;  $p=0.009$ ) and duration of NJ ( $r=0.327$ ;  $p=0.001$ ). The average of the amount of rainfall by Day 14 also affects the levels of NBs BR at Day 14 ( $r=0.252$ ;  $p=0.014$ ) (Figure 3).

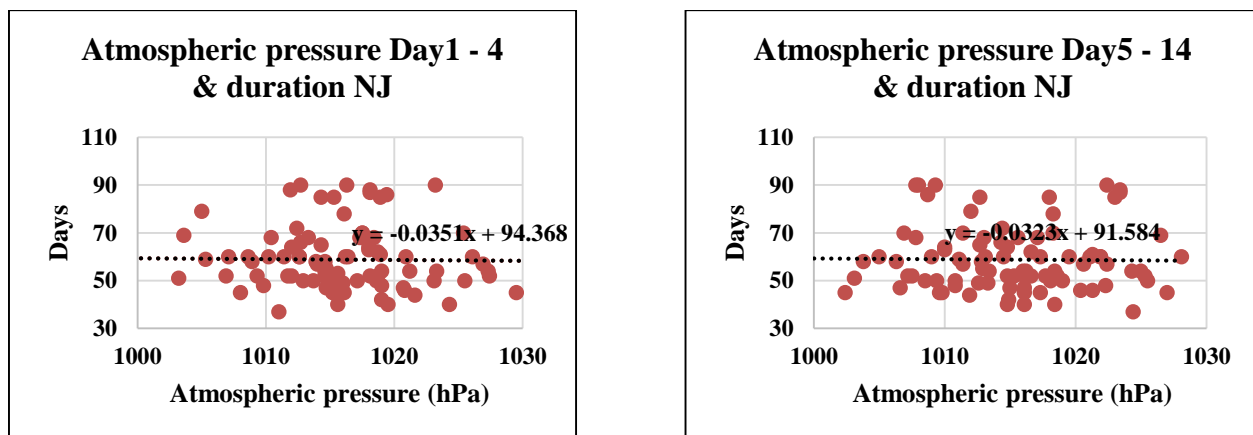


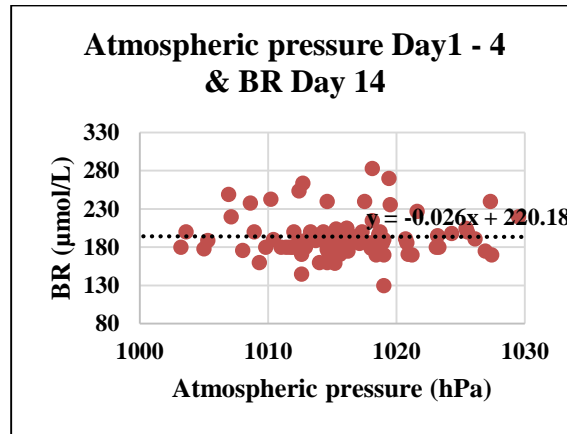
**Figure 3** Relationship between rainfall and bilirubin levels on Day 14, Day 28 and duration of PrNJ

An inverse correlation between duration of NJ and mean atmospheric pressure values between Day 1 - 4 ( $r = -0.247$ ;  $p = 0.017$ ), Day 5 - 14 ( $r = -0.226$ ;  $p = 0.030$ ) we calculated. We found a similar relationship between atmospheric pressure levels up to Day 4 and BR on Day 14 ( $r = -0.250$ ;  $p = 0.016$ ) (Figure 4).

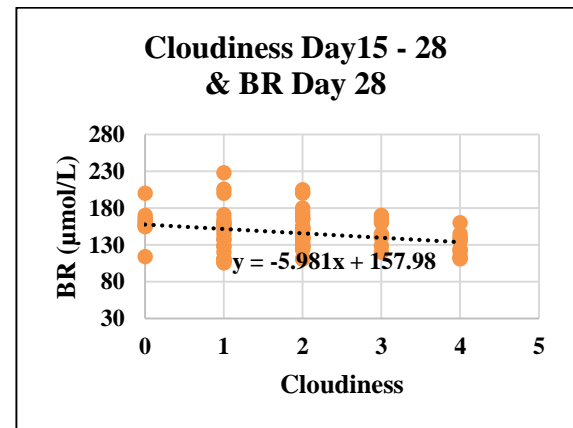
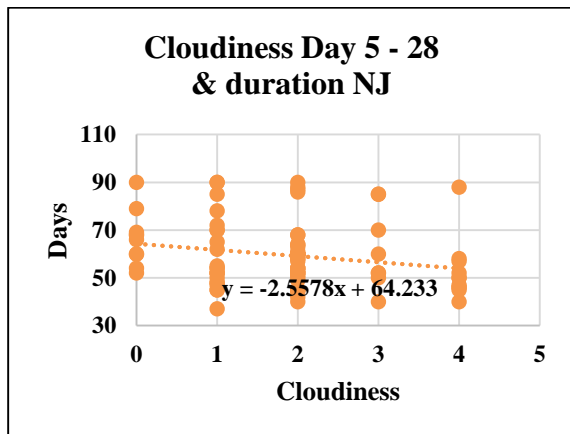
We reported the degree of cloudiness as a scale from 1 to 4 for the first 28 days of NB's life. We found that cloudiness between Day 15 - 28 had an inverse carelational with the BR on Day 28 ( $r = -0.266$ ;  $p = 0.012$ ) and duration of NJ ( $r = -0.212$ ;  $p = 0.047$ ) (Figure 5 ).

Sunshine for the period Day 1 - 4 and Day 5 - 14 affects the duration of the NJ ( $r = 0.212$ ;  $p = 0.043$  and  $r = 0.222$ ;  $p = 0.033$ ). The sunshine duration for the Day 5 - 14 determines the level of BR at the end of the neonatal period ( $r = 0.209$ ;  $p = 0.046$ ) (Figure 6).

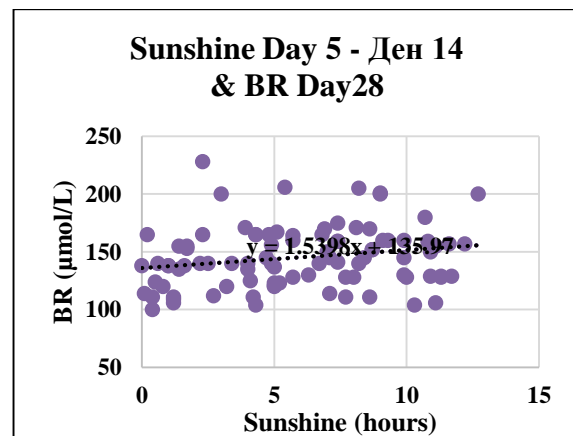
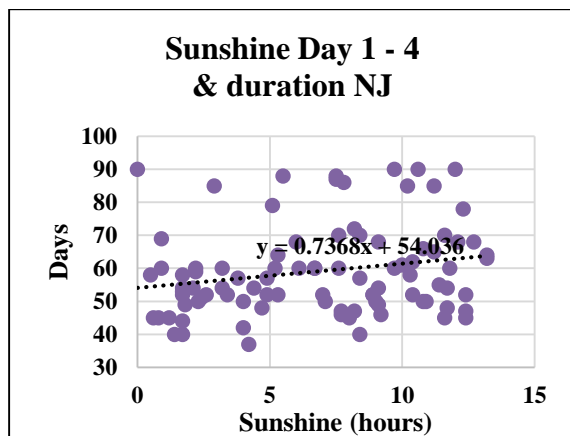


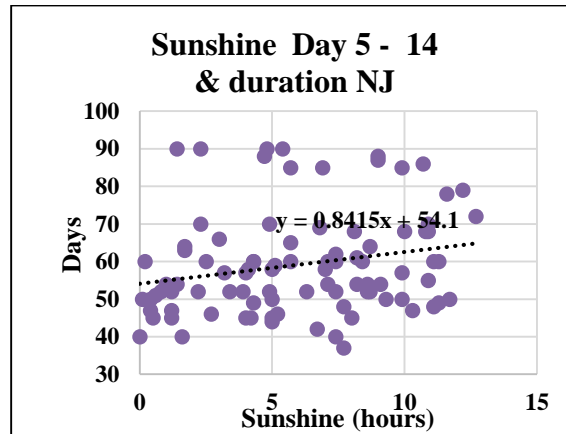


**Figure 4** Relationship between atmospheric pressure levels and bilirubin levels on Day 14 and duration of PrNJ



**Figure 5** Relationship between cloudiness degree and bilirubin levels on Day 28 and duration of PrNJ





**Figure 6** Relationship between duration of sunshine and bilirubin levels on Day 28 and duration of PrNJ

#### 4. Discussion

We followed the influence of climatic factors during the neonatal period on the manifestation of PrNJ. We found that air temperature directly affects the levels of BR for the entire neonatal period and the duration of PrNJ. The amount of rainfall during the first two weeks after birth directly correlated with bilirubinemia at end of neonatal period and the duration of PrNJ. A higher level of atmospheric pressure during the early neonatal period was associated with lower BR levels at the same and a shorter duration of PrNJ. The degree of cloudiness through the second half of the neonatal period is inversely related to the levels of BR and the duration of the PrNJ. Sunshine during the first two weeks affects the levels of BR on the end of neonatal period and the prolongation of PrNJ.

The first publication that investigated the influence of climatic factors on neonatal HB was in 1969 by Milby et al.[17] In their study, the incidence of neonatal unconjugated HB was significantly higher in the fourth trimester of each year. However, climatic information is not described and so the reason for the seasonal variation remains unclear.

Iijima et al [13] analyzed the influence of climatic factors on the expression of NJ during the early neonatal period for the NB cohort that were admitted to the neonatal structure of Hamamatsu University Hospital. They found that BR levels were significantly higher in children born during the cold season (October to March) than those born during the warm season. Only in the male population found that the BR level had a weak but significant negative correlation with the mean daily air temperature at birth. The climatic conditions in which the observation was carried out in Japan are different from those during our observation. We have formed four seasons with large temperature amplitudes in them.

Unlike the Japanese study in newborns in Iran, Hojat M et al [12] found no difference in bilirubinemia in the first week of life according to birth season, with the study done in southern Iran in Fars province. While another observation in northern Iran of Sajjadian et al [18] in the Tehran region concluded that the season acts as an independent etiological factor of neonatal HB and the mean increase in serum BR in winter is higher than the other seasons. In a study of the factors that influence the incidence of NJ in NB of in Nepal, Scrafford et al [14] considered that there was an increased risk of jaundice with increasing environmental temperature. This can be explained by the reluctance of the family to be outdoors during the warm season due to extreme heat. Thus reducing the potential for natural phototherapy. On warmer days, children are likely to lose more water and feel more thirsty. This leads on the one hand to a greater reduction in weight. On the other hand, they are breastfed more often. This suggests that jaundice is more common in exclusively breastfed children.

In China, in the southern regions, newborns in the first week of life have higher average rates of BR compared to northern and northeastern parts of the country, as the regions have different climatic conditions. Children who are born in the summer season have significantly higher levels of BR in the first week according to results of Ding et al [19]. These results are similar to those published by Gonazales et al (20), who recorded an increase in levels of BR in summer. The main reason for the increase in its level is probably the summer heat leading to a higher degree of dehydration in NB.

Cerna et al [21] analysing data on the proportion of NB with hyperbilirubinemia in a cohort from the Czech Republic, found a higher incidence in summer. Simultaneously the frequency of phototherapy is also higher in summer. These data are similar to ours. We have not been able to find studies that take into account the influence of climatic factors on the manifestation of PrNJ.

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## 5. Conclusion

According to our data climatic factors: air temperature, amount of rainfall, atmospheric pressure, degree of cloudiness, duration of sunshine affect the degree of manifestation and duration of PrNJ.

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## Compliance with ethical standards

### *Statement of ethical approval*

The study was approved by the ethics committee at the University Hospital Medica Ruse.

### *Statement of informed consent*

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

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