

Heart rate in newborns is associated with age, sex and maternal levothyroxine therapy

Asta Uusitalo^{1,2}  | Antti Tikkakoski³  | Pieta Lehtinen³  | Kaisa Ylänen^{1,2}  |
 Tuija Poutanen^{1,2}  | Päivi H. Korhonen^{1,2} 

¹Department of Pediatrics, Tampere University Hospital, Tampere, Finland

²Tampere Center for Child, Adolescent and Maternal Health Research, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

³Department of Clinical Physiology and Nuclear Medicine, Tampere University Hospital, Tampere, Finland

Correspondence

Asta Uusitalo, Department of Paediatrics, Tampere University Hospital, PO BOX 2000, Tampere FI-33521, Finland.
 Email: asta.uusitalo@tuni.fi

Funding information

The Finnish Society of Perinatology; Instrumentariumin Tiedesäätiö, Grant/Award Number: 200066

Abstract

Aim: To evaluate the definition and causes of neonatal bradycardias.

Methods: This retrospective study included 135 term-born newborns referred for 24-hour Holter monitoring due to bradycardia. Bradycardia was defined as either a heart rate below 80 beats per minute (standard definition) or a heart rate below our recently published age-specific reference values for neonatal heart rate.

Results: The mean (SD) age was 6.1 (1.3) days. With standard definition, 107 newborns (79%) had bradycardia, whereas only 20 (15%) had a minimum heart rate lower than the age-specific reference. Younger newborns had lower heart rates. Each day increased the minimum, mean and maximum heart rate by 1.8 (95% CI: 1.0, 2.6), 4.2 (95% CI: 3.0, 5.3) and 2.1 beats per minute (95% CI: 0.3, 3.8), respectively. Male sex and maternal levothyroxine medication were negatively associated with the mean and maximum heart rate. None of the newborns had a cardiac cause for low heart rate.

Conclusion: Among term newborns with bradycardias, younger age, male sex and maternal levothyroxine medication were associated with a lower heart rate on Holter monitoring. Given the age-related increase in heart rate, the 80 beats per minute limit as a universal threshold for abnormal heart rate in newborns appears inappropriate.

KEYWORDS

bradycardia, Holter, neonatal

1 | INTRODUCTION

Bradycardia in newborns is defined as a heart rate (HR) below 80 beats per minute (bpm).¹ However, occasional bradycardias below this limit seem to be common in newborns.^{1,2} Sinus bradycardia can be caused by various physiological states and is often an incidental finding during neonatal period.^{1,3} Cardiac causes of bradycardia

include sinus node dysfunction, complete atrioventricular (AV) block, long QT syndrome and atrial bigeminy.³

Admitted newborns are routinely placed under continuous electrocardiographic (ECG) monitoring. A frequently encountered clinical dilemma of continuous ECG monitoring relates to a decrease in HR below 80 bpm in an otherwise healthy-appearing newborn. Is it safe to consider this a normal phenomenon among

Abbreviations: APC, atrial premature contraction; AV, atrioventricular; bpm, beats per minute; CI, confidence interval; ECG, electrocardiogram; GA, gestational age; HR, heart rate; SD, standard deviation; VPC, ventricular premature contraction.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](https://creativecommons.org/licenses/by-nc/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2024 The Authors. *Acta Paediatrica* published by John Wiley & Sons Ltd on behalf of Foundation Acta Paediatrica.

newborns if there is no suspicion of a cardiac cause for bradycardia? This study aims to assess the definition and causes of bradycardias in term newborns, employing fixed criteria (HR below 80 bpm) along with our recently published age-specific reference values for HR in newborns.⁴

2 | METHODS

A retrospective chart review was performed among newborns referred for 24-h Holter monitoring due to bradycardias below 80 bpm at Tampere University Hospital from 2011 to 2017. The exclusion criteria were poor or inadequate recording, recording duration under 18 h, age over 10 days or gestational age (GA) under 37 + 0/7 weeks at birth.

For 24-h Holter monitoring, a SEER Light or SEER Light Extend Holter recorder (GE Medical Systems Information Technologies, Milwaukee, WI, USA) with two- or three-channel recording was used. Analysis of the recorded Holter data was performed with the MARS V8 software (GE Medical Systems Information Technologies, Milwaukee, WI, USA). The software automatically analysed the HR, maximum R-R interval, number of QRS complexes and number of atrial premature contractions (APCs) and ventricular premature contractions (VPCs), and number and length of tachyarrhythmias. The software calculated HR in bpm from 10 R-R intervals. After automated analysis, Holter data were checked for any misinterpretation of the software and edited manually. If the minimum and maximum HRs occurred during non-sinus rhythm, they were manually corrected for measurements of actual sinus rhythm.

The newborns were examined for clinical signs of heart disease, and a 12-lead ECG was performed. Echocardiography was performed if clinically indicated. Demographic data, diagnoses and blood test results were obtained from medical records. Age was calculated in hours from birth and converted into days. Blood test values analysed were either the highest value during the hospital stay (C-reactive protein) or the nearest value to the Holter monitoring.

Our recently published age-specific reference values for HR in newborns were used.⁴ The definition for bradycardia was either a HR < 80 bpm or a minimum HR < -2 standard deviations (SDs) of age-specific reference data.

In statistical analyses, means and SDs were calculated for normally distributed variables and medians, ranges and interquartile ranges (IQR) for skew-distributed variables. Frequencies and percentages were used for categorical variables. For two-group comparisons, the independent sample *t*-test (two-sided) for normally distributed continuous variables and the Mann-Whitney *U*-test for nonparametric variables were used. The Fisher's exact test was used for categorical variables. Linear regression analysis and Spearman's correlation were used whenever appropriate. In case of missing data, complete case analysis was used. The statistical significance level was defined as *p* (two-sided) < 0.05, and 95% confidence intervals (CIs) were presented whenever appropriate. Statistical analyses

Key notes

- Bradycardia below 80 beats per minute is frequently observed in continuous electrocardiographic monitoring of newborns.
- Using age-specific heart rate reference values, bradycardia was less frequent in newborns than with the fixed 80 beats per minute criteria.
- Utilising age-specific criteria for abnormal heart rate rather than a fixed limit may spare newborns from unnecessary assessments and monitoring.

were performed using IBM SPSS Statistics for Macintosh version 28.0 (IBM, Armonk, NY, USA).

3 | RESULTS

The study population consisted of 135 newborns (62% males) with a mean age of 6 days (Table 1). The median GA at birth was 41 + 0/7 weeks (IQR: 40 + 0/7–41 + 5/7) and 18 newborns (13%) were born at 42 + 0/7 weeks or later. Echocardiography was performed on 62 newborns (46%), and none of them had hemodynamically significant findings. None was on antiarrhythmic medication during the Holter monitoring. Nine newborns (7%) had short, 3-to-23-beat long, tachycardias (five ventricular tachycardias, four supraventricular tachycardias) (Table 2). Long QT syndrome, AV block, or multiple (>10%) APCs or VPCs were not found within the study population.

The mean (SD) HR was 126 (10) bpm and the minimum and maximum 74 (7) and 199 (14) bpm, respectively (Table 2). Age at the start of the monitoring was positively associated with HR. Each consecutive day increased the minimum, mean and maximum HR by 1.8 (95% CI: 1.0, 2.6; *p* < 0.001), 4.2 (95% CI: 3.0, 5.3; *p* < 0.001) and 2.1 bpm (95% CI: 0.3, 3.8; *p* = 0.024), respectively. The minimum HR correlated with the mean HR on Holter (ρ : 0.69; *p* < 0.001).

Male sex was negatively associated with the maximum HR (-5.4 bpm; 95% CI: -10.1, -0.7; *p* = 0.024). GA in weeks at birth was negatively associated with the mean HR (-1.8 bpm; 95% CI: -3.3, -0.3; *p* = 0.021). Apgar scores, umbilical cord pH, birth weight, or maternal age, smoking or body mass index, or birth method showed no statistically significant associations with HR.

Bradycardia defined as a minimum HR < 80 bpm was found in 107 (79%) newborns and was associated with younger age (Table 1). Bradycardia defined as a minimum HR < -2 SDs of age-specific reference data was found in 20 (15%) newborns and was associated with older age and higher umbilical cord arterial pH (Table 1). The study population's mean and minimum HRs were lower than the reference data population's HRs (Figures 1 and 2).

TABLE 1 Study population characteristics by different bradycardia definitions.

Characteristics	All	HR <80bpm		Minimum HR < -2 SD ^d	
	N = 135	Yes, n = 107	No, n = 28	Yes, n = 20	No, n = 115
Sex, male, n (%)	83 (62)	70 (65)	13 (46)	11 (55)	72 (63)
Age, d, mean (SD)	6.1 (1.3)	6.0 (1.3)^b	6.7 (1.1)^b	6.9 (1.5)^c	6.0 (1.2)^c
GA, wk, median (range)	41 (38–42)	41 (38–42)	41 (38–42)	41 (38–42)	41 (38–42)
Birth weight, g, mean (SD)	3660 (500)	3680 (480)	3570 (550)	3620 (390)	3670 (510)
Apgar at 1 min, median (range)	9 (2–9)	9 (2–9)	9 (4–9)	9 (2–9)	9 (2–9)
Apgar at 5 min, median (range)	9 (3–10)	9 (3–10)	9 (5–9)	9 (3–10)	9 (6–10)
Cord pH, mean (SD)	7.24 (0.09) ^a	7.25 (0.09)	7.22 (0.10)	7.30 (0.07)^d	7.23 (0.09)^d
Caesarean section, n (%)	13 (9.6)	11 (10)	2 (7)	4 (20)	9 (8)
Maternal age, median (range)	31 (19–45)	31 (19–45)	31 (19–43)	32 (21–40)	30 (19–45)
Maternal medication, n (%)	20 (15)	13 (12)	7 (25)	2 (10)	18 (16)
Antidepressants, n (%)	5 (3.7)	2 (1.9)	3 (11)	0 (0.0)	5 (4.3)
Antiepileptics, n (%)	1 (0.7)	0 (0.0)	1 (3.6)	0 (0.0)	1 (0.9)
Antipsychotics, n (%)	1 (0.7)	1 (0.9)	0 (0.0)	0 (0.0)	1 (0.9)
Betablockers, n (%)	2 (1.4)	2 (1.9)	0 (0.0)	1 (5)	1 (0.9)
Beta sympathomimetics, n (%)	2 (1.4)	1 (0.9)	1 (3.6)	0 (0.0)	2 (1.7)
Levothyroxine, n (%)	12 (8.9)	10 (9.3)	2 (7.1)	2 (10)	10 (8.7)
Infection, suspected, n (%)	62 (46)	51 (48)	11 (39)	10 (50)	52 (45)
Respiratory distress, n (%)	17 (13)	12 (11)	5 (18)	3 (15)	14 (12)
Hypoglycaemia, n (%)	12 (8.9)	7 (7)	5 (18)	1 (5)	11 (10)
Length of stay, median (range)	8 (3–20)	8 (3–20)	8 (6–17)	8 (3–12)	8 (4–20)

Note: ^aEight cases missing; ^b $p=0.005$; ^c $p=0.002$; ^d $p=0.005$.

Bold values indicate statistical significance.

Abbreviations: bpm, beats per minute; GA, gestational age; HR, heart rate.

TABLE 2 Holter results (N = 135).

Minimum HR (bpm), mean (SD)	74 (7)
Mean HR (bpm), mean (SD)	126 (10)
Maximum HR (bpm), mean (SD)	199 (14)
Maximum R-R interval (seconds), mean (SD)	0.91 (0.09)
Recording duration (hours), median (range)	19 (18–25)
APCs (%), median (range)	<0.1 (0–5)
VPCs (%), median (range)	<0.1 (0–6)
Supraventricular tachycardia, n (%)	4 (3.0)
Ventricular tachycardia, n (%)	5 (3.7)

Abbreviations: APC, atrial premature contraction; bpm, beats per minute; HR, heart rate; VPC, ventricular premature contraction.

Twelve newborns (9%) were exposed to maternal levothyroxine medication during pregnancy (Table 1). The minimum, mean and maximum HRs among the newborns without and with levothyroxine exposure were 75 and 71 bpm (-3.5 bpm; 95% CI: $-7.4, 0.4$; $p=0.079$), 127 and 119 bpm (-7.7 bpm; 95% CI: $-13.6, -1.8$; $p=0.011$), and 200 and 190 bpm (-10.3 bpm; 95% CI: $-18.3, -2.3$; $p=0.012$), respectively. Other maternal medication showed no statistically significant associations with HR.

In total, 62 (46%) newborns had a suspected infection during their first 10 days of life (Table 1). None had proven bacterial sepsis, and the median duration of antibiotic therapy was 3 days (range: 2–6 days). The median length of stay was 8 days (Table 1). Infection diagnosis or the level of C-reactive protein, or the diagnosis of hypoglycaemia ($n=12$), birth asphyxia ($n=6$) or jaundice ($n=9$) were not associated with HR. The diagnosis of respiratory distress ($n=17$) was positively associated with the mean and maximum HR (effect size: 8.6 bpm [95% CI: 3.6, 13.6; $p<0.001$] and 9.0 bpm [95% CI: 2.2, 15.9; $p=0.010$], respectively).

Plasma glucose value nearest to the Holter monitoring (range: 3.0 to 6.7 mmol/L) was positively associated with the minimum HR (effect size: 1.8; 95% CI 0.4, 3.2; $p=0.014$) but not with the mean or maximum HR ($p=0.170$ and $p=0.492$, respectively). The association between glucose and the minimum HR persisted when chronological age was added to the model. Other blood test results (blood haemoglobin, or plasma sodium, potassium or magnesium, or serum ionised calcium) were not associated statistically significantly with HR in models with chronological age.

Multivariate linear regression analyses were performed on HR (Table 3). Age and plasma glucose were associated with the minimum HR. Age, sex, respiratory distress, and maternal levothyroxine therapy were associated with the mean and maximum HR.

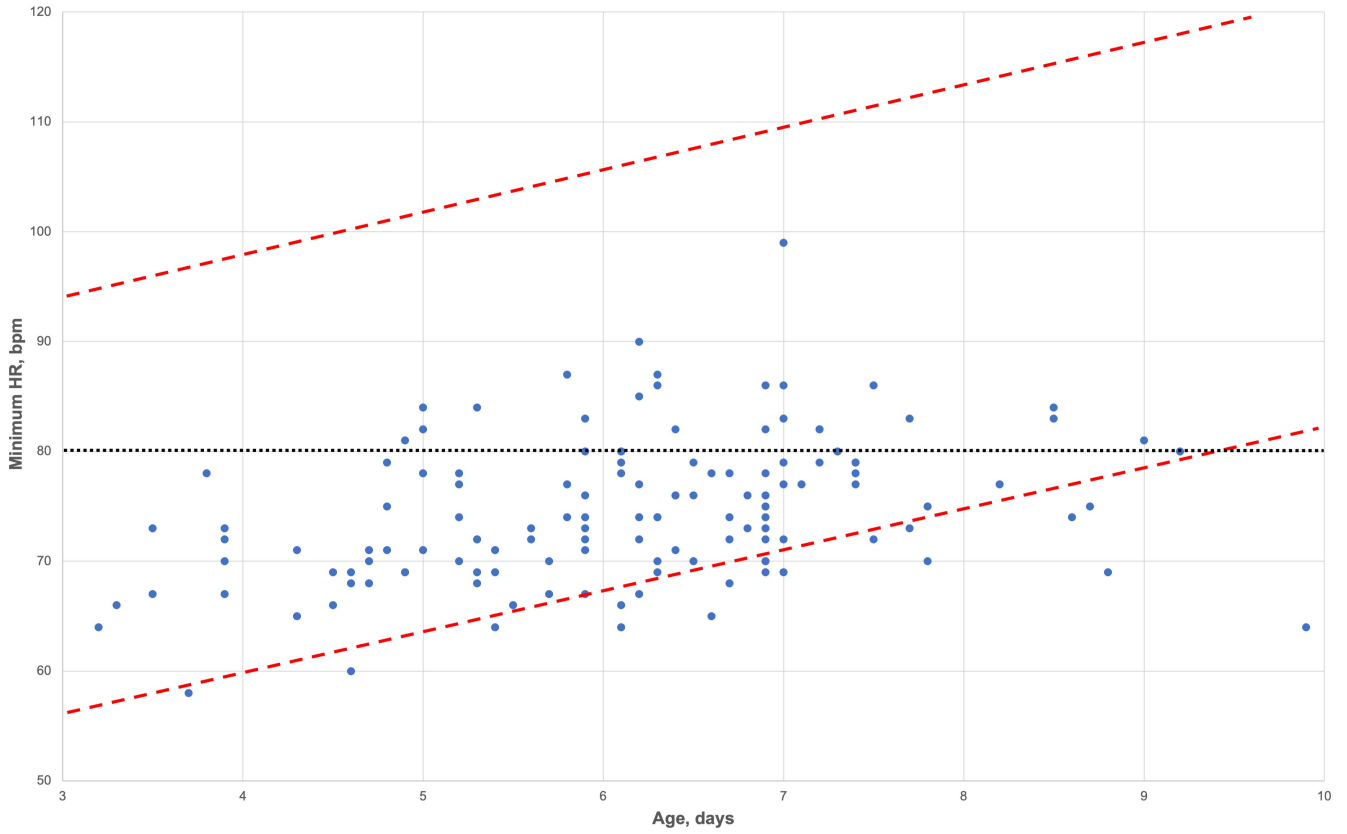


FIGURE 1 Minimum HR. Blue dots, study population. Red dashed lines, ± 2 standard deviation values for minimum HR from our previous publication.⁴ Black dashed line, 80bpm limit. bpm, beats per minute; HR, heart rate.

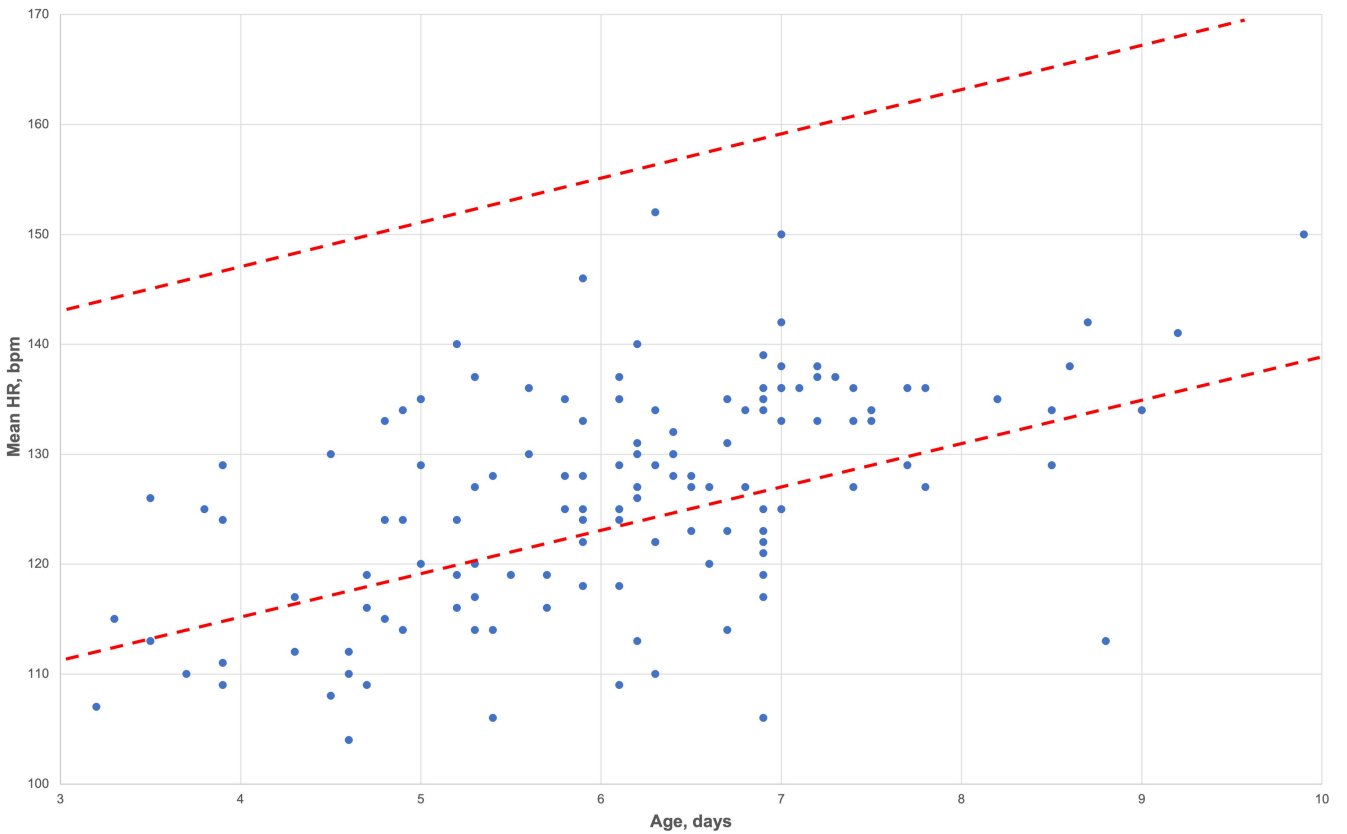


FIGURE 2 Mean HR. Blue dots, study population. Red dashed lines, ± 2 standard deviation values for mean HR from our previous publication.⁴ bpm, beats per minute; HR, heart rate.

TABLE 3 Multivariate linear regression analyses of HR (N=135).

Variables	B (95% CI)	p
Minimum HR (n=127)		
HR (Constant), bpm	56.9 (48.6, 65.2)	<0.001
Age, days	1.7 (0.8, 2.5)	<0.001
Glucose, nearest	1.6 (0.3, 3.0)	0.018
Levothyroxine	-1.9 (-5.7, 2.0)	0.337
R ² =0.156		
Mean HR (n=135)		
HR (Constant), bpm	105.1 (98.0, 112.3)	<0.001
Age, days	3.8 (2.8, 4.9)	<0.001
Male sex	-3.3 (-6.1, -0.5)	0.023
GA, weeks	-0.9 (-2.1, 0.4)	0.179
Respiratory distress	6.4 (2.2, 10.6)	0.003
Levothyroxine	-4.9 (-9.8, -0.1)	0.047
R ² =0.393		
Maximum HR (n=135)		
HR (Constant), bpm	191.8 (108.8, 202.8)	<0.001
Age, days	1.7 (0.0, 3.5)	0.045
Male sex	-5.5 (-10.0, -1.0)	0.017
Respiratory distress	7.8 (1.2, 14.4)	0.022
Levothyroxine	-8.3 (-16.0, -0.5)	0.036
R ² =0.150		

Note: Bold values indicate statistical significance.

Abbreviations: bpm, beats per minute; HR, heart rate; GA, gestational age.

4 | DISCUSSION

This study explored the Holter recordings of term newborns whose HRs fell below the established reference value of bradycardia during routine monitoring in the hospital. The majority of recordings revealed a minimum HR of less than 80bpm. However, when bradycardia was defined using the new age-specific reference values for newborn HR, most of the newborns exhibited a normal HR. Factors associated with a lower HR on Holter monitoring were younger postnatal age, male sex, and maternal levothyroxine therapy during pregnancy. None of the newborns had a cardiac cause for bradycardia.

In this study, HR below 80bpm was associated with younger age. The association between advancing age and HR was linear – as we have previously demonstrated in healthy newborns.⁴ While previous studies have reported an increase in the mean or median HR from birth to approximately 1 month of age,^{5,6} our findings suggest that the impact of chronological age is evident in all aspects of HR, including the minimum, mean, and maximum HR. According to HR variability studies, the increase in HR during neonatal period is explained by postnatal autonomic nervous system maturation.⁷

Using a HR threshold below 80bpm, nearly 80% of newborns in the study exhibited bradycardia on Holter monitoring, while applying our new age-specific reference values⁴ reduced the prevalence to 15%. In a previous study, bradycardias were reduced from 30%

to 7% when the definition of bradycardia was based on the baseline HR during the monitoring instead of a HR below 80bpm.² In the present study, the mean HR was influenced by more factors than the minimum HR. As the minimum and maximum HR measurements were single extreme values obtained during a 1-day HR monitoring, the mean HR stands out as a more reliable indicator when assessing the factors that influence HR. Moreover, it correlated well with the minimum HR observed on Holter.

In this study population of newborns, where the majority were boys, males exhibited lower HRs compared to females. The observed association between HR and sex in neonates is supported by some previous studies,^{4,8–10} whereas other studies observed sex differences in HR among older children but not in newborns.^{11,12} It is plausible that the sex difference in HR is inherently present from birth but becomes more pronounced with age.

In a large prospective general population study, the analysis of newborn ECG parameters showed a trend of decreasing HR as GA increased.¹³ This inverse correlation between GA and HR is supported by previous studies.^{14,15} In the present study, GA was negatively associated with the mean HR in univariate analysis, but not in the multivariate regression analysis. Many of the newborns in the present study were born late-term or even post-term. Probably, the effect of GA on HR might have been more evident if the sample had included more infants born early term. In our previous study, the association between HR and GA was statistically significant.⁴

None of the newborns received HR-lowering medication. Maternal sedative and antiarrhythmic medications can cross the placenta and reduce foetal HR.¹ The prevalence of levothyroxine treatment among the mothers of newborns was 9%, which surpasses the prevalence of any thyroid medication use among pregnant females in Finland from 2012 to 2016, recorded at 5.5%.¹⁶ We found a 5–10bpm reduction in postnatal HR when the foetus was exposed to levothyroxine. For other maternal medication, the sample size was too small to adequately assess associations between medication and HR.

In one foetal study, foetuses under maternal levothyroxine treatment showed a 5bpm reduction in basal HR with a significant positive correlation between the levothyroxine dose and foetal HR.¹⁷ The authors speculated that the effect seen on foetal HR was due to maternal hypothyroidism acting on foetal thyroid and that adequate dosage of maternal levothyroxine is important to foetal well-being. Unfortunately, we were not able to collect the dosage of levothyroxine during pregnancy.

Based on our unit's clinical observations, newborns with suspected infections frequently exhibit HRs below 80bpm on continuous ECG monitoring. While suspected infection was a common reason for hospitalisation in this study population, a low HR was not associated with the infection diagnosis. Antibiotics are typically discontinued around 2–3 days of age if no infection is detected, aligning with the timeframe of the lowest HRs in newborns, potentially explaining the presumed link between infection and bradycardia. Of the medical conditions, only respiratory distress showed an association with HR by increasing the HR of the affected newborns.

Preterm newborns with respiratory distress syndrome have been reported to have higher HRs than those without this condition.¹⁸

The incidental finding of bradycardia may have resulted in prolonged hospital stay. Using our new age-specific neonatal HR reference limits most of the study's newborns might have been discharged earlier and without Holter monitoring. Thus, the use of appropriate reference values could lead to savings in healthcare costs. None of the newborns had a finding on Holter that could have caused bradycardia (sinus node dysfunction, complete AV block, long QT syndrome, or atrial bigeminy). Instead, few of them had an incidental tachyarrhythmia on their Holter monitoring leading to further evaluation. However, the incidence of short tachyarrhythmias was similar in healthy controls.⁴

Blood test results were available in most of the newborns. The nearest plasma glucose value, but not the diagnosis of hypoglycaemia, was associated with the minimum HR. The glucose values of this study were single measurements and do not necessarily depict the overall glycaemia of the newborn. Nonetheless, hypoglycaemia is a known cause for bradycardia.^{3,19} The arterial umbilical cord blood pH was higher in those with a minimum HR below the age-specific limit. We do not consider this finding clinically significant, as the pH values were within normal limits in both groups.

We found factors contributing to low HR in newborns, but they explained only a small proportion of the variance in HR in the multivariate linear regression model. In previous studies, genetic factors accounted for about 25% of the variation among HR measurements, and about 50% of the variation remained unexplained.^{20,21} We were not able to collect data on parental HRs to assess the genetic factor behind bradycardia.

This was a retrospective study with a small sample size for some factors, such as maternal medication, to be assessed adequately. Otherwise, we consider our sample size adequate, compared with the previous studies on neonatal HR monitoring.^{6,8,11} The lowest HR on Holter was a single measurement. As a result, the data on frequency and duration of bradycardic episodes during Holter monitoring was lacking. Nevertheless, we consider that the mean HR generally described bradycardia at a sufficient level in this study.

5 | CONCLUSION

A large proportion of full-term neonates with suspected low HR did not have bradycardia when HR was assessed using age-specific neonatal reference values. The use of a HR below 80bpm as a general definition for an abnormal HR in newborns may lead to unnecessary monitoring of newborns with brief bradycardias. Additional studies with larger sample sizes are needed to evaluate the duration of the effect and the effect size of maternal levothyroxine medication on newborns' HR.

FUNDING INFORMATION

The study was supported by the Instrumentarium Science Foundation and the Finnish Society of Perinatology.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

ETHICS STATEMENT

The research project was approved by the Regional Ethics Committee of Tampere University Hospital (ETL R18083).

ORCID

Asta Uusitalo  <https://orcid.org/0000-0001-6620-360X>
 Antti Tikkakoski  <https://orcid.org/0000-0003-4706-9673>
 Pieta Lehtinen  <https://orcid.org/0000-0002-6613-8737>
 Kaisa Ylänen  <https://orcid.org/0000-0002-2189-1020>
 Tuuji Poutanen  <https://orcid.org/0000-0002-0805-0569>
 Päivi H. Korhonen  <https://orcid.org/0000-0002-1747-5526>

REFERENCES

1. Miller MS, Shannon KM, Wetzel GT. Neonatal bradycardia. *Prog Pediatr Cardiol*. 2000;11(1):19-24. doi:10.1016/S1058-9813(00)00032-1
2. Bohnhorst B, Seidel K, Böhne C, Peter C, Pirr S. Heart rate, respiratory rate, apnoeas and peripheral arterial oxygen saturation in healthy term neonates during quiet sleep. *Acta Paediatr*. 2019;108(2):231-8. doi:10.1111/apa.14470
3. Baruteau AE, Perry JC, Sanatani S, Horie M, Dubin AM. Evaluation and management of bradycardia in neonates and children. *Eur J Pediatr*. 2016;175(2):151-61. doi:10.1007/s00431-015-2689-z
4. Uusitalo A, Tikkakoski A, Lehtinen P, Ylänen K, Korhonen P, Poutanen T. Younger postnatal age is associated with a lower heart rate on Holter monitoring during the first week of life. *Eur J Pediatr*. 2023;182(5):2359-67. doi:10.1007/s00431-023-04914-4
5. Fleming S, Thompson M, Stevens R, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. *Lancet*. 2011;377(9770):1011-8. doi:10.1016/S0140-6736(10)62226-X
6. Richards JM, Alexander JR, Shinebourne EA, de Swiet M, Wilson AJ, Southall DP. Sequential 22-hour profiles of breathing patterns and heart rate in 110 full-term infants during their first 6 months of life. *Pediatrics*. 1984;74(5):763-77. doi:10.1542/peds.74.5.763
7. Javorka K, Lehotska Z, Kozar M, et al. Heart rate variability in newborns. *Physiol Res*. 2017;66(2):S203-S214. doi:10.33549/physiolres.933676
8. Nagy E, Orvos H, Bardos G, Molnar P. Gender-related heart rate differences in human neonates. *Pediatr Res*. 2000;47(6):778-80. doi:10.1203/00006450-200006000-00016
9. Makarov L, Komoliatova V, Zevald S, Schmidt G, Muller A, Serebruany V. QT dynamicity, microvolt T-wave alternans, and heart rate variability during 24-hour ambulatory electrocardiogram monitoring in the healthy newborn of first to fourth day of life. *J Electrocardiol*. 2010;43(1):8-14. doi:10.1016/j.jelectrocard.2009.11.001
10. Patural H, Pichot V, Flori S, et al. Autonomic maturation from birth to 2 years: normative values. *Heliyon*. 2019;5(3):e01300. doi:10.1016/j.heliyon.2019.e01300
11. Salameh A, Gebauer RA, Grollmuss O, Vít P, Reich O, Janoušek J. Normal limits for heart rate as established using 24-hour ambulatory electrocardiography in children and adolescents. *Cardiol Young*. 2008;18(5):467-72. doi:10.1017/S1047951108002539
12. Semizel E, Öztürk B, Bostan OM, Cil E, Ediz B. The effect of age and gender on the electrocardiogram in children. *Cardiol Young*. 2008;18(1):26-40. doi:10.1017/S1047951107001722
13. Hartmann J, Pærregaard MM, Norsk J, et al. Gestational age and neonatal electrocardiograms. *Pediatrics*. 2021;148:6. doi:10.1542/peds.2021-050942
14. Paliwoda M, Bogossian F, Davies MW, Ballard E, New K. Physiological vital sign differences between well newborns greater than 34 weeks gestation: a pilot study. *J Neonatal Nurs*. 2020;26(4):226-31. doi:10.1016/j.jnn.2020.02.002

15. Burtchen N, Myers MM, Lucchini M, Ordonez Retamar M, Rodriguez D, Fifer WP. Autonomic signatures of late preterm, early term, and full term neonates during early postnatal life. *Early Hum Dev.* 2019;137:104817. doi:[10.1016/j.earlhumdev.2019.06.012](https://doi.org/10.1016/j.earlhumdev.2019.06.012)
16. Ellfolk M, Heino A, Kiuru-Kuhlefelt S, Malm H, Saastamoinen L, Gissler M. *Raskausajan lääkkeiden käyttö ja syntyneiden lasten terveys 1996–2016*. 2020 Accessed December 18, 2023. <http://urn.fi/URN:ISBN:978-952-343-584-1>
17. Buscicchio G, Gentilucci L, Baldini E, Giannubilo SR, Tranquilli AL. Computerized analysis of heart rate in fetuses from mothers under levothyroxin treatment. *Gynecol Endocrinol.* 2009;25(10):679-82. doi:[10.1080/09513590903015452](https://doi.org/10.1080/09513590903015452)
18. Aarimaa T, Oja R. Transcutaneous PO₂, PCO₂ and heart rate patterns during normal postnatal adaptation and respiratory distress. *Early Hum Dev.* 1988;16(1):3-11. doi:[10.1016/0378-3782\(88\)90082-5](https://doi.org/10.1016/0378-3782(88)90082-5)
19. Nordin C. The proarrhythmic effect of hypoglycemia: evidence for increased risk from ischemia and bradycardia. *Acta Diabetol.* 2014;51(1):5-14. doi:[10.1007/s00592-013-0528-0](https://doi.org/10.1007/s00592-013-0528-0)
20. Xhaard C, Dandine-Roulland C, Villemereuil P, et al. Heritability of a resting heart rate in a 20-year follow-up family cohort with GWAS data: insights from the STANISLAS cohort. *Eur J Prev Cardiol.* 2021;28(12):1334-41. doi:[10.1177/2047487319890763](https://doi.org/10.1177/2047487319890763)
21. Singh JP, Larson MG, O'Donnell CJ, Tsuji H, Evans JC, Levy D. Heritability of heart rate variability: the Framingham heart study. *Circulation.* 1999;99(17):2251-4. doi:[10.1161/01.cir.99.17.2251](https://doi.org/10.1161/01.cir.99.17.2251)

How to cite this article: Uusitalo A, Tikkakoski A, Lehtinen P, Ylänen K, Poutanen T, Korhonen PH. Heart rate in newborns is associated with age, sex and maternal levothyroxine therapy. *Acta Paediatr.* 2024;113:973–979. <https://doi.org/10.1111/apa.17140>