European Journal of Pediatrics (2019) 178:403–411
https://doi.org/10.1007/s00431-018-03311-6

ORIGINAL ARTICLE

Apgar score and long-term respiratory morbidity of the offspring: a population-based cohort study with up to 18 years of follow-up

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Received: 3 October 2018 / Revised: 27 November 2018 / Accepted: 17 December 2018 / Published online: 9 January 2019

Abstract

The objective of this study is to investigate whether a significant association exists between low 5-min Apgar scores (< 7) and respiratory morbidity of the offspring. A population-based cohort analysis was performed comparing subtypes of respiratory morbidity leading to hospitalizations among children (up to age 18 years) stratified by their 5 min Apgar scores. Data were collected from two databases of a regional tertiary center. All singleton deliveries occurring between 1991 and 2014 were included in the analysis. A Kaplan-Meier survival curve was constructed to compare cumulative respiratory-related hospitalization incidence and a Cox proportional hazards model to control for confounders. Deliveries (238,622) met the inclusion criteria. Low 5-min Apgar scores were recorded in 742 (0.3%) newborns. Incidence of respiratory hospitalizations was higher among the low 5 min Apgar score group (7.3 vs. 4.8% in the normal [≥ 7] 5 min Apgar score group; OR = 1.5, 95%CI 1.2–2.0, $p = 0.003$). Association remained significant in the Cox model (aHR = 1.4, 95%CI 1.1–1.9, $p = 0.01$). Incidence of respiratory-related hospitalizations in preterm born offspring was higher among the low vs. the normal 5 min Apgar score groups (13.4 vs. 7.2%, OR = 2.0, 95%CI 1.2–3.1 , $p = 0.008$). Association remained significant in the multivariable analysis (aHR = 1.6, 95%CI 1.1–2.5, $p = 0.03$). The survival curves demonstrated significantly higher cumulative respiratory morbidity in the low Agar score group for the entire cohort and for the preterm born subgroup.

Elisha Ernest and Tamar Wainstock contributed equally to this work.

Accepted for poster presentation at the SMFM annual meeting, February 2019, Las-Vegas, Nevada.
This study was conducted as part of the requirements for MD degree from the Goldman Medical School at the Faculty of Health Sciences, Ben-Gurion University of the Negev.

Communicated by Peter de Winter

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00431-018-03311-6) contains supplementary material, which is available to authorized users.

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Conclusion: Newborns, of any gestational age, with low 5 min Apgar scores appear to be at an increased risk for pediatric respiratory morbidity.

What is Known:

- *Apgar score is a method for assessment of the medical condition of a newborn, and of the need for medical intervention and/or resuscitation. Studies assesing the correlation between low Apgar score and short or long term outcomes report a sgnificant correlation with different outcomes including neurological development and more. As two of its five components (color and respiratory effort) are utilizing the respiratory status, low Apgar scoreis associated with a higher risk for immedisate respiratory morbidity.*

What is New:

- *Low Apgar score increases the chances for several long-term respiratory-related morbidities, independent of gestational age and other obstetrical circumstances.*

Keywords Newborn · Child · Respiration · Pneumonia · Asthma

Introduction

The Apgar score is a method for quick assessment of the medical condition of a newborn, and of its need for medical intervention and/or resuscitation. Since its development and introduction by the anesthetist Virginia Apgar in 1952 [3], the use of the Apgar score has grown in popularity, and for years, every baby delivered in modern hospitals worldwide has been assessed by the Apgar score. Despite being introduced over 60 years ago, the Apgar score is still the most popular predictor for neonatal death, among both preterm and term newborns [5, 8]. Certain modern interventions may, however, significantly improve the status of newborns born with a low Apgar score thus making the role of low Apgar score as a predictor to newborns' survival limited [11, 13, 18]. Originally, the Apgar score was not developed as a prognostic tool for short- or long-term morbidity, and 20 years ago, the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists published a statement (later revised) regarding the abuse of Apgar scores as predictors of certain outcomes [25]. In addition, some components of the Apgar score are subjective and the inter-observer and interdisciplinary Apgar scoring variability is a limitation of this scoring method [25]. Nevertheless, studies assessing the correlation between low Apgar score and short- or long-term outcomes were and are being done, reporting a significant correlation with different outcomes such as asphyxia, cerebral palsy (CP), neurological development (seizures, intracranial hemorrhage, epilepsy, mental retardation, etc.) [21], hearing problems [10, 12], and even several types of childhood cancers [26] and gastrointestinal morbidity [14]. Yet, an association between low Apgar scores and future health remains controversial and has yet to be studied and proved.

Children's respiratory diseases are a major cause of death in developing countries and of morbidity in developed countries [23, 24, 27]. Most of these diseases have an immense impact on infants, children, and adolescents. Pneumonia, for example, is a primary cause of death in children worldwide, and asthma is the most common non-communicable disease in children.

Two out of the five components of the Apgar score—color and respiratory effort—are utilizing the respiratory status of the newborn to assess its general status. Therefore, it is expected that a low Apgar score will increase the chances for immediate respiratory morbidity. Our hypothesis was that low 5 min Apgar score (< 7) at birth is associated with long-term respiratory morbidity of the offspring.

Material and methods

In this retrospective cohort study, all deliveries taking place at the Soroka University Medical Center (SUMC) between 1991 and 2014 were included. SUMC is a 1000-bed university-affiliated tertiary referral center in Southern Israel and is the sole tertiary hospital for a population of more than 1 million. It includes the largest birth center in the country with approximately 16,000 deliveries annually (2016).

The primary objective of the study was to investigate the association between low 5 min Apgar score (< 7) and pediatric respiratory morbidity-related hospitalization rates of offspring up to the age of 18 years.

Study population consisted of all singleton deliveries taking place at SUMC during the study period. Multiple gestations, fetuses with congenital malformations (identified during pregnancy or immediately following birth prior to discharge), and all perinatal deaths (intrauterine fetal death, intra-partum death, and post-partum death) were excluded from all analyses.

Apgar scores were taken from maternal delivery charts. At SUMC, scores are given by the attending midwife 1 and 5 min following the delivery unless the delivery occurs prior to 35 weeks' gestation, fetal monitoring was

non-reassuring, or if the birth is expected to be complicated (for example placental abruption, uterine rupture, severe hemorrhage, etc.), in which case a pediatrician is called to attend beforehand. In addition, if the midwife feels that the newborn needs respiratory or other support, a pediatrician is called to the delivery room immediately following the delivery. In these cases, the pediatrician will be the one to give the Apgar scores.

One minute after birth, the midwife or pediatrician assesses each of the five components of the Apgar score, and scores it between 0 to 2 points, resulting in a total score between 0 and 10. The components are heart rate (none, less than 100 beats per minute, or more than 100 beats per minute), respiratory effort (no breathing, irregular breathing, or regular breathing), muscle tone (limp, some flexion, or active motion), reflex irritability (no response, grimace, or cry), and skin color (totally blue, bluish extremities, or pink). This process is repeated at 5 min of life, and the results are documented. In medical risk situations, every 5 min until 20 min following birth. Information regarding the first two Apgar scores any newborn was given were documented in the database.

Pediatric hospitalizations of the offspring up to the age of 18 years involving respiratory morbidity (i.e., not necessarily the primary diagnosis for the current hospitalization) according to a pre-defined set of ICD-9 respiratory morbidity codes (see Supplementary Table) were evaluated. Respiratory-related hospitalizations occurring immediately following birth and prior to the first post-partum discharge were not included in the analyses. Following the initial discharge, the first respiratory-related hospitalization for each child was included in all analyses. Follow-up time was defined as time to an event (respiratory related hospitalization) from birth or until censored. Censoring occurred in case of death (during hospitalization, other than respiratory morbidity related) or at age 18 (which was calculated for each child based on date of birth).

Data were collected from an electronic database and included demographic, obstetrical, and general maternal and fetal data for the entire cohort. For the long-term analysis, two databases were cross-linked and merged using identity numbers of mothers and offspring. In Israel, all newborns are issued a national security number (ID number) which is then registered in the mother formal identification card. These identification numbers are not changed nor duplicated within the population at any given time. This allowed us to be certain of the relationship between any mother and child in the database. The computerized hospitalization database of SUMC ("Demog-ICD9") and the computerized perinatal database of the Obstetrics and Gynecology Department. The Demog-ICD9 database includes demographic information and ICD-9 codes for all medical diagnoses made during any hospitalization at SUMC. The perinatal database consists of information recorded immediately following delivery by an obstetrician. Experienced medical secretaries routinely review the information prior to entering it into the database to insure its maximal completeness and accuracy. Coding is performed after assessing medical prenatal care records as well as routine hospital documents. Records/information were anonymized and de-identified prior to analysis.

The study received the approval of the Institutional Review Board Committee of the Soroka University Medical Center (SUMC IRB). As this was a database study, informed consent was exempted.

Statistical analysis

Statistical analysis was performed using SPSS (version 23.0) software. Assumptions were two-sided with $\alpha = 0.05$ and $\beta = 0.2$. Initial analysis compared background, pregnancy, and perinatal characteristics between the study groups (low or normal 5 min Apgar scores), using Fischer exact χ^2 test for categorical variables and t test based on variable characteristics and normal distribution. Data on continuous variables with normal distribution is presented as mean ± standard deviation (SD). Categorical data is shown in counts and percentages. Kaplan-Meier survival curves were constructed in order to take into account "time to event" as appropriate. Survival and hazard function were computed, and the cumulative hospitalization incidence was compared between the groups using the Cox-Mantel Log-rank test. Multivariate survival analysis was assessed using a Cox proportional hazards model. Variable selection for the multivariable modeling was based on clinical and statistical significance. Variables found to be significantly different between the two study groups and any available potential confounder were added to model. A sub-analysis was performed in which preterm (< 37 weeks' gestation) born offspring were evaluated separately.

Results

During the study period, 238,622 cases met the inclusion criteria. Low 5 min Apgar scores were recorded in 742 (0.3%) newborns, while normal 5 min Apgar scores were recorded in 237,880 (99.7%) newborns. Table 1 presents baseline maternal, delivery, and newborn characteristics in both groups. Mean maternal age and maternal diabetes rates were comparable between the groups, although maternal hypertension was more common among the low 5 min Apgar score group (8.1 vs. 5% among the comparison group, $p < 0.001$). Non-reassuring fetal heart rate monitoring (NRFHRM) and meconium-stained amniotic fluid (MSAF) were more common among the low 5 min

Table 1 Maternal, pregnancy, and neonatal characteristics in low and normal 5 min Apgar score groups

	Apgar < 7%(n = 742)	Apgar ≥ 7%(n = 237,880)	OR (95% CI)	p value
Maternal characteristics				
Maternal age at delivery (years, mean ± SD)	28.49 ± 6.45	28.15 ± 5.82	–	0.15
Ethnicity				
Bedouin	61.6 (457)	52.2 (124287)	0.68 (0.59–0.79)	< 0.001
Jew	38.4 (285)	47.8 (113593)		
Parity				
1	29.6 (219)	23.9 (56739)	–	< 0.001
2–4	42.9 (318)	51.2 (121760)		
5+	27.5 (204)	25 (59347)		
Diabetes[a]	6.2 (46)	5 (11977)	1.25 (0.92–1.68)	0.15
Hypertension[b]	8.1 (60)	5 (11991)	1.66 (1.27–2.16)	< 0.001
Fetal and delivery characteristics				
Non-reassuring fetal heart rate	28.7 (213)	4.9 (11762)	7.74 (6.6–9.09)	< 0.001
Meconium stained amniotic fluid	24 (178)	14.8 (35311)	1.81 (1.53–2.14)	< 0.001
Gestational age (weeks, mean ± SD)	38.1 ± 3.1	39.16 ± 1.74	–	< 0.001
Preterm delivery (% < 37 weeks gestational age)	21.2 (157)	6.4 (15221)	3.93 (3.29–4.69)	< 0.001
Induced labor	23.7 (176)	26.4 (62883)	0.87 (0.73–1.03)	0.1
Mode of delivery (% cesarean delivery)	51.9 (385)	13.6 (32270)	6.87 (5.95–7.94)	< 0.001
Gender				
Male	55.7 (413)	50.9 (120991)	1.21	0.00
Female	44.3 (329)	49.1 (116889)	(1.05–1.4)	9
Weight (grams, mean ± SD)	2979.01 ± 700.64	3216.95 ± 492.09	–	< 0.001
Birth weight ≤ 2500 g	20.2 (150)	6.3 (14881)	3.8 (3.17–4.55)	< 0.001
Birth weight ≥ 4000 g	3.6 (27)	4.7 (11248)	0.76 (0.52–1.12)	0.2
Apgar 1 min < 7	83.2 (617)	3.2 (7556)	150 (123–182)	< 0.001
Follow-up time (years, mean ± SD)	8.66 ± 6.3	10.03 ± 6.07	–	< 0.001

[a] Including all types of gestational and pre-gestational diabetes

[b] Mild or severe gestational hypertension, chronic hypertension, preeclampsia with or without severe features

Apgar score group (28.7 vs 4.9%, $p < 0.001$, and 24 vs. 14.8%, $p < 0.001$, respectively). Mean gestational age upon delivery and mean birth weight also differed between the groups although all were within the normal range. Preterm delivery (< 37 weeks gestational age) was more common in the low 5 min Apgar score group (21.2 vs 6.4%, $p < 0.001$), as were cesarean deliveries (51.9% within the low 5 min Apgar score group vs 13.6%, $p < 0.001$). Cases of low (< 7) 1 min Apgar scores were significantly more common in the low 5 min Apgar group (83.2 vs. 3.2% within the normal 5 min Apgar score group, $p < 0.001$).

Hospitalizations of the offspring involving respiratory morbidity up to 18 years of age were recorded, with a total of 11,582 events during the follow-up period. Selected respiratory morbidities are presented in Table 2 for the entire study population and for the preterm subgroup. Rates per 1000 person-years of follow-up were calculated (incidence rate or incidence density rate−the number of new cases per population at risk in a given time period, when the denominator is the sum of the person-time of the at risk population) and are also presented in Table 2. Total respiratory-related hospitalizations were significantly more common among the low 5 min Apgar score group (8.4 vs. 4.8 per 1000 person years) with a hazard ratio (HR) of 1.6 (95%CI 1.3–2.1 $p < 0.001$). In a sub-analysis of the different types of respiratory morbidities evaluated, several subcategories evaluated were more common in the low 5 min Apgar group. This difference reached statistical significance in asthma-related hospitalizations, and in "other" respiratory morbidity (respiratory failure, asphyxia, emphysema, and other dyspnea and respiratory abnormality, see Supplement Table).

In a sub-analysis of preterm (< 37 weeks' gestation) born offspring, total respiratory-related hospitalizations per 1000 person-years was significantly more common among the low 5 min Apgar score group (14.5 vs 7.3) with a HR of 2.0 (95%CI 1.3–3.0, $p = 0.002$). Evaluation of the different respiratory morbidities revealed that

Table 2 Selected respiratory morbidities among newborns with low (< 7) and normal (≥ 7) Apgar scores, for the entire study population and for preterm offspring only

	Entire study population (term and preterm)						Preterm group: <37 weeks gestation age					
	Apgar < 7		Apgar ≥ 7		HR (95% CI)	*p* value	Apgar < 7		Apgar ≥ 7		HR (95% CI)	*p* value
	n (%)	Rate per 1000 person-years	*n* (%)	Rate per 1000 person-years			*n* (%)	Rate per 1000 person-years	*n* (%)	Rate per 1000 person-years		
Asthma	28 (3.8)	4.36	6001 (2.5)	2.51	1.66 (1.14–2.4)	0.008	13 (8.3)	8.98	540 (3.5)	3.60	2.52 (1.46–4.38)	0.001
Pneumonitis	1 (0.1)	0.16	68 (<0.001)	0.03	5.24 (0.73–37.71)	0.1	1 (0.6)	0.69	3 (< 0.001)	0.02	33.7 (3.5–324)	0.002
Pleural diseases	1 (0.1)	0.16	188 (0.1)	0.08	1.94 (0.27–13.85)	0.51	1 (0.6)	0.69	14 (0.1)	0.09	7.32 (0.96–55.68)	0.054
Obstructive sleep apnea	3 (0.4)	0.47	1592 (0.7)	0.67	0.68 (0.22–2.12)	0.51	2 (1.3)	1.38	135 (0.9)	0.90	1.58 (0.39–6.39)	0.52
Other long term respiratory diseases	31 (4.2)	4.82	4621 (1.9)	1.94	2.29 (1.61–3.26)	<0.001	11 (7)	7.60	498 (3.3)	3.32	2.25 (1.24–4.09)	0.008
Total respiratory hospitalizations	54 (7.3)	8.40	11,528 (4.8)	4.83	1.64 (1.26–2.15)	< 0.001	21 (13.4)	14.50	1102 (7.2)	7.34	1.98 (1.28–3.04)	0.002

asthma, pneumonitis, and "other" respiratory morbidity were all significantly more common among the low 5 min Apgar score group (Table 2).

Among term-born offspring only, more total respiratory-related hospitalizations per 1000 person-years were noted (6.6 vs. 4.6); however, this did not reach statistical significance (HR = 1.3, 95%CI 0.9–1.9, $p = 0.11$, results not shown in the table).

Survival analysis

Three Kaplan-Meier survival analyses are presented in Figs. 1, 2, and 3 (total, preterm, and term groups). The figures demonstrate a significantly higher cumulative incidence of respiratory morbidity in the low 5 min Apgar score group in general, as well as in the preterm subgroup of newborns (log rank p values of < 0.001, and 0.002, respectively).

Several additional Kaplan-Meier survival curves were performed, in which analysis was done according to follow-up time until 1 year of age, and from age 1 to 18 years. For the entire population (both term and preterm), results were significant for both follow-up time groups—up to age 1 and from age 1 to age 18 years (Log-rank p value = 0.004 and 0.018, respectively).

For term newborns, only the survival curve constructed for the first year of life was significant (Log-rank p value = 0.009), while for preterm newborns, only the survival curve from age 1 to age 18 was significant (Log rank p value < 0.001).

Multivariate analysis

The following variables were introduced in the Cox proportional hazards model: maternal diabetes (gestational and pre-gestational diabetes), maternal hypertensive disorders, maternal age, and gestational age (in weeks, analyzed as a continuous variable, Table 3). Low 5 min Apgar score was found to be a significant and independent risk factor for respiratory morbidity of the offspring with an adjusted hazard ratio of 1.4 (95%CI 1.1–1.9, $p = 0.01$).

In a sub-analysis, preterm-born offspring with low 5 min Apgar scores were found to be at a significantly higher risk for childhood respiratory morbidity as compared to preterm-born offspring with normal 5 min Apgar scores (adjusted HR 1.6, 95%CI 1.1–2.5, $p = 0.03$).

Discussion

Apgar scores have been long established as a prediction tool for short-term neonatal survival and morbidity. Their value in

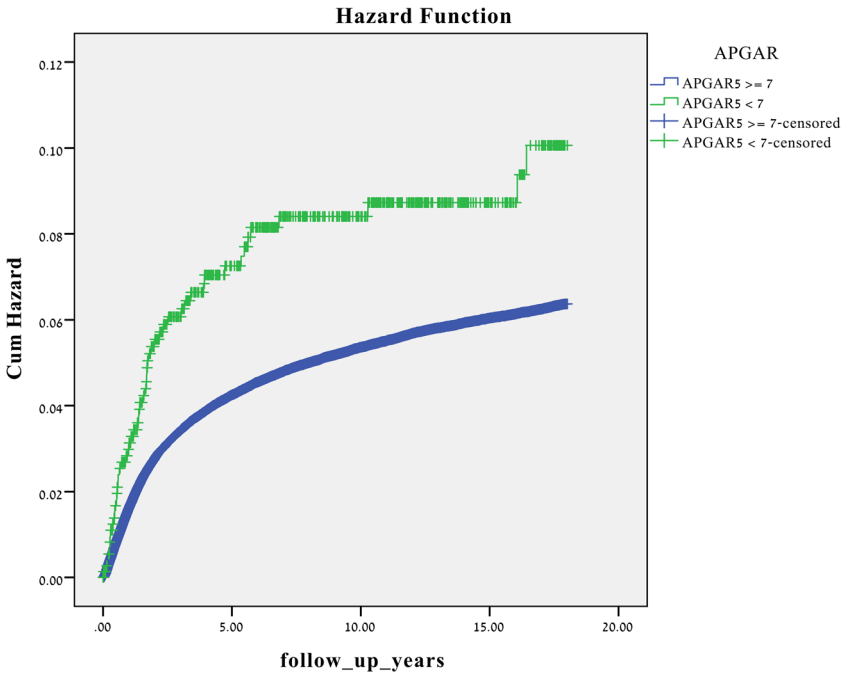

Fig. 1 The cumulative hazard for respiratory-related hospitalizations among newborns with 5 min Apgar scores of less than 7 (green line) and 7 or more (blue line). The p value of the Log-rank test is $p < 0.001$

prediction of long-term outcome has been questioned in recent years. In this large population-based cohort, with a long follow-up period, a low 5-min Apgar score was proven to be independently associated with pediatric respiratory-related hospitalizations, and specifically among preterm offspring.

Two out of the five components of the Apgar score—color and respiratory effort—are utilizing the respiratory status of the newborn. Thus, respiratory morbidity, at least in the short term, is expected to be more prevalent among newborns with low Apgar scores.

When examining the different Apgar score components, reduced values (0–1) of heart rate, and of respiratory effort, were independently associated with increased relative risks of neonatal mortality [2, 6]. As for the color component, several studies have shown different findings and some studies have even questioned the ability of medical providers who routinely assign Apgar scores to asses this component correctly especially for neonates of color who are not usually expected to be "pink all over" and are, therefore, likely to get a lower score.

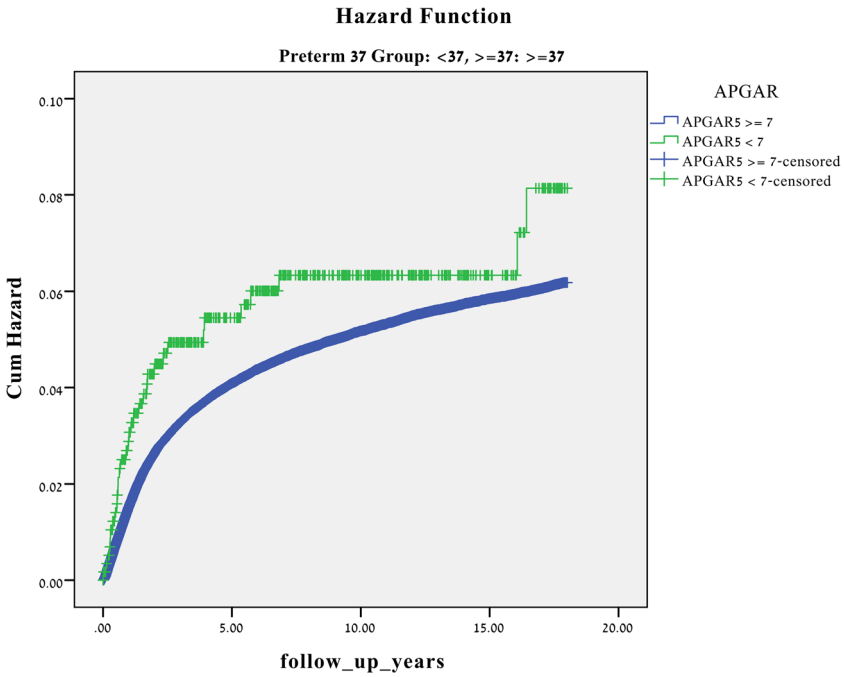

Fig. 2 The cumulative hazard for respiratory-related hospitalizations within term births only (≥ 37 weeks), among newborns with 5 min Apgar scores of less than 7 (green line) and 7 or more (blue line). The p value of the Log-rank test is $p = 0.107$

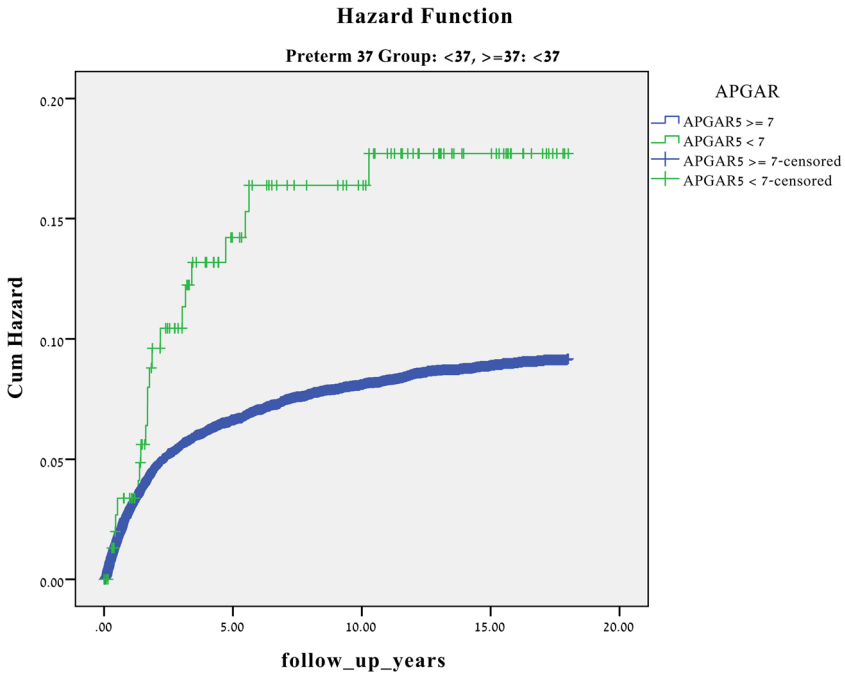

Fig. 3 The cumulative hazard for respiratory-related hospitalizations within preterm births only (< 37 weeks), among newborns with 5 min Apgar scores of less than 7 (green line) and 7 or more (blue line). The *p* value of the Log rank test is $p = 0.002$

Prematurity is known to be associated with an increased risk for long-term morbidity due to immaturity of different systems, and specifically the respiratory system [9, 15]. Our results suggest that the 5 min Apgar score may be pointing out preterm offspring more prone for later respiratory morbidity than others.

In addition, respiratory difficulties in the first minutes of the newborn's life can lead to different iatrogenic interventions often critical for life support. It is possible for these interventions to cause long-term or even permanent damages explaining the higher rate of respiratory-related hospitalizations among newborns with low Apgar scores. The fact that these interventions are more common among preterm newborns could be one of the explanations for why the findings were more pronounced in this subgroup. Nevertheless, initial interventions like these are often lifesaving.

Since alveolar lung development continues into the postnatal period, respiratory iatrogenic interventions such as intubation or mechanical high-pressure ventilation may lead to hyperoxia, volutrauma, and barotrama. These can interrupt normal pulmonary development and thus create a clinical scenario of chronic lung disease with pathophysiological effects that may extend beyond infancy into adulthood. This is more likely to occur among preterm newborns since their lung development is in its earlier stages and therefore more sustainable for injuries. For this reason, a variety of neonatal strategies have been developed, all with short-term advantages, and their long-term effects are still being studied. When we separated the follow-up time in the term group, results were significant for the first year of life, proving that the difference in respiratory morbidity rate between low Apgar score newborns and normal Apgar score newborns is more pronounced in the

Table 3 Cox proportional hazards model for the association between a low (< 7) 5-min Apgar score and total respiratory morbidity in the offspring

Cox variable controlled for	Entire study population (term and preterm) Adjusted HR; 95% CI	Preterm group < 37 weeks Adjusted HR; 95% CI	Term group ≥ 37 weeks Adjusted HR; 95% CI
Low 5 min Apgar score	1.42; 1.09–1.86	1.63; 1.06–2.52	1.31; 0.93–1.85
Diabetes mellitus[a]	1.07; 0.99–1.16	0.92; 0.72–1.16	1.09; 1.00–1.19
Hypertensive disorders[b]	0.95; 0.88–1.03	0.98; 0.82–1.16	0.94; 0.86–1.03
Gestational age[c]	0.91; 0.90–0.91	0.90; 0.88–0.92	0.90; 0.89–0.92
Maternal age	1.00; 0.99–1.00	1.00; 0.99–1.01	0.99; 0.99–1.00

[a] Including all types of gestational and pre-gestational diabetes

[b] Mild or severe gestational hypertension, chronic hypertension, preeclampsia with or without severe features

[c] In weeks, analyzed as a continuous variable

first year of life. This is consistent with previous findings regarding respiratory morbidity in the first year of life [7, 22].

Surprisingly, when we separated the follow-up time in the preterm group, results were significant only from age 1 to age 18 years but not during the first year of life. This finding is possibly a result of the fact that only hospitalizations following the initial post-partum discharge were included. Preterm newborns are often hospitalized in the NICU for long periods of time until they are ready to be discharged. This initial post-partum hospitalization was not included in our analysis.

In the analysis of the subcategories of respiratory morbidities, the highest hazard ratio was found for pneumonitis in the preterm group. The database does not include the initial hospitalization related to the birth itself, but rather hospitalizations that took place later on, after the newborn was discharged. Since the respiratory distress syndrome occurring much more often in preterm newborns usually manifests during the initial hospitalization, it cannot be the direct explanation for the high hazard ratio of pneumonitis among the preterm group. As mentioned above, it is possible that in preterm births, low Apgar scores can point out newborns in which the pulmonary system is under developed in a way that will cause their inflammatory reaction in case of aspiration to be more severe.

That being said, despite showing the highest hazard ratio among preterm births, the number of cases of pneumonitis within this group was very small. Thus, these small numbers do not allow performing a separate statistical analysis for the pneumonitis cases only or reaching any firm conclusions.

A significantly higher rate of preterm deliveries was found among the low Apgar score group. This finding is consistent with previous findings [6, 19]. As previously mentioned, preterm newborns have a respiratory system which is not fully developed. This fact itself may result in scoring less than 2 points for the respiratory effort and color components, and a lower total Apgar score [6].

In addition, a significantly higher rate of maternal hypertension was found among the low Apgar score group. This finding is also consistent with previous reports [1] and possibly related to antihypertensive drugs use, [16] maternal obesity, and maternal diabetes, all known to be more prevalent among mothers of newborns with low Apgar score [4, 17].

In order to adjust for the potential effect of prematurity and maternal hypertension on both the exposure (i.e., low Apgar score) and the outcome (i.e., childhood respiratory morbidity), we included maternal diabetes (gestational and pre-gestational), maternal hypertension, and gestational age in the regression model.

The study's retrospective nature is a significant limitation. On one hand, it allowed us to analyze a very large cohort of newborn but on the other hand, it holds all inherent weaknesses of a database study. Notably, Apgar score is subjective, being assigned by the staff (midwife or a pediatrician) and thus inter-observer and inter-disciplinary Apgar scoring variability is expected [25]. However, there is no reason to suspect that this distribution was different in the different groups compared.

Our database does not include information regarding respiratory morbidity dealt within an ambulatory setting but rather severe morbidity necessitating hospitalization. This limits the generalizability of our findings. Nevertheless, this was true for both the exposed and unexposed group and thus should not bias our results.

Our aim was to evaluate the predictive value of a low 5 min Apgar score in relation to later pediatric respiratory health. Since cases of perinatal deaths were excluded from the long-term follow-up, and only newborns that were discharged from the hospital following delivery were included, the study population represents the relatively "healthy" offspring.

Notably, we were able to analyze a long follow-up period while addressing the associations between low Apgar scores and the long-term respiratory-related pediatric hospitalizations including the less frequent respiratory morbidities, due to the large cohort size.

Low 5 min Apgar score monitoring may identify needs for focused educational programs and improvement in systems of perinatal care [20, 25]. Although Apgar scores are not intended for prediction of childhood respiratory-related outcomes [25], our findings suggest Apgar score may be used, possibly independently, or in combination with other measures, as a predictor of later respiratory vulnerability. Early detection of newborns, and specifically preterm newborns, at a higher risk for long-term adverse health outcomes can lead to early treatment and potentially reduce the odds for long-term disability.

Authors' contributions Elisha Ernst has participated in all the phases of this study including planning, literature search, data interpretation and has written the first draft of the manuscript.

Tamar Wainstock PhD is an equal first author contributor. Dr. Wainstock is a specialist in performing all aspects of the statistical analysis needed for this study. She has participated in all phases of this study and has performed most of the analyses presented in this paper and has taken a significant part in the manuscript preparation and drafting.

Eyal Sheiner MD PhD has initiated the study and supervised actively throughout its conduct. Specifically, he was involved in the data interpretation, statistical analysis, and has revised the manuscript.

Daniella Landau MD has participated in all phases of this study including literature search and research planning, data collection, and review and took part in the data interpretation and manuscript preparation.

Asnat Walfisch MD has initiated and participated in all phases of this study including study planning, literature search, data collection and review, and interpretation of the results and has supervised and extensively revised the manuscript.

Compliance with ethical statements

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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