Reference ranges for SpO_2, respiratory rate, and tidal volume in term newborn infants after birth: a narrative review

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Background and Objective: Post-natal adaptation implies respiratory and hemodynamic changes that contribute to the successful switching from transplacental to lung-based respiration and from serial to parallel circulation after cord clamping. Initial respiratory efforts extrude lung fluid to the interstitial space, facilitate alveolar aeration, and alveolar-capillary gas exchange contributing to an increase in the arterial partial pressure of oxygen (paO_2). Consequently, there is a decrease in pulmonary vascular resistance and the closure of the intra-and-extracardiac shunts. The establishment of a functional residual capacity contributes to the stabilization of the respiratory rate (RR) and the arterial paO_2. This study sought to update the reference ranges for respiratory function, oxygen saturation, and heart rate (HR) to guide neonatologists in the stabilization and/or resuscitation of newborn infants in the delivery room (DR).

Methods: Data on the respiratory function and oxygenation pattern of normal term infants in the stabilization period during the first minutes after birth were retrieved and stored by employing continuous pre-ductal pulse oximetry and respiratory function monitoring. The electronic databases searched included MEDLINE, Embase, CINAHL, and Scopus. Statistical methods were employed to establish the percentile curves for each parameter.

Key Content and Findings: We provide data of HR and oxygen saturation measured by pulse oximetry and RR and tidal volume (VT) measured by a respiratory function monitor and recorded during the first 10 minutes after birth in healthy term infants. Post-natal respiratory and cardiorespiratory adaptation in healthy term babies is enhanced by delayed cord clamping. HR and oxygen saturation achieved values of 140–160 bpm and 90–95% in the first 2–3 minutes after birth, respectively, and a VT and RR between 5–10 minutes.

Conclusions: Updated reference ranges for clinical parameters in the DR constitute a useful tool for guiding neonatologists in the stabilization of newborn infants.

Keywords: Newborn; oxygen saturation; heart rate (HR); tidal volume; fetal-to-neonatal transition

Received: 16 June 2021; Accepted: 21 December 2022; Published online: 09 January 2023.
doi: 10.21037/pm-21-75
View this article at: https://dx.doi.org/10.21037/pm-21-75

Introduction

During fetal life, the mean arterial partial pressure of oxygen (paO_2) ranges from 25 to 40 mmHg. The umbilical vein containing oxygenated blood is re-directed through specific intra-and-extracardiac shunts (in the foramen ovale and ductus arteriosus) to the brain and myocardium. The first and most critical step in establishing airborne respiration after birth requires the clearance of the liquid filling the lungs. The first profound breaths generate a negative transthoracic pressure relative to the atmospheric pressure (ΔP_{Aa}: –40 and –50 cmH_2O). The transthoracic pressure constitutes the driving force that extrudes the fluid filling the lungs to the interstitial space and contributes to the aeration of the alveolar space, thus facilitating the alveolar-capillary gas exchange. Additionally, braking maneuvers, crying, and the surfactant lining the alveolar surface contribute to the establishment of a functional residual capacity (FRC).

The increment of the arterial blood oxygen content is a major factor that causes lung vasculature dilatation, a drop in pulmonary vascular resistance and increased pulmonary blood flow. Consequently, the entire right ventricular output is re-directed through the lungs and replaces the right umbilical venous return as the main source of the left ventricular preload after the umbilical cord is either clamped or flow spontaneously ceases (1-5).

This review sought to describe the physiological steps that occur in the first minutes after birth that contribute to air respiration and adult-type circulation. We also describe the recently updated reference ranges for respiratory parameters, heart rate (HR), and arterial oxygen saturation (SpO_2). Reference ranges are a valuable guide for neonatologists to provide optimal ventilation and oxygenation to newborn infants during the fetal-to-neonatal transition when resuscitation maneuvers are requested. The following article is presented in accordance with the Narrative Review reporting checklist (available at https://pm.amegroups.com/article/view/10.21037/pm-21-75/rc).

Methods

Data on the respiratory function and oxygenation pattern of normal term infants in the stabilization period during the first minutes after birth were retrieved and stored by employing continuous pre-ductal pulse oximetry and respiratory function monitoring. The electronic databases searched included MEDLINE, Embase, CINAHL, and Scopus (see *Table 1*). Statistical methods were employed to establish the percentile curves for each parameter.

Lung-based respiration after birth

Initiation of respiration

During intrauterine life, fetal breathing activity is intermittently present and largely contributes to lung growth and development (6). The mechanisms that regulate the change from fetal intermittent respiration to newborn continuous respiration are yet unknown. However, a series of factors have been identified that notably affect the initiation of a regular respiratory pattern after birth. The role of chemoreceptors responding to hypercarbia and/or hypoxia in the first minutes after birth and especially in pre-term infants are yet unclear. Thus, while hypoxia inhibits respiratory efforts *in utero*, it appears to be a potent stimulator in new born infants (7,8). Conversely, pre-term infants display an immature response to hypoxia that appears to suppress respiratory activity (7,8).

Oxygen supplementation, especially the use of pure oxygen, has a negative effect on the respiratory drive, especially after hypoxic-ischemic events, such as in asphyxia. The initiation of diaphragmatic contractions and breathing activity occurred earlier in asphyctic rats ventilated with a lower than those ventilated with a higher inspired fraction of oxygen (9). Additionally, in a series of studies performed in asphyxiated term newborn infants, it was shown that the time to the first cry and/or initiation of spontaneous respiration was achieved earlier when newborn infants were ventilated with room air instead of 100% oxygen (10-12).

As van Vonderen *et al.* (5) noted: "*Physical stimuli are also relevant to trigger respiration. Hence, to lower the environmental temperature, rubbing the newborn's back, or using bright lights, may trigger respiratory efforts that may contribute to ensuing a regular pattern of respiration*".

Aerating the lung, and creating an FRC

In utero, the continuous secretion of fluid contributes to keeping the lung distended, which further promotes lung growth and development. Conversely, a reduction in lung fluid production leads to lung collapse and the arrest of lung growth (7). Airborne breathing requires the clearing of the lungs in a few minutes to allow alveolar-capillary gas exchange. Currently, the first inspiratory movements are largely considered the exclusive mechanism for lung fluid

Table 1 The search strategy summary

Items	Specification
Date of search	30/6/2022
Databases and other sources searched	The electronic databases searched included MEDLINE, Embase, CINAHL, and Scopus
Search terms used	Oxygen saturation, HR, RR, V_T, term infants, delivery, reference ranges, and post-natal adaptation
Timeframe	01/01/2010–30/6/2022
Inclusion criteria	Prospective observational studies that included monitoring of physiological parameters in the delivery room (heart rate, oxygen saturation, respiratory rate, tidal volume)
	Retrieval and analysis of data
	Articles in English-language
Selection process	Independent selection by 2 authors with a data extraction form

V_T, tidal volume; HR, heart rate; RR, respiratory rate.

extrusion. The first intense respiratory efforts generate a transpulmonary pressure that forces the fluid filling the airways across the alveoli, especially type I pneumocytes, to the interstitium (13,14). Additionally, stress induced by fetal expulsion favors the release of adrenaline that stimulates the epithelial cells to activate luminal surface sodium channels. This reverses the Na^+ flux and the osmotic gradient across the epithelium, causing the reabsorption of the lung liquid. The relevance of sodium channels has been challenged by studies using phase X-ray imaging that clearly show liquid clearance and lung aeration during the first inspiratory movements (15). Finally, the role of aquaporins does not appear to be related to the rapid clearance of fluid immediately after birth but with slow ongoing clearance in the following days (16). During expiration, air retention in the lungs is caused by the end expiratory pressure secondary to the closure of the glottis, breath holds, and/or crying (4). Additionally, surfactant rapidly expands on the alveolar surface and drastically reduces the tensioactive forces, thus preventing lung collapse during expiration and increasing the uniformity of lung aeration contributing to the formation of a FRC (17,18). FRC is essential to establish effective airborne respiration.

Reference range for respiratory parameters after birth

Approximately 5–10% of all newborn infants will require respiratory assistance in the first minutes after birth. Lung ventilation is the cornerstone of neonatal resuscitation (19). Positive pressure ventilation (PPV) adequately performed homogeneously expands the lungs, facilitates lung fluid extrusion to the interstitial space, creates a FRC and normalizes blood gases (20). However, the optimization of ventilation and avoidance of lung damage requires that the respiratory parameters be kept within the physiologic ranges. For this purpose, the monitoring of the tidal volume (V_T) is more effective during PPV than the monitoring of the peak inspiratory pressure (PIP) (21,22). Thus, Kattwinkel *et al.* (22), proved that monitoring V_T was superior to monitoring pressure to detect changes of lung compliance during mechanical ventilation.

Additionally, excessive V_T even for short periods was shown to cause lung overdistension and damage in experimental studies (23). For example, administering 6 manual inflations of 35–40 mL/kg to lambs, which represents a V_T 6 times greater than average (6 mL/kg), hindered their response to rescue surfactant and caused important changes in lung cytoarchitecture (23). In a rabbit model, Hernandez *et al.* (24) showed that overdistension caused by high V_T rather than PIP was responsible for lung damage. Additionally, it has been shown that a wide range of V_T can be delivered by employing a fixed PIP (21). Consequently, adjusting V_T according to lung compliance within a safe volume range allows the desired PIP to be reached while minimizing lung overdistension.

Recently, Baixauli-Alacreu *et al.* (25) provided a reference range for the V_T and respiratory rate (RR). In a prospective observational study, these authors employed a respiratory function monitor (RFM) to retrieve the V_T and RR in healthy spontaneously breathing term newborn babies who did not require resuscitation maneuvers and had been born by C-section during post-natal stabilization in the

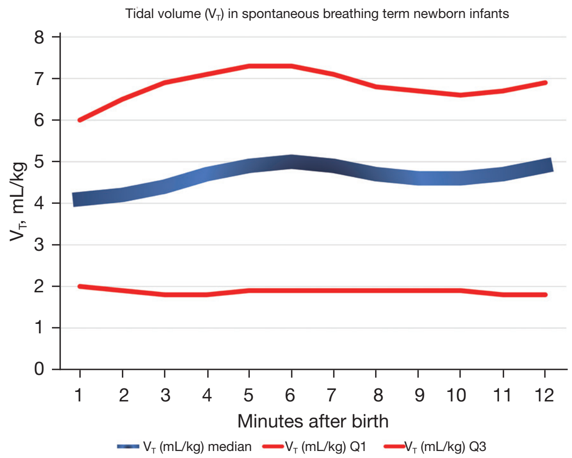

Figure 1 V_T median and IQR values expressed in mL/kg in the first 12 minutes after birth in spontaneous breathing term newborn infants based on data from reference (25). Copyright approval from Elsevier. V_T, tidal volume; IQR, interquartile range.

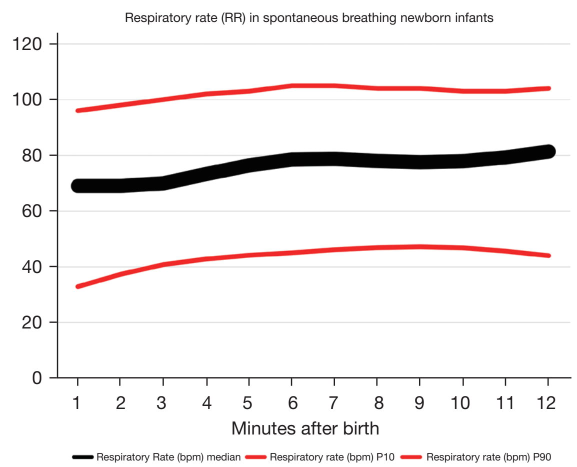

Figure 2 RR median and IQR values expressed in breaths per minute in the first 12 minutes after birth in spontaneous breathing term newborn infants based on data from reference (25). Copyright approval from Elsevier. RR, respiratory rate; IQR, interquartile range.

delivery room (DR). The RFM sensors for respiratory parameters and flow were connected to the mask interface, and the mask was sealed to ensure optimal hold during the monitoring. The mask was open to air with neglectable expiratory resistance (25). A total of 243 term newborn infants were included in the study. A total of 59,058 valid observations representing 32,801 breaths were subjected to breath-by-breath analysis using an *ad-hoc* software for respiratory research (Pulmochart; Advance Life Diagnostics, Germany). The percentiles for the V_T and RR were determined and graphically represented (see *Figures 1,2*, respectively). The median and interquartile ranges (IQRs) for the V_T at 2, 5, and 10 min were 4.2 [1.9–6.5], 4.9 [1.9–7.3], and 4.6 [1.9–6.6] mL/kg, respectively, and those for the RR were 69 [53–82], 76 [60–90], and 78 [61–92] breaths per minute (bpm), respectively.

Some interesting conclusions were drawn from this study. Notably, females had a significantly greater V_T at the 3 time points (2, 5, and 10 min) after birth, which may indicate, as has previously been suggested, that pulmonary maturation is more delayed in males than females (25,26). Additionally, a significant correlation between the evolving V_T and RR (P=0.96), and the V_T and SpO_2 (P=0.83) was established. We envision that in the future, optimal ventilation will be guided by airway pressure, gas flow, mask leak, and, most importantly, by the V_T.

Oxygenation after birth

Both the initiation of lung respiration and cord clamping have critical effects on oxygenation. Lung respiration and alveolar-capillary gas exchange enhance blood oxygenation flowing into the left atrium. Delayed cord clamping (DCC) increases blood hemoglobin content and right ventricular preload. Both circumstances will increase the availability of oxygen to tissue (2).

Pulse oximetry monitoring during post-natal adaptation

The use of pulse oximeters (POs) notably facilitates the monitoring of SpO_2. POs are easy to manage and do not require tedious calibration procedures. The use of POs became generalized in the DR in the 1980s in infants to assess SpO_2 during post-natal stabilization (27). A body of evidence has been rapidly gathered. The SpO_2 of 1,732 term newborn infants enrolled in 10 observational studies was recorded between 1987 and 2010 (28). In these studies, SpO_2 was continuously recorded during the first minutes after birth, and it was noted that in the first 2–3 min after birth, the SpO_2 was around 75%, but increased rapidly, achieving stable values >90% at 7–8 min after birth (28). Additionally, it was also stated that the post-ductal SpO_2 was 2–3% lower than the pre-ductal SpO_2, and this difference could persist for at least 24–48 hours after birth (29). Additionally, it was also established that babies born by C-section exhibited lower SpO_2 in the first minutes after birth than those born by vaginal delivery (30).

Reference range for oxygen saturation and HR after birth

In 2010, Dawson *et al.* (31), established a reference range by merging 3 pre-ductal SpO_2 data sets from the Royal Women's Hospital (Melbourne) and the Hospital Universitario y Politécnico La Fe (Valencia) that included 468 babies (ranging from 25 to 40 weeks of gestation) whose SpO_2 and HR had been continuously monitored for the first 10 min after birth. The newborn infants included in the study had not been resuscitated after birth. The SpO_2 and HR data were recorded every 2 seconds with maximum sensitivity totaling 61,650 SpO_2 data points. The population comprised a total of 465 babies, 64% of whom were term infants (≥37 weeks) and 36% of whom were pre-term (<37 weeks). The 3rd, 10th, 50th, 90th, and 97th percentiles minute by minute for the first 10 min after birth were calculated and graphically represented in 3 different graphs for the term (≥37 weeks), late pre-term (32–36 weeks), and very pre-term (<32 weeks) infants (31). Dawson's reference ranges have been widely employed since their publication in 2010 (31). In 2015, the American Heart Association (AHA) recommended the following target ranges for SpO_2: at 1 min 60–65%, at 2 min 65–70%, at 3 min 70–75%, at 4 min 75–80%, at 5 min 80–85%, and at 10 min 85–95% (32).

Reference ranges for SpO_2 and HR in newly born infants with DCC

The 2020 AHA guidelines recommend that "*after an uncomplicated term or late pre-term birth, it is reasonable to delay cord clamping until after the baby is placed on the mother, dried, and assessed for breathing, tone, and activity*." (33). In 2018, DCC had already become a standard practice in the DR in Spain as recommended by the Spanish Society for Obstetrics and Gynecology (34). Kc *et al.* (35) conducted a single-center study in which 1,510 women with uneventful deliveries were randomly assigned to cord clamping in ≤60 s of birth and cord clamping in ≥180 s. The babies with DCC exhibited significantly higher oxygen saturations during the first 10 min after birth; however, the babies with DCC had lower HRs in the first 5–6 min (35).

In 2018, we launched a prospective observational study to establish a normality range for SpO_2 and HR using pre-ductal POs in term babies born after an uneventful pregnancy by vaginal delivery and with >60-second DCC (36). We also aimed to compare the results to the Dawson reference range published in 2010 when immediate cord clamping was routine (31). Of the 392 eligible term newborn infants (≥37 weeks' gestation), we assessed 282 babies and registered a total of 70,257 SpO_2 and 79,746 HR measurements. The study was performed using a low noise cabled pulse oximetry sensor (Masimo SET Masimo-LNCS; Irvine; CA), which was placed on the infant's right hand or wrist for pre-ductal SpO_2 and HR. Immediately after placing the sensor, the cable was connected to the oximeter (Pulsi CO-Oximeter Radical 7 touch screen Masimo, Irvine, CA). The SpO_2 and HR were set at 2-second intervals and maximal sensitivity. Once the PO had been connected, the baby was put in the prone position on the mother's chest and covered to avoid hypothermia for 45 min. The cord was left patent for a median of 110±62 seconds. The results for the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentiles for SpO_2 and HR are shown in *Figure 3*, and the minute-by-minute data are shown in *Tables 2,3* (31). DCC significantly modified the reference ranges for SpO_2, especially in the first 5 min after birth. As *Table 2* shows, the reference range [median (IQR)] for SpO_2 was significantly higher (P<0.001) during the first 5 min after birth in neonates with DCC, but no differences were observed compared to the Dawson reference range from the 5th minute onwards. The HR of the neonates with DCC showed more stable values (which remained between 148–157 bpm), especially in the first 2–3 min, while the neonates with immediate cord clamping evolved from 99 bpm at 1 min to 160 at the 3rd min after birth as shown in Dawson's nomogram (see *Table 3*).

Final considerations and conclusions

In recent years, researchers in the field of fetal-to-neonatal

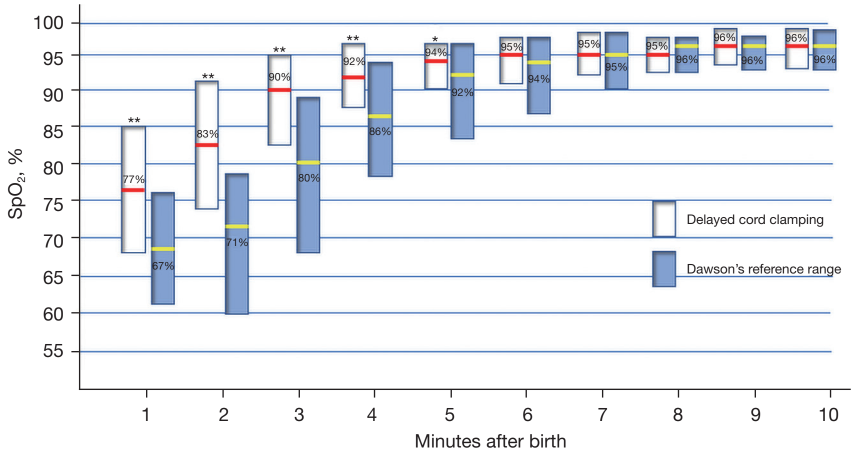

Figure 3 Comparison of percentiles (P50, P10, and P90) for oxygen saturation measured by pulse oximetry (SpO_2) in term newborn infants without [Dawson's reference range, reference (31)] and with DCC [reference (35)] in the first minutes after birth. *, P<0.05: **, P<0.01. SpO_2, arterial oxygen saturation; DCC, delayed cord clamping.

Table 2 SpO_2 median and IQR expressed in beats per minute during the first 10 minutes after fetal expulsion of term newborn infants with DCC (27) and Dawson's reference range (23)

Minutes after birth	DCC group (n=282), median [IQR]	Dawson's reference range (n=246), median [IQR]	P value
1	77 [68–85]	67 [62–76]	<0.001
2	83 [74–91]	71 [60–78]	<0.001
3	90 [82–95]	80 [68–89]	<0.001
4	92 [88–96]	86 [78–94]	<0.001
5	94 [90–96]	164 [147–180]	0.04
6	95 [91–97]	94 [87–97]	0.19
7	95 [92–97]	95 [90–97]	0.21
8	95 [92–98]	96 [92–98]	0.45
9	96 [94–98]	96 [93–97]	0.30
10	96 [93–98]	96 [93–98]	0.23

SpO_2, arterial oxygen saturation; IQR, interquartile range; DCC, delayed cord clamping.

transition and newborn resuscitation have been seeking to incorporate objectivity into their interventions in the DR. Thus, it is essential that reference ranges for the most vital clinical signs are established. Baixauli-Alacreu *et al.* (25) were the first to construct a reference range for the V_T and RR for term newborn infants. This study should be further developed and include late pre-term and extreme preterm infants to adequately guide ventilation during post-natal stabilization. The 2010 reference range for HR and SpO_2 elaborated by Dawson and his coworkers set the basis for guiding the oxygenation of newborn infants (31). The reference range developed by Padilla-Sánchez *et al.* (36), showed that DCC for approximately 2 min generates substantial changes in SpO_2 and HR, especially in the first 5 min after birth, which should be taken into consideration in the new resuscitation guidelines.

Table 3 HR median and IQR expressed in beats per minute during the first 10 minutes after fetal expulsion of term newborn infants with DCC (27) and Dawson's reference range (31)

Minutes after birth	DCC group (n=282), median [IQR]	Dawson's reference range (n=246), median [IQR]	P value
1	148 [84–170]	99 [66–132]	<0.001
2	154 [124–169]	144 [115–171]	<0.001
3	157 [143–170]	160 [138–180]	<0.001
4	158 [144–170]	163 [145–181]	<0.001
5	155 [143.167]	164 [147–180]	<0.001
6	152 [141–168]	163 [147–179]	<0.001
7	153 [142–163]	162 [146–178]	<0.001
8	152 [140–164]	159 [144–173]	<0.001
9	152 [142–161]	157 [143–172]	<0.001
10	151 [141–161]	157 [142–171]	<0.001

HR, heart rate; IQR, interquartile range; DCC, delayed cord clamping.

In the future, caregivers in the DR will likely have access to precise and valuable information in real time that will objectively guide their interventions and thus reduce iatrogenic damage and increase effectiveness.

Acknowledgments

Funding: M Vento received PI20/00964 and RD16/0022/0001 grants, and the ILC CM20/00187 grant from the Health Research Institute Carlos III (Ministry of Science and Innovation; Kingdom of Spain).

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Ola Didrik Saugstad) for the series "Oxygen in the Newborn" published in *Pediatric Medicine*. The article has undergone external peer review.

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://pm.amegroups.com/article/view/10.21037/pm-21-75/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://pm.amegroups.com/article/view/10.21037/pm-21-75/coif). The series "Oxygen in the Newborn" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved.

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(English Language Editor: L. Huleatt)

doi: 10.21037/pm-21-75
Cite this article as: Padilla-Sánchez C, Baixauli-Alacreu S, Solaz-García Á, Lara-Cantón I, Parra-Llorca A, Vento M. Reference ranges for SpO_2, respiratory rate, and tidal volume in term newborn infants after birth: a narrative review. Pediatr Med 2023.

