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Hemodynamic Trends in Full Term Newborns versus Late Preterms during Transition

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***Abstract*---**To define hemodynamic changes in the first 15 minutes of life and at one hour after birth in healthy full term and late preterm neonates using electrical cardiometry. This is a prospective observational study using EC in the first 15 minutes of life and one hour after birth. Two hundred newborns were included in the study and divided into two groups. Group A included 100 healthy full term newborns (≥37 weeks gestational age), while group B included 100 late preterms (≥34 weeks up to 36^6 weeks gestational age). Each group was further subdivided according to mode of delivery to vaginal delivery group and elective CS group. The study included 200 newborns. Higher values of PEP were observed in full term than preterm neonates. TFC is higher in CS group when compared to VD group. SVV tends to decrease over time. Oxygen saturation increases over time. The present study provides normative values for PEP, TFC, O2 saturation and SVV during the first hour of life using electrical cardiometry.

***Keywords*---**electrical cardiometry, full term newborns, hemodynamic trend, late preterms, neonatal transition.

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Introduction

The newborn may have a variety of hemodynamic problems with a variable and complex pathophysiology. This cardiovascular vulnerability results from particular features of the newborn, such as incomplete myocardial development, the presence of fetal shunts, changes in systemic and pulmonary vascular resistance, and more generally the complex hemodynamic changes that take place during transition to extra-uterine life (Corredera et al., 2014). Understanding the functional and structural characteristics of the neonatal circulation is essential, as therapeutic hemodynamic interventions must be based on the underlying pathophysiology (Vrancken et al., 2018).

At birth rapid clearance of the lung liquid is needed, to allow air entry and start pulmonary gas exchange. As it also triggers the increase in pulmonary blood flow (PBF) at birth, lung aeration is the central determining event for the successful transition to newborn life (Hooper et al., 2015). When the umbilical cord is clamped after birth it eliminates the placental function as a reservoir for blood, causing increase in the systemic vascular resistance (SVR), increase in blood pressure, and increase in pressures in the left side of the heart (Askin, 2009).

In normal situations, left ventricular output increases significantly because of an increased heart rate, increased left ventricular end-diastolic volume with increased pulmonary blood flow, increased inotropic function secondary to circulating catecholamines, and improvement of left ventricular wall compliance due to decreased right ventricular systolic and diastolic load (Mielke & Benda, 2001). Rapid and transient increase in cerebral blood flow results from increase in the systemic vascular resistance (SVR). Increased oxygenation will close the fetal cardiac shunts (Dawes, 1962).

Normal physiologic transition in the preterm newborn is affected by several factors, including but not limited to the immaturity of organ systems, maternal conditions, diseases, and medications, the timing of cord clamping, and resuscitation Procedures (Kluckow & Evans, 2000). Transition may proceed less smoothly for some neonates. Signs of mild to moderate respiratory distress may include mild temperature instability or borderline blood glucose levels. These newborns must be monitored closely to detect whether these signs indicate underlying disease (Askin, 2009).

PDA will result from the failure of the ductus arteriosus (DA) to close spontaneously in the early postnatal period leading to persistent shunting of blood between the systemic and pulmonary circulations. PDA has been linked to a variety of negative outcomes in preterm neonates in several studies (Clyman et al., 2012). Hemodynamic monitoring is a cornerstone of critical care for both management and diagnosis, but it is still very difficult for patients in neonatal intensive care units (NICUs). In fact, the techniques available for this purpose are unreliable, operator-dependent, or intermittent (Hsu et al., 2016).

Variable methods are used for hemodynamic monitoring mainly cardiac output, but not all are appropriate for newborns. Technical and size restraints, possible toxicity of indicators (lithium, carbon dioxide), risk of fluid overload, difficulties in vascular access, and the presence of shunts (transitional circulation, congenital heart defects) all contribute to this restriction (de Boodi, 2010). Ideally, hemodynamic monitoring in neonates should be accurate, practical, noninvasive, continuous in absolute measurements and feasible to entire spectrum of age and weight. Various guidelines have been published to standardize the use of functional echocardiography in the NICU. Its use is especially vital in the intensive care settings (Singh et al., 2016).

The motivation for validation of electrical cradiometry (EC) against echocardiography in cardiovascular monitoring for neonates, is that EC has the advantage of being non-invasive, operator-independent and continuous (Boet et al., 2016). Electrical cardiometry (EC) has been proposed as a safe, accurate and reproducible technique for hemodynamic measurement in children and infants. It is an impedance-based device that provides real-time cardiovascular assessment in an absolute number. Its principle is related to changes in thoracic electrical bio-impedance caused by cardiac cycle. The method of EC is based on the fact that the conductivity of the blood in the aorta changes during the cardiac cycle and orientation of erythrocyte (RBCs) prior and after opening of aortic valve (Osypka, 2009; Sanders et al., 2005).

Method

This is a prospective observational study carried out in Obstetrics and Gynecology hospital, Cairo University (Kasr EL Ainy school of medicine); in the resuscitation area of the delivery room over 20 months period from July 2019 till March 2021. Two hundred newborns were included in the study and divided into two groups. Group A included 100 healthy full term newborns (≥37 weeks gestational age) while group B included 100 late preterms (≥34 weeks up to 36^6 weeks gestational age). Each group was further subdivided according to mode of delivery to vaginal delivery group and elective CS group (using spinal anesthesia).

Inclusion criteria

- Newborns in need only for routine care without need for any medical or respiratory support during resuscitation;
- APGAR score ≥ 7 at 1 minute and ≥ 8 at 5 minutes.

Exclusion criteria

- Need for respiratory or medical support during resuscitation;
- Intrauterine fetal distress and perinatal asphyxia;
- Major congenital anomalies;
- Multiple pregnancies;
- APGAR score less than 7 at 1 minute.

Electrical cardiometry setting and parameters

EC (ICON; Osypka Medical, Berlin, Germany) ICON® was applied by means of four standard surface electrocardiogram electrodes and all measurements were performed on supine to avoid agitation. EC was set to record qualified measurements (i.e., signal quality index, provided by ICON, ⩾80%). EC hemodynamic parameters comprise of Stroke volume variation (SVV), Pre-ejection period (PEP), thoracic fluid content (TFC). The cord was clamped immediately within a period of 30 seconds after birth. A stopwatch was used to detect time accurately. Neonates were resuscitated by attending neonatologist (who was not member of the research team). APGAR score was documented at 1 and 5 minutes. After that four surface ECG electrodes (forehead, left lower neck, left mid-axillary line at the level of xiphoid process and lateral aspect of left thigh) are used to obtain a current flow.

Measurement/monitoring of the newborns hemodynamics was performed continuously for the first 15 minutes of life and at age of one hour after birth in both groups. The transducer for arterial oxygen saturation measurement was placed on the right hand or wrist. Monitoring started at minute 1 to 2 of life and was continued until minute 15 then we recorded measurements at age of one hour. Arterial oxygen saturation was measured using a Masimo radical 7 pulse oximeter (Masimo , Irvine, CA) with a LCNS Neo 3 sensor (Masimo) monitor (Philips, Eindhoven, Netherlands).

Statistics

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between groups were done using unpaired t test or ANOVA with post hoc test (Chan, 2003a).

For comparison of serial measurements within each group repeated measures ANOVA was used (Chan, 2004). For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003b). Correlations between quantitative variables were done using Pearson correlation coefficient (Chan, 2003c). P-values less than 0.05 were considered as statistically significant.

Results and Discussion

Results

Two hundred fifty three newborns were recruited for the present study, 53 newborns were excluded due to need of respiratory support (11 newborns), no informed consent was obtained from parents (32 newborns) and equipment failure (10 newborns).Two hundred neonates were finally included. We recorded 3000 ICON measurements in the first 15 minutes of life. 2100 (70%) measurements were excluded because of SQI <80%.

Included neonates are divided into two groups. Group A included 100 healthy full term newborns (≥37 weeks gestational age) while group B included 100 late preterm newborns (≥34 weeks up to 366 weeks gestational age). Each groups was further subdivided according to mode of delivery:

- Full Term Vaginal Delivery group (FT VD) included 50 full term newborns;
- Full Term Cesarean Section delivery group (FT CS) included 50 full term newborns;
- Late Preterm Vaginal Delivery group (PT VD) included 53 late preterm newborns;
- Late Preterm Cesarean Section delivery group (PT CS) included 47 late preterm newborns.

All neonates are appropriate for gestational age. Demographic and clinical characteristics of the studied population are presented in tables 1 and 2.

Table 1
Demographic characteristics of the studied full term neonates

	Cesarean section (n=50)	Vaginal (n=50)	P-value
Gestational age at delivery (weeks)	38.2 ± 1.0	38.3 ± 1.1	1
Birth weight (kg)	3.13 ± 0.41	2.97 ± 0.35	0.194
Length (cm)	48.5 ± 1.9	48.2 ± 2.0	1
SA (m^2)	0.21 ± 0.02	0.20 ± 0.01	0.114
Male (%)*	22(44%)	31(62%)	0.071
Apgar at 1 minute	7 (7 to 8)	8 (7 to 8)	0.497
Apgar 5 at minute	9 (9 to 9)	9 (9 to 9)	1

chi-squared test for nominal and unpaired t test for numerical data. Data were expressed as mean±SD for numerical data and number, percentage for qualitative data.

Table 2
Demographic characteristics of the studied late preterm neonates

	Cesarean section (n=47)	Vaginal (n=53)	P value
Gestational age at delivery (weeks)	35.1 ± 0.8	35.2 ± 0.8	1
Birth weight (kg)	2.63 ± 0.30	2.54 ± 0.35	1
Length (cm)	46.7 ± 2.1	45.8 ± 2.3	0.248
SA (m^2)	0.19 ± 0.01	0.18 ± 0.01	0.68
Male (%)*	23(48.9%)	31(58.5%)	0.339
Apgar at 1minute	8 (8 to 8)	8 (7 to 8)	1
Apgar at 5 minute	9 (9 to 10)	9 (9 to 10)	1
Antenatal steroids *	11(23.4%)	18(34%)	0.246

**.chi-squared test for nominal and unpaired t test for numerical data Data were expressed as mean±SD for numerical data and number, percentage for qualitative data.*
Surface area (SA); kilogram (Kg); centimeter (Cm)

Indications of Cesarean section are: Previous CS, fetal malpresentation, and maternal contracted pelvis.

Thoracic fluid content

Thoracic fluid content is defined as the electrical conductivity of the chest cavity, which is primarily determined by the intravascular, intra-alveolar, and interstitial fluids in the thorax. Thoracic fluid content decreases between minute 2 and minute 60 of life (P value 0.036) in late preterm CS group in the first hour of life. No significant difference is observed in TFC in the other 3 groups in the first hour of life. Trend of TFC changes over time was illustrated in figure 1.

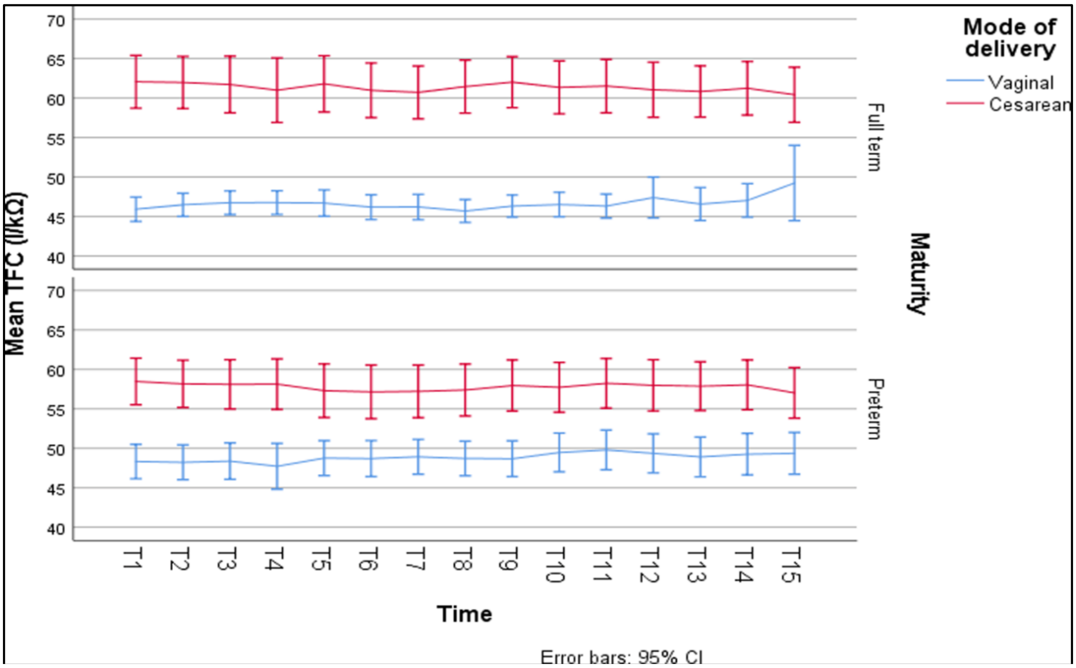

Figure 1. Change in Thoracic fluid content over time by mode of delivery in full term and late preterm babies. Time points: T1 = 2 minutes, T2 = 3 minutes, T3 = 4 minutes, T4 = 5 minutes, T5 = 6 minutes, T6 = 7 minutes, T7 = 8 minutes, T8 = 9 minutes, T9 = 10 minutes, T10 = 11 minutes, T11 = 12 minutes, T12 = 13 minutes, T13 = 14 minutes, T14 = 15 minutes, T15 = 60 minutes.

Regarding mode of delivery; TFC is higher in CS when compared to VD group (P value >0.001 and 0.003 respectively) for both full term and late preterm neonates over the first hour of life

Pre-ejection period (PEP)

It is defined as a valid index of myocardial contractility and beta-adrenergic sympathetic control of the heart defined as the time between electrical systole (ECG Q wave) to the initial opening of the aortic valve. Higher values of PEP were observed in full term than preterm neonates. Trend of PEP changes over time are illustrated in figure 2.

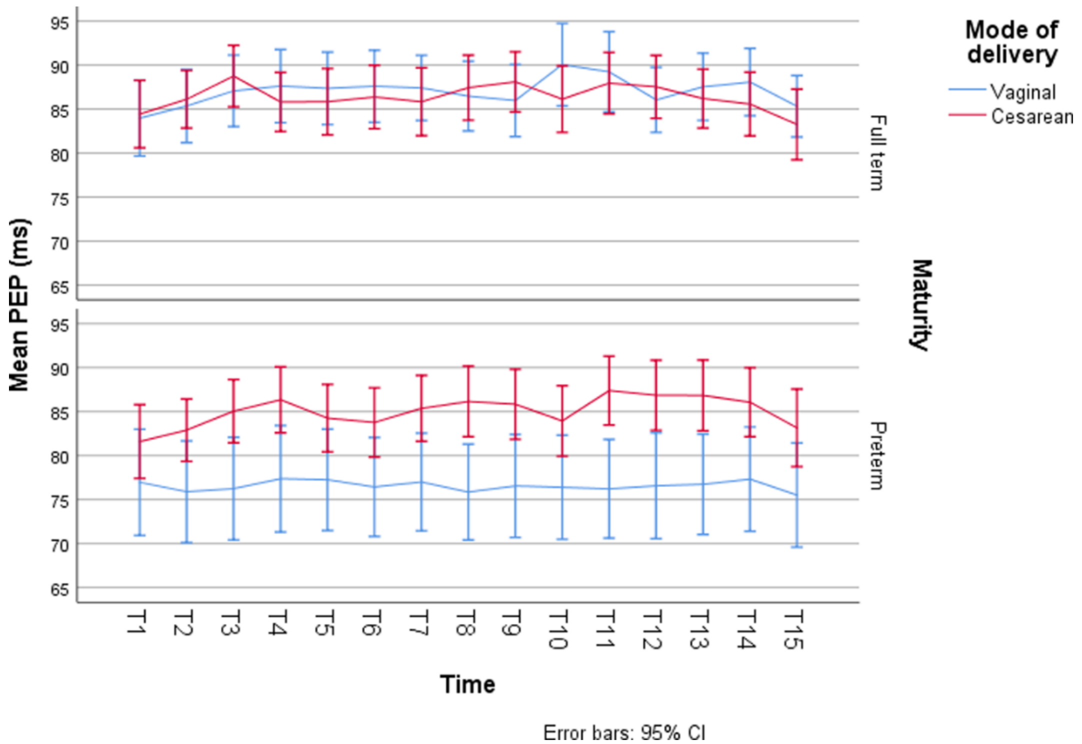

Figure 2. Change in PEP over time by mode of delivery in full term and late preterm babies. Time points: T1 = 2 minutes, T2 = 3 minutes, T3 = 4 minutes, T4 = 5 minutes, T5 = 6 minutes, T6 = 7 minutes, T7 = 8 minutes, T8 = 9 minutes, T9 = 10 minutes, T10 = 11 minutes, T11 = 12 minutes, T12 = 13 minutes, T13 = 14 minutes, T14 = 15 minutes, T15 = 60 minutes

Stroke volume variation

Stroke volume variation is defined as the difference in maximum SV and minimum SV during respiration. The greater the difference, the more fluid responsive a patient is likely to be. Stroke volume variation decreases over the first hour of life in full term and late preterm babies delivered both vaginal and CS. In FT VD group, no significant changes are observed at minute 5 versus minute 10 of life. In FT CS group no significant changes are observed at minute 2 versus minute 5, minute 5 versus minutes 10 and 15 of life, and at minute 10 of life versus minute 15. In Late PT VD group no significant changes are observed at minute 5 versus minute 10 and 15 of life, also at minute 10 versus minute 15 no significant changes are found. In Late PT CS groups; no significant decrease occurs at minute 2 versus minute 5, 10 and 15 of life as well as minute 5 versus minutes 10 and 15 and minute 10 versus minute 15 of life. Trend of Changes in SVV over time are illustrated in figure 3.

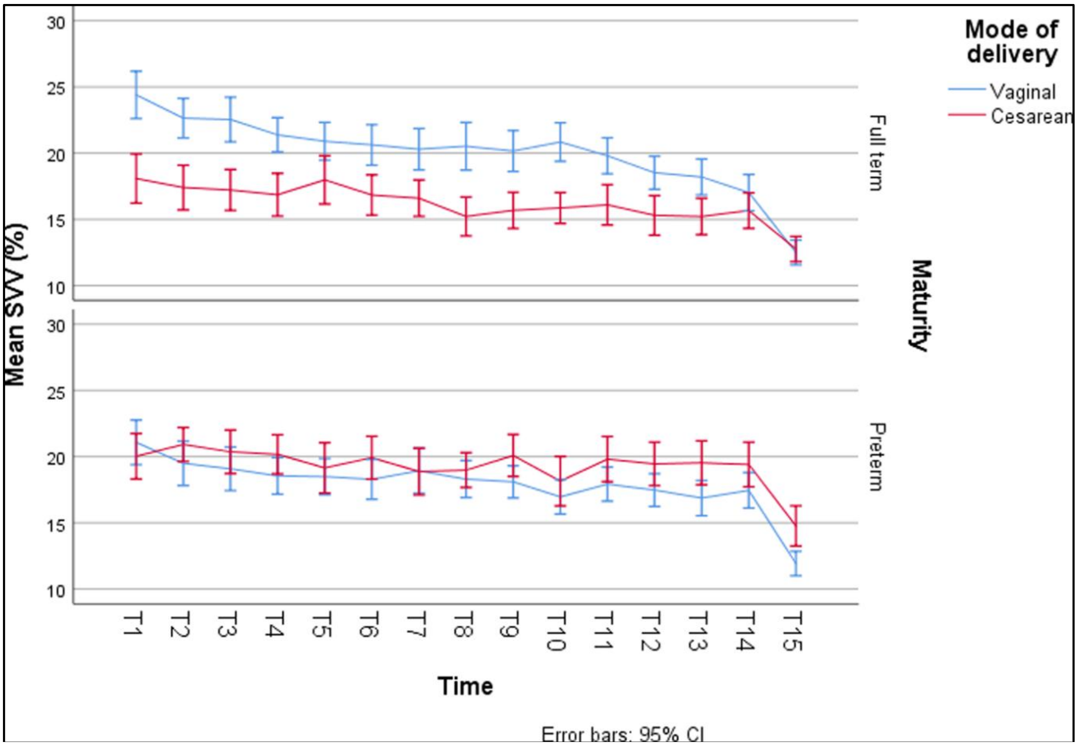

Figure 3. Change in SVV over time by mode of delivery in full term and late preterm babies. Time points: T1 = 2 minutes, T2 = 3 minutes, T3 = 4 minutes, T4 = 5 minutes, T5 = 6 minutes, T6 = 7 minutes, T7 = 8 minutes, T8 = 9 minutes, T9 = 10 minutes, T10 = 11 minutes, T11 = 12 minutes, T12 = 13 minutes, T13 = 14 minutes, T14 = 15 minutes, T15 = 60 minutes

Regarding mode of delivery; Full term vaginal delivery group has higher SVV than full term CS group with (p value <0.001) at minutes 2, 5 and 10 of life. On the contrary Late Preterm Vaginal Delivery group has lower measurements than Late Preterm CS group with p value (0.049 and <0.001 respectively) at minutes 10 and 60 of life. Regarding gestational age; Full Term VD group has higher SVV than Late PT VD group with significant p value (0.007, 0.005 and 0.038) at minute 2, 5 and 10 of life respectively. Late preterm CS delivery group has higher measurements than full term CS group with significant p value (0.002, <0.001, <0.001 and 0.011 respectively) at minutes 5, 10, 15 and 60 of life respectively.

Oxygen saturation changes during transition

Oxygen saturation increases significantly over time (P values <0.001) in all studied neonates over the first 15 minutes of life. From minute 15 to minute 60 of life significant increase occurs in Full Term Vaginal Delivery and Late Preterm CS groups (P value <0.001 and 0.003 respectively). Trend of Oxygen saturation over time was illustrated in figure 4.

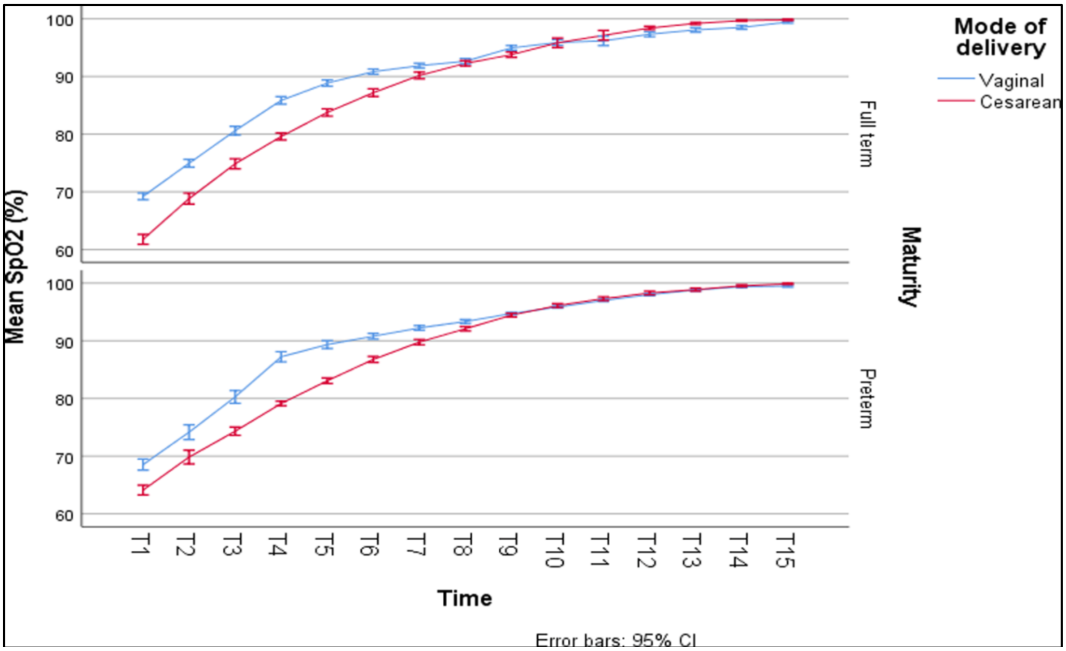

Figure 4. Change in SpO_2 over time by mode of delivery in full term and late preterm babies. Time points: T1 = 2 minutes, T2 = 3 minutes, T3 = 4 minutes, T4 = 5 minutes, T5 = 6 minutes, T6 = 7 minutes, T7 = 8 minutes, T8 = 9 minutes, T9 = 10 minutes, T10 = 11 minutes, T11 = 12 minutes, T12 = 13 minutes, T13 = 14 minutes, T14 = 15 minutes, T15 = 60 minutes

Regarding mode of delivery; O2 saturation is higher in FT VD group when compared to FT CS group over the first hour of life (p value <0.001 and 0.002 respectively). O2 saturation is higher in Late PT VD group than Late PT CS group at minute 2, 5 and 60 (P value >0.001,>0.001 and 0.001 respectively). Regarding gestational age; Oxygen saturation is lower in full term babies compared to late preterm babies delivered vaginally at minutes 5 and 15 of life (P 0.004 and <0.001 respectively).O2 saturation is higher in Late PT CS when compared to FT CS group group (p <0.001 and 0.01) at minutes 2 and 10 of life.

Discussion

Fetal transition from intrauterine to the extrauterine environment with the major rerouting of fetal hemodynamics could be the most significant and dramatic human adaptation to change. It occurs within the first few breaths of postnatal life (Wu et al., 2016). Until now, published haemodynamic changes during neonatal transition included a rise in HR, a decrease in pulmonary vascular resistance (PVR), and an increase in pulmonary blood flow (PBF) after onset of lung aeration (Freidl et al., 2017).

Hemodynamic assessment is essential for both diagnosis and management of critically ill newborns (Hsu et al., 2016). Electrical cardiometry (EC) has been proposed as a safe, accurate and continous technique for hemodynamic measurement in children and infants (de Boode, 2010). In the present study we used EC to measure hemodynamic changes that occur during transition. The current study is a pilot study using EC to detect hemodynamic changes during transition, involving newborns with different mode of delivery and comparing between them. Our data represent normative values of PEP, TFC, SVV and oxygen saturation during first hour of life.

In the present study we found mean SpO2 at 10 min after birth in NVD was 94.96±1.44 and 93.78±1.62 <0.001, while Bhargava et al. (2018), illustrated in their study that ; Mean SpO2 at 10 min after birth in NVD was 91.8% (±5.1) and 89.9% (±4.48) in CS (P = 0.005) respectively. In the current study; O2 saturation for included newborns delivered vaginally is higher than those delivered by CS over time, this agreed with Bhargava et al. (2018), studied babies born by normal vaginal delivery had significantly higher SpO2 levels and attained SpO2 >90% faster than those born by elective CS as it has been speculated that in vaginally delivered neonates, the catecholamine surge is significantly higher compared to neonates delivered by CS, which may be the reason for higher levels of SpO2 after vaginal delivery.

Our study revealed Oxygen saturation increases significantly over time (P values <0.001) in all studied neonates over the first 15 minutes of life. In all involved population, oxygen saturation reaches > 93% by minute 10 after birth this agrees with Anderson (2012), who described that oxygen saturation reaches 85-95 % by 10 minutes after birth accrording to NRP resuscitation program. Thoracic fluid content is defined as the electrical conductivity of the chest cavity, which is primarily determined by the intravascular, intra-alveolar, and interstitial fluids in the thorax.

The main pathophysiological feature of transient tachypnoea of the neonate (TTN) is delayed lung fluid re-absorption during the foetal life transition and this creates a mainly interstitial, ab extrinseco lung oedema (Riamondi et al., 2021). Consistently, Copetti & Cattarossi (2007), showed that neonates with TTN have both interstitial oedema (represented by B-lines), and normal areas (represented by A-lines).

In the present study TFC for Late PT VD group and FT VD group is 49.36±9.59 and 49.24±16.76 successively, while Hsu et al. study (2016) showed that in neonates with GA (35 to 36 weeks), (37 to 38 weeks) and (39 to 41 weeks) TFC is 27.7±6.1, 27.8±5.1 and 27±5.5 successively. Higher values in the present study can be explained as Hsu et al. detected TFC at age 72 to 96 hours post natal, while we finished the measurement at age of one hour after birth, as TFC decreases over time.

Raimondi et al. (2021), used lung ultrasound found that substantial liquid retention has been demonstrated in 14% of healthy neonates, while 49%, 78% and 100% of neonates had completed airway liquid clearance at 2, 4 and 24 h, respectively. In the present study, thoracic fluid content decreases between minute 2 and minute 60 of life (P value 0.036) in late preterm CS group, while no significant difference is observed in TFC in the other 3 groups in the first hour of life.

TFC is higher in CS when compared to VD group (P value >0.001 and 0.003 respectively) for all studied neonates over the first hour of life, this agreed with Blank et al. (2018), who described that neonates born by an elective caesarean section have higher fluid retention early after birth than those vaginally delivered using lung ultrasound. In the current study; Full Term CS group has significantly higher values than PT CS group at minute 10 of life (p value 0.031). In our study Stroke volume variation decreases over the first hour of life in all studied neonates.

In the present study; SVV Mean value for Late PT VD and FT VD group is 11.92±3.34 and 12.50±3.30 successively, in Hsu et al. (2016), study they found that SVV varied greatly in their neonates; it ranged from 5.3 to 27, with a mean of 15.8 ± 4.4. Regarding mode of delivery; Full term vaginal delivery group has higher SVV than full term CS group with (p value <0.001) at minutes 2, 5 and 10 of life. On the contrary Late Preterm Vaginal Delivery group has lower measurements than Late Preterm CS group with p value (0.049 and <0.001 respectively) at minutes 10 and 60 of life.

Regarding gestational age; Full Term VD group has higher SVV than Late PT VD group with significant p value (0.007, 0.005 and 0.038) at minute 2, 5 and 10 of life respectively. Late preterm CS delivery group has higher measurements than full term CS group with significant p value (0.002, <0.001, <0.001 and 0.011 respectively) at minutes 5, 10, 15 and 60 of life.

Conclusion

- Electrical cardiometry (EC) is a thoracic impedance-based device and an interesting point-of-care technique that monitor blood flow parameters in full-term and late preterm neonates which will help to give a guidance for proper diagnosis and management of neonatal cardiovascular disorders during transition.
- The present data represents normative values for PEP, TFC, O2 saturation and SVV in healthy term infants after caesarean section.
- Oxygen saturation increases over time (P values <0.001) in all groups over the first 15 minutes of life.
- TFC is higher in CS when compared to VD group (P value >0.001 and 0.003 respectively) for both full term and late preterm neonates over the first hour of life.

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