EFFECT OF DECREASED SUPERIOR VENA CAVA FLOW ON VERY LOW BIRTH-WEIGHT INFANT

By

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ABSTRACT

Background: *The increasing knowledge of neonatal hemodynamics and the resultant increased understanding concerning the changing physiology of the neonate's cardiovascular system has been driven primarily by neonatologists,*

Aim and objectives: *To assess the relationship between SVC flow and velocity with adverse outcome in very low birth weight (VLBW) infants.*

Subjects and methods: *This is prospective, case control study where the patients were recruited from the neonatal intensive care unit (NICU), Al-Azhar university hospitals. 2021. The study included two groups of newly born infants: The case group: is composed of 40 very low birth weight infants. The control group is composed of 20 normal birth weight infants, Result; there was significant relation between SVC flow in day 1,7,14 and on discharge and occurrence of interventricular hemorrhage but as regard SVC velocity there was significant relation only in day 1, 7.*

Conclusion: *SVC flow is important for assessment of hemodynamic status in low-birth-weight neonates.*

Keywords: *SVC flow, interventricular hemorrhage, VLBW infant.*

INTRODUCTION

The diagnosis and management of circulatory compromise in the very low birth weight infant remains controversial **(Seri, 2001)**.

Many practitioners continue to rely on absolute blood pressure values to guide intervention **(Dempsey and Barrington, 2006)**.

This is an inaccurate approach as evidenced by the large number of ''normative'' blood pressure ranges, the marked variation in the incidence of hypotension **(Al-**

Aweel et al., 2001), and the even greater variation in those receiving treatment **(Laughon et al., 2007)**.

End-organ perfusion is determined by a combination of perfusion pressure and vascular resistance, and reliance on absolute blood pressure values may result in inappropriate therapeutic intervention. More reliable methods of detecting end-organ blood flow would help identify patients for whom intervention may be appropriate. Clinical evaluation at the bedside might provide more information than absolute blood pressure values alone. Concerns surrounding clinical assessment include lack of objectivity, relative importance or lack of individual parameters assessed, lack of normative values and their reproducibility.

It was previously shown that the inclusion of clinical parameters and blood pressure values in the management of hypotension reduced the number of infants treated with volume expanders, inotropes and corticosteroids, and resulted in a similar short-term outcome **(Dempsey et al., 2005)**.

It has recently been used to measure superior vena cava blood (SVC) flow, of which approximately 80% is estimated to be venous return from the brain. The SVC fulfils the criteria for Doppler assessment, and a normal range has been produced and the technique has been shown to be reproducible. SVC blood flow has been previously associated with adverse short-term outcome **(Kluckow et al., 2000)**.

The aim of study: To assess the relationship between SVC flow and velocity with adverse outcome in very low birth weight (VLBW) infants.

PATIENTS AND METHODS

This prospective, case control study that was conducted in neonatal intensive care unit (NICU), Al-Azhar university hospitals from September 2020 to April 2021.

The study included two groups of newly born infants: The case group: is composed of 40 very low birth weight infants. The control group: is composed of 20 normal birth weight infants.

Sample Size: This study base on study carried out by Cerbo et al., 2015 Epi Info STATCALC was used to calculate the sample size by considering the following assumptions: - 95% two-sided confidence level, with a power of 80%. & an error of 5% odds ratio calculated. The final maximum sample size taken from the Epi-Info output was 66. Thus, the sample size was increased to 70 subjects to assume any drop out cases during follow up.

Method of selection: by simple random method.

Ethical considerations: An informed consent taken from all parents before getting involved in study. Confidentiality of all data ensured. The parents have the right to withdraw from the study at any time without giving any reasons. The study was done after approval of ethical committees of Pediatrics department & faculty of medicine for Al-Azhar University. The author declared that there is no conflict of interest or financial support regarding to study and publication.

Inclusion Criteria: Very low birth weight (<1500 g) in the first day of life.

Exclusion Criteria: Newborns with lethal congenital heart disease (except patent ductus arteriosus, non-complicated atrial septal defect and no complicated muscular ventricular septal defect (VSD)), major congenital malformations will be excluded by echocardiography and IDM, meconium aspiration, diaphragmatic hernia, bleeding tendency and thrombcytopenia.

Study method:

All neonates included in the study were subjected to the following:

History taking: including (mode of delivery, gestational age, sex, admission diagnosis, prenatal history, natal history, postnatal history, family history, maternal history).

General examination of the neonate including: Measurements (length, weight, head, abdominal and chest circumference), vital signs (heart rate, respiratory rate, temperature and blood pressure), general condition and activity and neonatal reflexes (Moro and Suckling) and any evidence of bleeding disorders e.g petechiae and he.

Systemic examination: (chest, heart, abdominal, CNS).

Ultrasound Doppler examination of the neonate: All the neonates were underwent echocardiography on day 1 together with cranial ultrasonography which was repeated on day 1, 7 and day 14 of life and before discharge. The Doppler examinations were performed by a single radiologist on MyLab50 esaote ultrasonography with color Doppler ultrasound machine with curvilinear (3.5-5 MHz for ICA and MCA) and high frequency linear (7.5 MHz for VA) array transducer. PSV, EDV, PI and RI were calculated as per formulae of the ultrasound blood flow imaging technique. The examination was carried out through the anterior fontanelle in the coronal plane. The circle of Willis was located and the ICA and MCA were identified. The vertebral artery was assessed through either side of the neck of the neonate.

SVC Diameter assessment:

SVC diameter was assessed from a high parasternal long axis view by echocardography, rotated towards the true sagittal plane. The transducer head was placed as close to the midline as possible to acquire directly anteroposterior views of the SVC. Maximum and minimum SVC diameters were assessed for each cardiac cycle, and the mean of these used to quantify volume of flow.

SVC Flow assessment:

The SVC flow was calculated using the following formula: SVC flow = (velocity time integral × (π × (mean SVC diameter2/4) × heart rate)/body weight.

Statistical analysis of the data: Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Shapiro-Wilk test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

RESULTS

Table (1): Comparison between the two studied groups regarding to demographic data

	Cases (n = 40)		Control (n = 20)		Test of Sig.	P
	No.	%	No.	%		
Gender						
Male	15	37.5	5	25.0	χ^2= 0.938	0.333
Female	25	62.5	15	75.0		
Gestational age\wk						
Min. – Max.	34.0 – 37.0		38.0 – 40.0		t= 12.431*	<0.001*
Mean ± SD.	35.90 ± 0.96		38.95 ± 0.76			
Median (IQR)	36.0 (35.0 – 37.0)		39.0 (38.0 – 39.50)			
Postnatal age\(hr)						
Min. – Max.	4.50 – 12.0		5.0 – 12.0		U= 363.0	0.553
Mean ± SD.	6.58 ± 2.18		7.55 ± 3.02			
Median (IQR)	6.0 (5.50 – 6.50)		6.0 (5.50 – 12.0)			
Birth weight\(gm)						
Min. – Max.	890.0 – 1500.0		3000.0 – 3400.0		t= 42.143*	<0.001*
Mean ± SD.	1204.3 ± 177.8		3242.5 ± 174.2			
Median (IQR)	1225.0 (1050.0 – 1325.0)		3250.0 (3000.0 – 3400.0)			

IQR: Inter quartile range, SD: Standard deviation, χ2: Chi square test
U: Mann Whitney test, t: Student t-test

There were insignificant differences between cases and control as regard gender and age at scan but as regard gestational age, birth weight there was significant lower in gestational age and birth weight of cases versus control.

Table (2): Comparison between the two studied groups regarding to SVC flow

SVC flow (ml/kg/min)	Cases	Control	t	p
Day1	**(n = 40)**	**(n = 20)**		
Min. – Max.	43.0 – 78.0	89.0 – 115.0	11.740*	<0.001*
Mean ± SD.	65.30 ± 10.48	98.65 ± 10.15		
Median (IQR)	66.0 (60.0 – 76.0)	96.0 (89.0 – 105.5)		
Day 7	**(n = 36)**	**(n = 20)**		
Min. – Max.	54.0 – 80.0	99.0 – 120.0	17.122*	<0.001*
Mean ± SD.	71.92 ± 7.71	109.20 ± 7.99		
Median (IQR)	75.0 (70.0 – 77.0)	110.0 (99.0 – 115.0)		
Day 14	**(n = 33)**	**(n = 20)**		
Min. – Max.	75.0 – 86.0	113.0 – 125.0	33.430*	<0.001*
Mean ± SD.	81.48 ± 3.29	117.80 ± 4.61		
Median (IQR)	80.0 (80.0 – 85.0)	117.0 (113.0 – 121.0)		
On discharge	**(n = 33)**	**(n = 20)**		
Min. – Max.	85.0 – 90.0	110.0 – 125.0	20.998*	<0.001*
Mean ± SD.	87.27 ± 1.77	115.55 ± 5.86		
Median (IQR)	87.0 (86.0 – 89.0)	114.0 (110.0 – 119.5)		

IQR: Inter quartile range, SD: Standard deviation, t: Student t-test

This table shows that SVC flow was significant lower in cases than control with p-value <0.001.

Table (3): Comparison between the two studied groups regarding to to mean SVC diameter

Mean SVC diameter	Cases	Control	T	P
Day1	**(n = 40)**	**(n = 20)**		
Min. – Max.	2.0 – 4.0	4.90 – 5.40	18.212^{*}	$<0.001^{*}$
Mean ± SD.	3.17 ± 0.64	5.23 ± 0.22		
Median (IQR)	3.40 (2.75 – 3.50)	5.30 (4.90 – 5.40)		
Day 7	**(n = 36)**	**(n = 20)**		
Min. – Max.	2.40 – 4.10	5.40 – 6.40	17.321^{*}	$<0.001^{*}$
Mean ± SD.	3.42 ± 0.52	5.74 ± 0.40		
Median (IQR)	3.45 (3.34 – 3.70)	5.60 (5.40 – 6.0)		
Day 14	**(n = 33)**	**(n = 20)**		
Min. – Max.	2.50 – 4.20	5.70 – 6.60	23.029^{*}	$<0.001^{*}$
Mean ± SD.	3.55 ± 0.43	6.15 ± 0.34		
Median (IQR)	3.50 (3.50 – 3.80)	6.20 (5.70 – 6.40)		
On discharge	**(n = 33)**	**(n = 20)**		
Min. – Max.	3.0 – 4.30	5.70 – 6.70	24.440^{*}	$<0.001^{*}$
Mean ± SD.	3.69 ± 0.35	6.31 ± 0.42		
Median (IQR)	3.60 (3.60 – 4.0)	6.50 (5.70 – 6.60)		

IQR: Inter quartile range, SD: Standard deviation, t: Student t-test

Regarding to Mean SVC diameter there was significant lower in cases in 1st day ,7th day, 14th day and on discharge than control with p-value <0.001.

Table (4): Comparison between the two studied groups regarding to Interventricular haemorrhage and Neonatal death

	Cases (n = 40)		Control (n = 20)		X^2	P
	No.	**%**	**No.**	**%**		
Interventricular haemorrhage						
No	22	55.0	20	100.0	12.857^{*}	$<0.001^{*}$
IVH	18	45.0	0	0.0		
Neonatal death						
No	33	82.5	20	100.0	3.962	$^{FE}p=$ 0.084
Died	7	17.5	0	0.0		

χ^2: Chi square test, FE: Fisher Exact, p: p value for comparing between the studied groups

interventricular haemorrhage founded in 18 cases (45%) with neonatal mortality 17.5% in comparison to control no interventricular haemorrhage nor deaths occurred.

Table (5): Relation between interventricular haemorrhage with SVC flow

	Interventricular hemorrhage		Test of Sig.	P
	No (n = 22)	IVH (n = 18)		
Day1				
Min. – Max.	65.0 – 78.0	43.0 – 70.0	t= 5.682*	<0.001*
Mean ± SD.	71.82 ± 5.53	57.33 ± 9.59		
Median	76.0	56.0		
Day 7				
Min. – Max.	70.0 – 80.0	54.0 – 75.0	t= 4.552*	<0.001*
Mean ± SD.	76.0 ± 3.63	65.50 ± 8.13		
Median	77.0	70.0		
Day 14				
Min. – Max.	80.0 – 86.0	75.0 – 80.0	t= 4.669*	<0.001*
Mean ± SD.	82.91 ± 2.74	78.64 ± 2.34		
Median	85.0	80.0		
On discharge				
Min. – Max.	87.0 – 90.0	85.0 – 86.0	t= 10.006*	<0.001*
Mean ± SD.	88.27 ± 1.24	85.27 ± 0.47		
Median	89.0	85.0		

This table shows significant relation between SVC flow in day 1, 7, 14 and on discharge and occurrence of interventricular hemorrhage.

Table (6): Relation between interventricular hemorrhage with SVC velocity time

	Interventricular hemorrhage		Test of Sig.	P
	No (n = 22)	IVH (n = 18)		
Day1				
Min. – Max.	0.09 – 0.98	0.05 – 0.12	U= 76.0*	0.001*
Mean ± SD.	0.31 ± 0.37	0.08 ± 0.03		
Median	0.11	0.06		
Day 7				
Min. – Max.	0.10 – 0.99	0.05 – 0.13	U= 39.500*	<0.001*
Mean ± SD.	0.32 ± 0.37	0.09 ± 0.03		
Median	0.14	0.10		
Day 14				
Min. – Max.	0.10 – 0.15	0.08 – 0.14	U= 73.500	0.069
Mean ± SD.	0.13 ± 0.02	0.11 ± 0.02		
Median	0.14	0.12		
On discharge				
Min. – Max.	0.13 – 0.15	0.10 – 0.16	U= 96.0	0.355
Mean ± SD.	0.14 ± 0.01	0.14 ± 0.03		
Median	0.15	0.15		

This table shows that significant relation between SVC velocity and occurrence of interventricular hemorrhage only in day 1, 7.

DISCUSSION

The increasing knowledge of neonatal hemodynamics and the resultant increased understanding concerning the changing physiology of the neonate's cardiovascular system has been driven primarily by neonatologists. Indirect measures for assessment of tissue perfusion, including urine output and serum lactate levels, are especially problematic with the very early preterm neonate in the first postnatal days when complex hemodynamic changes occur during the transition to postnatal life **(McNamara & Lai, 2020)**.

The role of functional echocardiography in neonatal intensive care unit is rapidly evolving, and increasingly neonatologists are using it in making clinical decisions in sick infants. Functional echocardiography can provide a direct assessment of hemodynamics on bedside, and may be considered as an extension of the clinical examination to evaluate cardiovascular wellbeing in the critically-ill infant **(Hébert et al., 2019)**.

The main aim of this study was to assess the relationship between follow up of SVC flow at 1, 7, 14 day and adverse outcome in very low birth weight (VLBW) infants.

In This prospective, case control study our patients were recruited from the neonatal intensive care unit (NICU), Al-Azhar university hospitals. From September 2020 to April 2021. The study included two groups of newly born infants: The case group: is composed of 40 very low birth weight infants. The control group is composed of 20 normal birth weight infants.

There were insignificant differences between cases and control as regard gender and post natal age there was difference between cases and control. Regarding Apgar score 1 min and 5 min there was significant lower score in cases than control p-value <0.001.

While in the study of Hassan **Saad et al., 2019**, there was significant decrease in gestational age, Apgar score, weight and length of preterm and low birth weight groups, compared to control group.

Also **Soni et al., 2021**, median gestational ages of late preterm and term group were 35 weeks and 39 weeks respectively. Median birth weight of preterm group was 1900gm and for term group it was 3000 gm with statistically significant decrease between them.

The present study showed that regarding SVC flow there was significant lower measurements in cases in 1st day, 7th day, 14th day and on discharge than control with p-value <0.001. Regarding SVC velocity time there was significant lower in cases in 1st day, 7th day, 14th day and on discharge than control with p-value <0.001. Regarding Mean SVC diameter there was significant lower in cases in 1st day, 7th day, 14th day and on discharge than control with p-value <0.001.

Our results were supported by the study of **Hassan Saad et al., 2019** as they found that SVC flow was significantly decreasing in preterm and low birth weight groups in comparison with full term group.

This in agree with **Hunt et al., 2004** who found that low superior vena cava flow is common in the first hours after preterm birth. They said that it has a strong association with subsequent periventricular/ intraventricular hemorrhage.

Groves et al., 2007 stated that wide range of flow volumes (40–

193 ml/kg/min) means that quantification of SVC flow volume may be a relatively sensitive technique for detecting hemodynamic change in the clinical setting. These measurements are mostly taken at the first 48 hrs of life.

Severe intraventricular hemorrhage (IVH) in the premature infant is an acquired lesion with a potentially enormous impact on morbidity, mortality and long-term neurodevelopmental outcome.

The present study showed that interventricular hemorrhage found in 18 cases (45%) with neonatal mortality 17.5% in comparison to control neither interventricular nor deaths occurred.

Kluckow & Evans, 2000 demonstrated that early IVH was already present in 9 babies at 5 hours of age. Normal SVC flows were seen in these babies except in 3 with IVH, which later extended, who all had SVC flow below the normal range at 5 and/or 12 hours.

Our results showed that there was significant relation between SVC flow in day 1, 7, 14 and on discharge and occurrence of interventricular hemorrhage but as regard SVC velocity there was significant relation only in day 1, 7.

However, in the study of **Miletin and Dempsey, 2008**, there was a poor correlation between SVC flow and left and right ventricular output. Incidence of patent ductus arteriosus at the time of echocardiography was 100% in the low SVC flow group and 83% in the normal SVC flow group (p = 0.56).

According to **Kluckow & Evans, 2000**, IVH was first seen after the SVC flow had improved, and the grade of IVH related significantly to the severity and duration of low SVC flow.

CONCLUSION

SVC flow is important for assessment of hemodynamic status in low-birth-weight neonates. There was significant relation between SVC flow in day 1,7,14 and on discharge and occurrence of interventricular hemorrhage but as regard SVC velocity there was significant relation only in day 1, 7.

Limitations of study:

- Difficulties of exclusion of multiple factors causing inter ventricular hemorrhage.
- V.L.B.W infant mortality.

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