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Determination of the Prevalence of Patent Ductus Arteriosus in Infants with Very Low Birth Weight Admitted in Hospital during 2011-2016

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Abstract

Introduction: The ductus arteriosus is one of the most common cardiac anomalies in premature neonates. Understanding its dimensions among high-risk groups such as infants with very low birth weight (VLBW) can be helpful in preventing and timely treatment.

Methods: This study was conducted to determine the prevalence of patent ductus arteriosus (PDA) in VLBW infants in Shahid Akbar Abadi Hospital during the years of 2011-2016. In this observational and cross-sectional study, 286 extremely low birthweight (ELBW) infants (<1000 gr) were selected by census and the incidence of ductus arteriosuswas determined via echocardiography by a pediatric cardiologist.

Results: In the present study, the mean (SD) of the gestational age, birth weight, Apgar score were determined to be 27.27 ± 0.15 weeks, 835.20 ± 42.6 and 5.31 ± 0.13, respectively. Based on the data presented herein, 57.70% of the neonates were found to be female. Our findings indicated that 95.9% of the LBW infants showed PDA, of which 14% exhibited spontaneous closure. The ductus arteriosus was closed spontaneously in 14% of patients, and small, moderate and large PDA were observed in 34.25%, 3.5% and 4.15%, respectively.

Conclusion: Our results showed that there was a significant relationship between the PDA with sepsis (P=0.032) andsmall PDA was more common in sepsis cases. Furthermore, the mean score of Apgar score was found to be significantly different (P=0.001), when severe cases were observed to be higher in neonates with lower Apgar score. Taken together, our results revealed that PDA is present in more than half of the infants with VLBW.

Keywords: Prevalence; Patent ductus arteriosus; Very low birth weight

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Introduction

The ductus arteriosus is a fetal vascular connection between the pulmonary artery and the aorta which transmit blood from the pulmonary artery to the systemic circulation during the fetal period. The duct contracts and usually closes up to 72 hours after birth. If this contraction does not occur after birth, the ductus arteriosus will remains patent, which result in patent ductus arteriosus (PDA), leading to inappropriate blood transmission between the aorta and the pulmonary artery [1,2].

Usually, this contraction causes the functional closure of the ductus arteriosus within 10 to 15 hours after birth that starts from the pulmonary artery and ultimately progresses to the aortic end. Such changes do not occur in patent ductus arteriosus, which indicates the presence of specific anatomical differences in the ductus arteriosus tissue [3]

Very low birth weight (VLBW) is considered as a term to define babies who are less than 1500 grams. Approximately 1% of infants are VLBW, but they account for 50% of infant mortality. VLBW infants face a 200-fold risk of death compared with other infants [4]. The incidence of PDA is inversely associated with gestational age. A large PDA with a left to right shunt in the VLBW infant can cause pulmonary edema, congestive heart failure (CHF), pulmonary hemorrhage, and an increased risk of pulmonary dysplasia [5].

Drug therapy with indomethacin or ibuprofen is successful in 75-80% of newborns, but also has an adverse effect on neonates, such as gastrointestinal bleeding, perforation, and necrotizing enterocolitis [6].

Studies have shown that the incidence of congenital heart defects is about 1 in 200 births in normal populations. Recent statistics indicate that the incidence of congenital heart defects is 12 to 14 per 1,000 live births. PDA as a single congenital defect in neonates is estimated to account for 5-10% of all congenital heart defects [7]. A study indicated that clinical symptoms alone were not sufficient to detect PDA. In addition, routine echocardiography was necessary for early detection

of PDA in premature babies in the first few days after birth [8]. Another studyreported that the ductus arteriosus is closed spontaneously at the beginning of the infancy in most of the newborns with VLBW and PDA [9]. Another study looked at the extent of the spontaneous closure of the ductus arteriosus in the VLBW neonates in an observational and prospective manner in which ductus arteriosus was closed in 49% of the newborns on day 7, based on echocardiographic findings [10]. There is no detailed data on the association between PDA and VLBW in Iran and the need for accurate diagnostic procedures seems to be necessary for proper treatment with regard to various supportive, pharmaceutical and surgical treatments.

The study of companion (VLBW) and PDA in Iran's largest referral centers (Iranian maternity hospitals) can be the basis for further studies in favor of appropriate treatment and reduction of the mortality rate in these infants. Therefore, in this study, the prevalence of PDA was evaluated in VLBW infants admitted to Shahid Akbar Abadi Hospital in 2011-2016.

Materials and Methods

In this observational and cross-sectional study, the data were collected from medical records of 286 VLBW neonates (<1000 grams) admitted to the NICU of Shahid Akbar Abadi Hospital during the years 2011 to 2016. In the present study, a checklist was used in which variables such as gender (boy, girl), gestational age (week), birth weight (g), neonate Apgar score, need for respiration (requiring auxiliary ventilation; positive, negative) Cardiac anomalies (positive, negative), sepsis (positive, negative), PDA (neg, closing, small, medium, large), treatment (positive, negative) and response to treatment (positive, negative) were recorded. Echo was performed by a skilled pediatric cardiologist after the first 48 hours of birth and before 72 hours in all extremely low birth weight (ELBW) infants.

If there were indications (hemodynamic instability, oxygen dependence and large PDA), the infant with open ductus arteriosus was treated with ibuprofen for 3 days at a dose of 10 mg/kg and then 5 mg/kg for the next two doses at intervals of 24 hours. After the end of the treatment period, the echocardiographywas performed again, if the PDA still remained, a re-treatment course with ibuprofen was performed. In the absence of treatment indication, the baby was re-echoed for 7 days. In the absence of treatment indication, the echo was repeated for the baby at 7 days of age.

In the presence of contraindications for the use of ibuprofen, the baby was excluded from the study Contraindications include: internal bleeding such as gastrointestinal or pulmonary hemorrhage or IVH grade 3 and 4, platelets less than 50,000, creatinine above 1.2, or jaundice close to or near the exchange transfusion based on the Bhutani curve. In addition, diagnosis of sepsis in the newborn was performed based on positive blood culture.

Inclusion criteria included;all infants less than 1000 gr who were admitted to Shahid Akbar Abadi hospital during 2011-2012.

Exclusion criteria included contraindication of ibuprofen administration, incidence of complications such as gastrointestinal bleeding, abdominal distension, necrotizing enterocolitis during study, infant death for any reason during the study.

In this research, ethicalprinciples were fully followed, first the ethical codewas taken from the Ethics Committee and the information extracted from the cases remained confidential.

ANOVA and Chi-square analyses were conducted using the statistical software SPSS for Windows, version 13.0 with a significance level of 0.05.

Results

In the present study, the mean (SD) of the gestational age, birth weight, Apgar score were determined to be 27.27 ± 0.15 weeks, 835.20 ± 42.6 and 5.31 ± 0.13, respectively. Frequency distribution and frequency of qualitative variables are shown in Table 1.

As indicated in the Table 1, 57.70% of the neonates were female, most neonates (93.40%) needed respiration, and heart anomalies were detected in most neonates (82.20%), and sepsis was negative in most neonates (92%). Most neonates (44.10%) did not show PDA, while the lowest PDA frequency was reported in neonates (3.50%). In addition, 22 neonates needed treatment, of which 12 responded to ibuprofen therapy, but 10 did not respond to treatment (Table 2).

The relationship between PDA in neonates based on qualitative variables is presented in Table 2. The results show that PDA frequency distribution was significantly different in neonates (P=0.032), which small PDA was more positive in cases of sepsis.

The relationship between PDA in neonates based on gestational age (week), birth weight (g), and neonatal Apgar score are shown in Table 3. Our findings demonstrated that PDA frequency distribution was not significantly different in terms of gestational age and birth weight (P>0.05), but the mean score of Apgar score was found to be significantly different (P=0.001), whensevere cases were found to be higher in neonates with lower Apgar score.

Discussion

Ductus arteriosus closurehas been indicated to be often delayed in preterm infants, which incidence of patency at less than 30 weeks has been reported to be up to 60% [11]. PDA has been defined to be liked to an increase in the mortality of premature neonates, however, the causal correlationof these adverse situation has not been appropriately documented. The PDA may be merely considered as an intermediate stage of hemodynamic changes during the first weeks of life of the infant [12-14].

In the current study, the prevalence of PDA in newborns with

Table 1. General population characteristics and demographic data.

percentage	Study Patients	Characteristic	
42.3	121	**Boy**	**sex**
57.7	165	Girl	
93.4	276	Positive	Need to breathe in newborns requiring auxiliary ventilation with ventilator
6.6	19	Negative	
17.8	51	Positive	Cardiac anomalies
82.2	235	Negative	
8	23	Positive	Sepsis based on positive blood culture
92	263	Negative	
44.1	126	Negative	PDA in neonatal
14	40	Closing	
34.3	98	Small	
3.5	10	Medium	
4.2	12	Large	
7.7	22	Positive	Neonatal treatment
92.3	264	Negative	
54.5	12	Positive	Response to treatment in newborns
45.5	10	Negative	

Table 2. Relationship between PDA in neonates and other qualitative variables.

	Number (present)						
p-value*	**Large**	**Medium**	**Small**	**Closing**	**Negative**		
0.12	4(3.30)	4(3.30)	44(36.40)	18(14.90)	51(42.10)	**Boy**	**Sex**
	8(4.80)	6(3.60)	54(32.70)	22(13.30)	75(45.50)	Girl	
0.23	10(3.70)	10(3.70)	94(35.20)	39(14.60)	144(42.70)	Positive	Newborn breathing
	2(10.50)	0	4(21.10)	1(5.30)	12(63.20)	Negative	
0.098	2(3.90)	2(3.90)	23(45.10)	8(15.70)	16(31.40)	Positive	Neonatal cardiac anomalies
	10(4.30)	8(3.40)	75(31.90)	32(13.60)	110(46.80)	Negative	
0.032	0	2(8.70)	13(56.50)	0	8(34.80)	Positive	Sepsis in Neonates
	12(460)	8(3.00)	85(32.30)	40(15.20)	118(44.90)	Negative	

Table 3. Relationship between PDA in neonates based on gestational age (week), birth weight (g) and neonatal Apgar score.

p-value*	**Large**	**Medium**	**Small**	**Closing**	**Negative**	
	Sd±Mean					
0.13	2.38±27.75	1.16±26.70	2.30±27.21	1.48±27.15	2.88±27.35	Pregnancy age (week)
0.17	73.19±858.33	136.36±830.00	108.96±832.76	110.26±850.70	109.04±830.40	Birth weight (g)
0.001	1.97±3.67	2.17±4.40	2.33±5.06	2.11±5.05	1.87±5.82	Apgar neonates

VLBW was investigated in Shahid Akbar Abadi Hospital during 2011-2016. In this study, 55.9% of the infants with ELBW showed PDA. The ductus arteriosus was closed spontaneously in 14% of them, and small, moderate and large PDA were observed in 34.25%, 3.5% and 4.15%, respectively. There was a significant relationship between the PDA and sepsis, where small PDAs were found to be more positive in case of sepsis. There was also a significant difference between PDA based on Apgar score when most cases were severe in infants with low Apgar score.

Radvar et al. (2014) examined the efficacy of clinical symptoms in detecting PDA in premature neonates in Iran. They reported that Clinical signs were not reliably capable of diagnosing PDA in premature neonates; therefore, routine echocardiography is needed in this regard. Furthermore, aforementioned study indicated that hyperdynamic precordium and worsening respiratory have been found to be attributing to high sensitivity at 48-72 h of life. Furthermore, in conjunction with echocardiography are valuable tools for early detection of PDA in premature infants [15].

Recent studies suggest that supportive care should be taken during the first week and be followed by selective anti-inflammatory drugs. Spontaneous closure of PDA has been reported in more than 40-60% of VLBW infants in 7 days [16]. In our study, 7.7% of newborns were treated and the response to treatment was observed in 54.5% of infants. In addition, only 14% of the PDA cases were closed spontaneously.

Current evidence indicates that management of PDA can be wide-ranging and controversial findings have been also recorded; these conditions may even represent a diverse approach in this regard [17]. The paucity of literatures in terms of supportive care of PDA has remained controversial in very premature infants [18-20].

Another study by Herrman et al. (2009) examined spontaneous closure of the PDA and treatment of PDA-associated statues in VLBW neonates with ductal patency. They stated that spontaneous closure has been reported in most VLBW neonates with PDA at initial neonatal unitdischarge [18].

A prospective observational study by Nemerofsky (2008) evaluated the rate of spontaneous closure of PDA in VLBW neonates with birth weight (BW) <1500 g, in which echocardiography were applied for neonates on day of life 3 and 7, once a week in the first month, and bimonthly until ligation, discharge, or death. The ductus arteriosus was found to be spontaneously closed in 49% infants at day 7 (67% in weight more than 1000 and 31% in weight less than 1000 g) [10]. In our study, the spontaneous closure of the ductus arteriosus was determined to be 14% in infants weighing less than 1000 g.

Conservative management of PDA has elevated for preterm imoenates, however, assessment of PDA treatment is currently controversial, leading to remarkable heterogeneity in clinical practice [14,21,22].

It has been demonstrated that 30% of preterm neonates born at <1000 g exhibited spontaneous ductus closure in the first week of life. Nevertheless, the long-term management and treatment of PDA has yet to be confirmed [14,23,24].

A study by Lee et al. (2014) aimed at determining the usefulness and safety of surgical ligation (after 15 days) in VLBW infants undergoing surgical correction for PDA for a 6-year period [25].

Early ligation for the treatment of PDA that failed treatment or contraindicated therapeutic drug may be desirable in reducing the incidence of necrotizing enterocolitis and reducing feeding intolerance in preterm neonates [25]. Of course, Based on the data presented herein, response to treatment was observed in 54.5% of newborns.

Taken together, our results revealed that PDA is present in more than half of the infants with VLBW. However, further development requires in-depth understanding of PDA and its therapeutic approaches through conducting comprehensive and multicenter trial by considering other intervening variables.

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References

1. Bordbar A, Mohagheghi P, Yoonesi L, Kalani M, Kashaki M, et al. (2018) Value of physical examination in the diagnosis of developmental hip dislocation in preterm infants. J Compr Ped 9: e14049.

2. Kashaki M, Mazouri A, Bordbar A, Saboute M, behnamfar Z, et al. (2018) Effect of protein supplementation on the growth of infants weighing less than 1,000 grams hospitalized on the neonatal intensive care unit of akbarabadi hospital in Tehran, Iran (2015-2016). Iranian J Neonatology 9: 49-56.

3. Fanaroff AA, Martin RJ (1987) Neonatal-perinatal medicine: diseases of the fetus and infant.

4. Abbott MB (2010) Nelson essentials of pediatrics. JAMA 304: 1724-1728.

5. Bancalari E, Claure N, Gonzalez A (2005) Patent ductus arteriosus and respiratory outcome in premature infants. Biol Neonate 88: 192-201.

6. Bhat R, Das UG (2015) Management of patent ductus arteriosus in premature infants. The Indian J Pediatr 82: 53-60.

7. Pees C, Obladen M (2005) Epidemiology of persisting ductus in preterm infants. Interventions for Persisting Ductus Arteriosus in the Preterm Infant: Springer 19-23.

8. Radvar M, Fakor Z, Aghayar MA, Gheibi S, Sadeghi E (2014) Values of clinical criteria compared with echocardiographic findings in diagnosing of pda in premature neonates. The J Urmia Uni Med Sc 25: 268-274.

9. Herrman K, Bose C, Lewis K, Laughon M (2008) Spontaneous closure of the patent ductus arteriosus in very low birth weight infants following discharge from the neonatal unit. Archives of Disease in Childhood-Fetal and Neonatal Edition.

10. Nemerofsky SL, Parravicini E, Bateman D, Kleinman C, Polin RA, et al. (2008) The ductus arteriosus rarely requires treatment in infants>1000 grams. American J Perinatol 25: 661-666.

11. Clyman RI, Couto J, Murphy GM (2012) Patent ductus arteriosus: are current neonatal treatment options better or worse than no treatment at all? Semin Perinatol 36: 123-129.

12. Perez KM, Laughon MM (2015) What is new for patent ductus arteriosus management in premature infants in 2015? Curr Opin Pediatr 27: 158-164.

13. EL-Khuffash A, Weisz DE, McNamara PJ (2016) Reflections of the changes in patent ductus arteriosus management during the last 10 years Arch Dis Child Fetal Neonatal Ed 101: 474-478.

14. Borras NC, Riverola A, Aldecoa BV, Izquierdo M, Domingo M, et al. (2018) Clinical outcomes after more conservative management of patent ductus arteriosus in preterm infants. J Pediatr (Rio J) 18: 30819-2.

15. Radvar M, Fakor Z, Aghayar MA, Gheibi S, Sadeghi E (2014) Values of clinical criteria compared with echocardiographic findings in diagnosing of pda in premature neonates. The J Urmia Uni Med Sc 25: 268-274.

16. Yurttutan S, Oncel MY, Arayıcı S, Uras N, Altug N, et al. (2013) A different first-choice drug in the medical management of patent ductus arteriosus: oral paracetamol. J Matern Fetal Neonatal Med 26: 825-827.

17. Edstedt Bonamy AK, Gudmundsdottir A, Maier RF, Toome L, Zeitlin J, et al. (2017) Collaborators from the EPICE research group, patent ductus arteriosus treatment in very preterm infants: a european population-based cohort study (EPICE) on variation and outcomes. Neonatology 111: 367-375.

18. Herrman K, Bose C, Lewis K, Laughon M (2009) Spontaneous closure of the patent ductus arteriosus in very low birth weight infants following discharge from the neonatal unit. Arch Dis Child Fetal Neonatal Ed 94: 48-50.

19. Vanhaesebrouck S, Zonnenberg I, Vandervoort P, Bruneel E, Van Hoestenberghe MR, et al. (2007) Conservative treatment for patent ductus arteriosus in the preterm. Arch Dis Child Fetal Neonatal Ed 92: 244-247.

20. Kaempf JW, Wu YX, Kaempf AJ, Kaempf AM, Wang L, et al. (2012) What happens when the patent ductus arteriosus is treated less aggressively in very low birth weight infants? J Perinatol 32: 344-348.

21. Mitra S, Florez ID, Tamayo ME, Mbuagbaw L, Vanniyasingam T, et al. (2018) Association of placebo, indomethacin, ibuprofen, and acetaminophen with closure of hemodynamically significant patent ductus arteriosus in preterm infants: a systematic review and meta-analysis. JAMA 319: 1221-1238.

22. Hagadorn JI, Brownell EA, Trzaski JM, Johnson KR, Lainwala S, et al. (2016) Trends and variation in management and outcomes of very low-birth-weight infants with patent ductus arteriosus. Pediatr Res 80: 785-792.

23. Semberova J, Miletin SJ, Kucera J, Berka I, Sebkova S (2017) Spontaneous closure of patent ductus arteriosus in infants ≤ 1500 g. Pediatrics 140: e20164258.

24. Benitz WE (2016) Committee on fetus and newborn, american academy of pediatrics. Patent ductus arteriosus in preterm infants Pediatrics 137: e20153730.

25. Lee JH, Ro SK, Lee HJ, Park HK, Chung WS, et al. (2014) Surgical ligation on significant patent ductus arteriosus in very low birth weight infants: comparison between early and late ligations. The Korean J Thoracic Cardiovas surg 47: 444.