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ORIGINAL ARTICLE

# Incidence of Spontaneous Closure of Patent Ductus Arteriosus in Preterm

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## ABSTRACT

**Background:**The ductus, an essential component of foetal circulation, normally closes within the first days of life. 5 However, in preterm infants, closure of the ductus arteriosus is frequently delayed or fails to eventuate. We aimed in this study to determine the frequency of spontaneous closure of PDA among preterm infants at Zagazig University Hospitals.

**Methods:** We performed this prospective study on 57 preterm neonates with patent ductus arteriosus admitted at NICU, Zagazig University Hospital.Routine laboratory investigations were done to all neonates.All PDAs were assessed by Echocardiography before 4$^{th}$ day of life and were followed up by once or twice echocardiography per week, the date of the echocardiogram was used as the ductal closure date when it was closed.

**Results:**Among the total cases (n=57), 19.30% experienced spontaneous PDA closure, while 80.70% had persistent DA.Initially, the mean PDA diameter was 1.84 ± 0.85 millimeters, with a median of 1.60 millimeters and a range from 1 to 5 millimeters. Upon follow-up, the mean PDA diameter decreased to 1.33 ± 1.03 millimeters, with a median of 1.10 millimeters and a range from 0 to 5 millimeters. This represents a closure percentage of 25.07%.There were highly statistically significant results between spontaneous PDA closure with gestational age and albumin. The results showed that duct closure increases with increased gestational age andhigh albumin level (p-value = 0.009, and 0.02 respectively).Persistent PDA was associated with a significant lower gestational age, p-value 0.012.

**Conclusions:**The rate of spontaneous PDA Closure in our study was 19.30%, so we concluded giving a chance for spontaneous closure of the duct.Factors associated with persistence of the duct opened included low gestational age and low albumin levels.

**Keywords:** Spontaneous Closure, Patent Ductus Arteriosus, Preterm

## INTRODUCTION

The Aorta and the pulmonary artery are connected by a continuous opening known as patent ductus arteriosus (PDA). As part of the typical fetal circulatory system, the opening (ductus arteriosus) often closes not long after birth. The leading cause of death in premature infants, patent ductus arteriosus is linked to an eight-fold rise in mortality rates as well as various detrimental long-term consequences such as bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC), intraventricular hemorrhage (IVH), and even death itself. Normal closure of the ductus, a critical component of fetal circulation, occurs within the first few days of life. A small PDA may not manifest any symptoms at all and remain undiagnosed for a long period, possibly until adulthood [1].Sweating when crying or eating, quick heart rate, easy fatigue, chronic fast breathing, and poor growth can all be symptoms of a big PDA. Fluid restriction, pharmacological intervention with paracetamol or non-steroidal anti-inflammatory medicines (NSAIDs), or surgical ligation or cardiac catheterization to close the duct are all potential treatments [2].There are dangers and adverse effects associated with each of these treatment choices for premature babies. As a result, the best way to handle PDA in premature babies is a topic of continuous debate around the globe. The paucity of comprehensive understanding on the pathophysiology of the ductus arteriosus in premature newborns adds complexity to this conversation[3].Because of the hypoxic fetal environment and prostaglandins E2 (PGE2) produced by the placenta, the ductus arteriosus needs to remain open intrauterine. The ductus arteriosus wall produces nitric oxide (NO), which further enhances vasodilatation. The ductus arteriosus often closes within hours of a full-term delivery [4].The ductus arteriosus, on the other hand, often stays open after a premature delivery. Reopening of the ductus arteriosus in premature newborns may occur as a result of infection or elevated inflammation even after functional closure of the ductus arteriosus has occurred, whether naturally or as a result of pharmaceutical therapy [5].Even though the placenta's high prostaglandin levels decrease after premature birth, the ductus arteriosus appears to be significantly more responsive to PGE2 and NO in premature newborns than term-born infants. Thus, spontaneous closure must be considered in any discussion on preterm infant PDA care, even though there is currently no comprehensive analysis of spontaneous closure rates [6].

So, we aimed at this study to determine the frequency of spontaneous closure of PDA among preterm infants at Zagazig University Hospitals.

## METHODS

We performed this prospective study on 57 preterm neonates with patent ductus arteriosus admitted at NICU of Pediatrics Department, Zagazig University Hospital from June 2023 to January 2024. Informed consent was obtained from all parents. The approval for performing the study was obtained from the pediatric departments of Zagazig University Hospitals after receiving **approval from the Institutional Review Board (#9348).** The study was done according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All Preterm neonates from both sexes who had confirmed patent ductus arteriosuswere included in this study. Cases with following criteria were excluded: Neonates with other cardiac or any blood disease, systemic disease, CNS or congenital problems.

All patients were subjected to **a full history** (age, sex, and Antenatal, Natal (mode of delivery), postnatal) and thorough **clinical assessment**: with a focus on vital data and all systems, to analyze Signs of prematurity (Abnormal breathing patterns (shallow, irregular pauses in breathing called as apnea, Soft, flexible ear cartilage, Body hair, Enlarged clitoris in female infants or Small scrotum that is smooth and has no ridges, and undescended testicles in male infants, Less body fat, Lower muscle tone and less activity than full-term infants, Problems feeding due to trouble sucking or coordinating swallowing and breathing, and Thin, smooth, shiny skin that is often transparent).Gestational age assessment was done by Ballard score [7].

Anthropometric measurements; weight, height, head circumference, BMI. Weight was measured by weighing scale and classified as follows: Low birth weight (LBW) neonates weigh less than 2500 g at birth. Very low birth weight (VLBW) neonates weigh less than 1500 g at birth. Extremely low birth weight (ELBW) neonates weigh less than 1000 g at birth [8].

**Chest examination:** for signs of respiratory distress; Grade 1: tachypnea (more than 60 breaths/mi) and nasal flaring, Grade 2: subcostal and intercostal retraction, Grade 3: grunting, Grade 4: cyanosis. Downes score was used to assess respiratory distress clinically and determine the need of oxygen supplementation [9].

**Laboratory investigations** included: All the laboratory tests were assessed only once, according to the routine lists of Zagazig University hospitals laboratories: complete blood count (CBC), blood group, blood glucose, liver functions, and kidney functions.**A complete echocardiographic assessment** was performed by staff of Pediatric cardiology using Philips device model HD5.the ductus arteriosus diameter was measured on the suprasternal view of the aorta at its narrowest part identified via color Doppler and measured on 2D.

**Echocardiography before day 4 of life.** All PDAs were assessed by Echocardiography before 4th day of life and were followed up by once or twice echocardiography per week, the date of the echocardiogram was used as the ductal closure date when it was closed.Examination was done till discharge.

**Causes of neonate intensive care unit (NICU) admission** included: Respiratory distress, Jaundice and Low birth weight. **Respiratory interventions** involved: Nasal oxygen, Incubator oxygen, Continuous positive airway pressure (CPAP), or mechanical Ventilation.

**Statistical Analysis:**

Excel 2010 (Microsoft Corporation, Redmond, WA, USA) and SPSS 27.0 (IBM Inc., Chicago, IL, USA) were used for data collection, tabulation, and statistical analysis. We displayed the mean ± standard deviation (SD) and median with range for continuous quantitative data, and frequencies and percentages for categorical qualitative variables. The continuous data was tested for normality using the Shapiro-Wilk test. When comparing two groups with normally distributed data, an independent T-test was employed. When dealing with data that did not follow a normal distribution, we used the Kruskal-Wallis H test for comparisons involving more than two groups and the Mann-Whitney U test for two groups. We used the Chi-square test for categorical data.

## RESULTS

The study consisted of 57 neonates, with 64.9% being male and 35.1% female. The mean gestational age was 35 weeks with a standard deviation of 1.44, and maternal age ranged from 32 to 37 years, with a mean of 35 years. Among the participants, 14% reported positive consanguinity, while 86% reported negative consanguinity. Cesarean section was the predominant mode of delivery, accounting for 82.5%, with vaginal delivery at 17.5%. Among 57 neonates, 15.8% did not require NICU admission. Respiratory distress was the most common cause, accounting for 47.4% of admissions. Jaundice was the reason for admission in 17.5% of cases, while a combination of respiratory distress and jaundice led to admission in 7.0% of cases. Additionally, 12.3% of admissions were due to low birth weight (Table 1).

**Table (1): Baseline characteristics of studied cases.**

| Variables | Cases (n=57) | |
|---|---|---|
| **Sex, n (%)** | Male | 37 (64.9) |
| | Female | 20 (35.1) |
| **Gestational age (wk)** | Mean ± SD | 35 ± 1.44 |
| | Median (range) | 35 (32-37) |
| **Residence, n (%)** | Rural | 27 (47.4) |
| | Urban | 30 (52.6) |
| **Consanguinity, n (%)** | Positive | 8 (14) |
| | Negative | 49 (86) |
| **Mode of delivery, n (%)** | Cesarean section | 47 (82.5) |

| Variables | Cases (n=57) | |
|---|---|---|
| | Vaginal | 10 (17.5) |
| **ABO, n (%)** | A+ | 12 (21.1) |
| | A- | 2 (3.5) |
| | B+ | 9 (15.8) |
| | B- | 4 (7) |
| | AB+ | 5 (8.8) |
| | O+ | 24 (42.1) |
| | O- | 1 (1.8) |
| **Weight at birth (gm)** | Mean ± SD | 2230.18 ± 218.24 |
| | Median (range) | 2200 (1850 – 2750) |
| **Causes of NICU admission** | | |
| **Causes** | **Number (n=57)** | **%** |
| **Not admitted** | 9 | 15.8 |
| **Respiratory distress** | 27 | 47.4 |
| **Jaundice** | 10 | 17.5 |
| **Respiratory distress and jaundice** | 4 | 7.0 |
| **Low birth weight** | 7 | 12.3 |

SD, standard deviation.

The mean Hb level was 11.12 ± 0.95 grams per deciliter. White blood cell count had a mean of 9.17 ± 2.75 thousand cells per microliter. The mean serum total bilirubin level was 0.38 ± 0.22 milligrams per deciliter. Serum direct bilirubin had a mean of 0.17 ± 0.12 milligrams per deciliter. The mean serum total protein level was 5.78 ± 1.09 grams per deciliter. Albumin levels had a mean of 3.98 ± 0.46 grams per deciliter.The mean prothrombin time was 14.07 ± 1.60 seconds. Prothrombin concentration had a mean of 109.75 ± 17.54%. The mean INR was 1.07 ± 0.12. PTT had a mean of 39.90 ± 3.73 seconds (Table 2).

**Table (2): Laboratory investigations of the studied cases.**

| Variables | Total cases (n=57) | |
|---|---|---|
| **RBCs (million/mcL)** | Mean ± SD | 4.07 ± 0.46 |
| | Median (range) | 4.10 (3.20 – 4.90) |
| **Hgb (g/dl)** | Mean ± SD | 11.12 ± 0.95 |
| | Median (range) | 10.80 (9.60 – 12.70) |
| **WBCs (thousand/mcL)** | Mean ± SD | 9.17 ± 2.75 |
| | Median (range) | 8.80 (5.80 – 14.4) |
| **Platelet (thousand/mcL)** | Mean ± SD | 328.98 ± 87.78 |
| | Median (range) | 323 (182 – 490) |
| **Serum total bilirubin (mg/dl)** | Mean ± SD | 0.38 ± 0.22 |
| | Median (range) | 0.33 (0.11 – 0.91) |
| **Serum direct bilirubin (mg/dl)** | Mean ± SD | 0.17 ± 0.12 |
| | Median (range) | 0.16 (0.03 – 0.90) |
| **Serum total protein (g/dl)** | Mean ± SD | 5.78 ± 1.09 |
| | Median (range) | 5.44 (4.06 – 7.90) |
| **Albumin (g/dl)** | Mean ± SD | 3.98 ± 0.46 |
| | Median (range) | 3.82 (3.17 – 4.91) |

| Variables | Total cases (n=57) | |
|---|---|---|
| **SGPT (unit/L)** | Mean ± SD | 20.92 ± 15.20 |
| | Median (range) | 19.20 (4 – 60.80) |
| **SGOT (unit/L)** | Mean ± SD | 38.61 ± 21.49 |
| | Median (range) | 29.40 (9.10 – 80.40) |
| **Creatinine (mg/dl)** | Mean ± SD | 0.32 ± 0.07 |
| | Median (range) | 0.33 (0.21 – 0.53) |
| **Blood urea nitrogen (mg/dl)** | Mean ± SD | 15.14 ± 8.49 |
| | Median (range) | 11.50 (7.20 – 32.80) |
| **Prothrombin time (s)** | Mean ± SD | 14.07 ± 1.60 |
| | Median (range) | 13.70 (10.60 – 17.60) |
| **Prothrombin concentration (%)** | Mean ± SD | 109.75 ± 17.54 |
| | Median (range) | 112.60 (74.20 – 133.30) |
| **INR** | Mean ± SD | 1.07 ± 0.12 |
| | Median (range) | 1.07 (0.91 – 1.35) |
| **PTT(s)** | Mean ± SD | 39.90 ± 3.73 |
| | Median (range) | 39.50 (33.90 – 47.40) |

SD, standard deviation; RBCs, red blood count; Hgb, hemoglobin; WBCs, white blood count.SD, standard deviation; SGPT, serum glutamate pyruvate transaminase; SPOT, serum glutamic oxaloacetic transaminase.

No need for oxygen interventions accounted for 35.1% of cases, while nasal oxygen was utilized in 42.1% of cases. A combination of CPAP followed by nasal oxygen was administered in 3.5% of cases. Additionally, incubator oxygen was provided in 5.3% of cases, CPAP alone in 10.5% of cases, and mechanical ventilation in 3.5% of cases (Table 3).

**Table (3): Types of respiratory interventions among included studies.**

| Variables | Frequency (n=57) | % |
|---|---|---|
| **No O2 intervention** | 20 | 35.1 |
| **Nasal O2** | 24 | 42.1 |
| **CPAP then nasal O2** | 2 | 3.5 |
| **Incubator free O2** | 3 | 5.3 |
| **CPAP** | 6 | 10.5 |
| **Ventilator** | 2 | 3.5 |

DA, ductus arteriosus; NICU, neonatal intensive care unit; CPAP, continuous positive airway pressure

Among the total cases (n=57), 19.30% experienced spontaneous PDA closure, while 80.70% had persistent DA. Initially, the mean PDA diameter was 1.84 ± 0.85 millimeters, with a median of 1.60 millimeters and a range from 1 to 5 millimeters. Upon follow-up, the mean PDA diameter decreased to 1.33 ± 1.03 millimeters, with a median of 1.10 millimeters and a range from 0 to 5 millimeters. (Table 4)

**Table (4): Distribution of spontaneous DA closure, persistent DA, and closure percentage of DA diameter**

| **Variables** | | **Total cases (57)** | | |
|---|---|---|---|---|
| **Spontaneous DA closure** | | 11 | 19.30% | |
| **Persistent DA** | | 46 | 80.70% | |
| **Variables** | | **Initial** | **Follow up** | **Closure percentage** |
| **DA diameter (mm)** | Mean ± SD | 1.84 ± 0.85 | 1.33 ± 1.03 | 25.07% |
| | Median (range) | 1.60 (1 – 5) | 1.10 (0 – 5) | |

SD, standard deviation; DA, ductus arteriosus

No significant difference between spontaneous PDA closure and persistent PDA was found in terms of gender, residence, consanguinity, mood of delivery, ABO, causes of NICU admission, and types of respiratory interventions (Table 5).

**Table (5): Comparison between cases with spontaneous DA closure and persistent DA.**

| **Variables** | **Spontaneous closure (n= 11)** | **Persistent DA (n= 46)** | **Chi square test** | **P-value** |
|---|---|---|---|---|
| **Gender** | | | | |
| **Male** | 8 | 29 | 0.37 | 0.55 |
| **Female** | 3 | 17 | | |
| **Residence** | | | | |
| **Rural** | 5 | 22 | 0.02 | 0.89 |
| **Urban** | 6 | 24 | | |
| **Consanguinity** | | | | |
| **Positive** | 3 | 5 | 1.98 | 0.16 |
| **No** | 8 | 41 | | |
| **Mode of delivery** | | | | |
| **Caesarian section** | 7 | 40 | 3.34 | 0.07 |
| **Vaginal delivery** | 4 | 6 | | |
| **ABO** | | | | |
| **A+** | 1 | 11 | 11.16 | 0.08 |
| **A-** | 0 | 2 | | |
| **B+** | 1 | 8 | | |
| **B-** | 0 | 4 | | |
| **AB+** | 0 | 5 | | |
| **O+** | 8 | 16 | | |
| **O-** | 1 | 0 | | |
| **Causes of NICU entry** | | | | |
| **No admission** | 1 | 8 | 1.56 | 0.82 |
| **Respiratory distress** | 6 | 21 | | |
| **Jaundice** | 1 | 9 | | |
| **Respiratory distress and jaundice** | 1 | 3 | | |
| **Low birth weight** | 2 | 5 | | |

| Variables | Spontaneous closure (n= 11) | Persistent DA (n= 46) | Chi square test | P-value |
|---|---|---|---|---|
| **Types of respiratory interventions** | | | | |
| **Free** | 2 | 18 | 5.04 | 0.41 |
| **Nasal O2** | 7 | 17 | | |
| **CPAP then nasal O2** | 1 | 1 | | |
| **Incubator O2** | 0 | 3 | | |
| **CPAP** | 1 | 5 | | |
| **Ventilator** | 0 | 2 | | |

DA, ductus arteriosus; NICU, neonatal intensive care unit; CPAP, continuous positive airway pressure; chi-square test was used.

There were highly statistically significant association between spontaneous PDA closure and both gestational age and albumin. The results showed that duct closure increases with increased gestational age and high albumin level (p-value = 0.009, and 0.02 respectively) (Table 6).

**Table (6): Comparison between spontaneous and persistent DA regarding gestational age, weight at birth and laboratory tests.**

| Variables, mean ± SD | Spontaneous closure (n=11) | Persistent DA (n=46) | T-test | p-value |
|---|---|---|---|---|
| **Gestational age (week)** | 35.24 ± 1.34 | 34 ± 1.48 | 2.71 | **0.009**** |
| **Weight at birth (gm)** | 2185.45 ± 130.49 | 2240.87 ± 234.26 | -0.75 | 0.45 |
| **RBCs (million/mcL)** | 4.16 ± 0.46 | 4.05 ± 0.46 | 0.72 | 0.47 |
| **Hgb (g/dl)** | 11.29 ± 0.91 | 11.08 ± 0.96 | 0.67 | 0.51 |
| **WBCs (thousand/mcL)** | 9.42 ± 3.11 | 9.11 ± 2.69 | 0.33 | 0.74 |
| **PLT (thousand/mcL)** | 320 ± 82.84 | 331.13 ± 89.67 | -0.38 | 0.71 |
| **Serum total bilirubin (mg/dl)** | 0.3209 ± 0.13 | 0.39 ± 0.23 | -0.001 | 0.32 |
| **Serum direct bilirubin (mg/dl)** | 0.16 ± 0.07 | 0.17 ± 0.13 | -0.42 | 0.68 |
| **Serum total protein (g/dl)** | 6.20 ± 5.68 | 1.17 ± 1.06 | 1.43 | 0.15 |
| **Albumin (g/dl)** | 4.27 ± 0.48 | 3.91 ± 0.43 | 2.44 | **0.02*** |
| **SGPT (unit/L)** | 16.65 ± 9.92 | 21.95 ± 16.13 | -1.04 | 0.30 |
| **SGOT (unit/L)** | 36.95 ± 20.80 | 39 ± 21.86 | -0.28 | 0.78 |
| **Creatinine (mg/dl)** | 0.34 ± 0.06 | 0.33 ± 0.08 | 0.47 | 0.64 |
| **Blood urea nitrogen (mg/dl)** | 15.17 ± 6.98 | 15.14 ± 8.88 | 0.01 | 0.99 |
| **Prothrombin time (s)** | 13.92 ± 1.96 | 14.11 ± 1.53 | 0.36 | 0.72 |
| **Prothrombin concentration (%)** | 113.77 ± 13.60 | 108.79 ± 18.35 | 0.84 | 0.40 |
| **INR** | 1.12 ± 0.17 | 1.06 ± 0.10 | 1.59 | 0.12 |
| **PTT (s)** | 39.45 ± 3.45 | 40.01 ± 3.82 | -0.45 | 0.66 |

SD, standard deviation; RBCs, red blood count; Hgb, hemoglobin; WBCs, white blood count; SGPT, serum glutamate pyruvate transaminase; SPOT, serum glutamic oxaloacetic transaminase; DA, ductus arteriosus; INR, international normalized ratio; PTT, partial thromboplastin time; *p-value less than 0.05 was considered statistically significant, ** highly significant results. Independent t-test was used.

The results of risk factors assessment showed that persistent PDA was associated with a significant lower gestational age, p-value 0.012. (Table 7).

**Table (7): Risk factors of persistent DA.**

| | Odds ratio | 95% confidence interval | p-value |
|---|---|---|---|
| **Female vs Male** | 0.64 | 0.15 – 2.73 | 0.59 |
| **Cesarean section vs vaginal** | 0.26 | 0.06 – 1.18 | 0.58 |
| **Gestational age (wk)** | 0.52 | 0.04 – 0.73 | **0.012*** |
| **Albumin (g/dl)** | 0.18 | 0.03 – 10.3 | 0.054 |
| **Weight at birth (gm)** | 1.001 | 0.99 – 1.004 | 0.45 |
| **Jaundice vs other types** | 0.48 | 0.09 – 2.56 | 0.39 |
| **Rural vs urban** | 0.91 | 0.24 – 3.40 | 0.88 |
| **Consanguinity (yes vs no)** | 0.33 | 0.06 – 1.64 | 0.16 |
| **Blood group (O+ vs other types)** | 0.86 | 0.21 – 3.53 | 0.83 |
| **Types of O2 need (nasal vs other types)** | 1.67 | 0.35 – 7.86 | 0.52 |

*p-value less than 0.05 was considered statistically significant.

## DISCUSSION

One of the most prevalent congenital heart abnormalities is patent ductus arteriosus (PDA). When the ductus arteriosus (DA) does not close within 72 hours of birth, a condition known as a perforated ductus (PDA), infants may suffer serious complications and can die at rates up to 30%. Patent ductus arteriosus is a common clinical condition in preterm infants. Preterm newborns with PDA are at greater risk for several morbidities and mortality.Medications such as paracetamol or non-steroidal anti-inflammatory medicines (NSAIDs) or fluid restriction are some of the treatment options for PDA. Surgical techniques such as ligation or cardiac catheterization are also possible. But there are dangers and negative effects associated with each of these treatments for preterm babies [10].Despite a decline in prostaglandin levels following premature delivery, the ductus arteriosus is still significantly more responsive to prostaglandin E2 (PGE2) and nitric oxide (NO) in premature babies than in full-term babies. Although exact closure rates are yet unknown, the possibility of spontaneous closure should be included in discussions about managing PDA in preterm newborns [5].

We conducted the current study to determine the frequency of spontaneous closure of PDA among preterm infants at Zagazig University Hospitals. The study consisted of 57 neonates, with 64.9% being male and 35.1% female. The mean gestational age was 35 weeks with a standard deviation of 1.44, and maternal age ranged from 32 to 37 years, with a mean of 35 years. Among the participants, 14% reported positive consanguinity, while 86% reported negative consanguinity. Cesarean section was the predominant mode of delivery, accounting for 82.5%, with vaginal delivery at 17.5%. Regarding ABO blood groups, O+ was the most common at 42.1%, followed by A+ at

21.1%. The mean birth weight was 2230.18 grams with a standard deviation of 218.24, and birth weights ranged from 1850 to 2750 grams.

Compared to other studies, Nielsen et al. [11] conducted a retrospective study, consisting of 167 infants. Of them, 97 infants (58%) were male. The median gestational age was 27 weeks and 6 days. The median birth weight was 1073 grams, based on 166 infants. In addition, 104 deliveries (62%) were via cesarean section.A study by Tolia et al. [12] enrolled a total of 201 premature infants, all born with a gestational age ranging from 23 to 32 weeks. The infants had a median gestational age of 27 weeks, with a range from the 10th to the 90th percentile of 24 to 31 weeks. Their median birth weight was 982 grams, with the 10th to the 90th percentile range spanning from 634 to 1618 grams. Another study by Romagnoli et al. [13] included a total of 593 infants; of them, 293 were males. The average gestational age was 28.7 ± 2.4 weeks and an average birth weight was 1028 ± 238 grams.

Our study shows that, among 57 neonates, 15.8% did not require NICU admission. Respiratory distress was the most common cause, accounting for 47.4% of admissions. Jaundice was the reason for admission in 17.5% of cases, while a combination of respiratory distress and jaundice led to admission in 7.0% of cases. Additionally, 12.3% of admissions were due to low birth weight.

Compared to other studies, Nielsen et al. [11] reported that respiratory distress was diagnosed in 151 infants (90%), and surfactant therapy was given to 115 infants (69%). Bronchopulmonary dysplasia (BPD) was present in 69 infants (41%), with 27 infants (16%) receiving steroid treatment for BPD. Necrotizing enterocolitis (NEC) and renal failure each affected 16 infants (10%). Intraventricular hemorrhage (IVH) occurred in 59 infants (35%), and sepsis was diagnosed in 107 infants (64%). Intrauterine growth restriction (IUGR) was observed in 20 infants (12%).

Our study showed that 35.1% of included cases did dot need for oxygen interventions accounted, while nasal oxygen was utilized in 42.1% of cases. A combination of CPAP followed by nasal oxygen was administered in 3.5% of cases. Additionally, incubator oxygen was provided in 5.3% of cases, CPAP alone in 10.5% of cases, and mechanical ventilation in 3.5% of cases.

Compared to other studies, Nielsen et al. [11] reported that 160 infants (96%) required continuous positive airway pressure (CPAP) or high flow treatment, 154 infants (92%) needed oxygen, and 89 infants (53%) required mechanical ventilation**.**

The current study showed that, 19.30% experienced spontaneous PDA closure, while 80.70% had persistent PDA among the total cases (n=57).

The study by Rolland et al. [14] reported that 8 (9%) had their ductus arteriosus close before 72 hours, and in 13 cases, the ductus could not be confirmed as patent. Out of the 70 infants with a persistent PDA, one required surgical ligation, and spontaneous closure was observed in 51 infants (73%). For the remaining 18 infants, the date of PDA closure could not be determined due to death (n=11) or discharge (n=7). Overall, spontaneous ductus arteriosus closure was observed in 59 out of the 91 infants

This difference may be due to difference in gestational age; their study included infants born before 28 weeks of gestation. Nielsen et al. [11] showed that spontaneous closure rate within the first year of life was 66% increasing to 80% five years after birth in infants born before 32 weeks of gestation, consistent with the results demonstrated by Romagnoli et al. [13] as Out of 593 newborns that fulfilled the inclusion criteria, 317 (53.4%) were found to have patent ductus arteriosus. Out of the total number of newborns, 283 (89.3% of the total) had a patent ductus arteriosus that was hemodynamically significant. Of those, 228 (80.6%) were able to have the condition closed with medication, and 20 (7.1%) underwent surgical ligation. At the time of hospital discharge, 39 out of 48 infants (81.3%) had a patent ductus arteriosus; 36 (92.3%) had spontaneous closure, two (5.1%) had surgical ligation, and one (2.6%) still had a patent ductus arteriosus.

Tolia et al. [12] who reported a 58% spontaneous closure rate after 18 months of follow-up.

Nielsen et al. [11] reported the highest rate of spontaneous PDA closure, which continued to increase, reaching 80% at five years of follow-up. This highlights the potential for spontaneous ductal closure long after hospital discharge. Additionally, a notable number of infants required assisted closure of the PDA after discharge, indicating the need for close follow-up.

However, when comparing our results with existing literature, caution is warranted. Given the variability of PDA sizes (small, moderate, and large), small or moderate-sized PDAs potentially leading to more favorable outcomes. Larger PDAs are more likely to need assisted closure, either pharmacological or surgical, while smaller PDAs tend to close spontaneously. Also,follow-up duration, gestational age and birth weight were different to those in other studies.

Initially, the mean PDA diameter was 1.84 ± 0.85 millimeters, with a median of 1.60 millimeters and a range from 1 to 5 millimeters. Upon follow-up, the mean PDA diameter decreased to 1.33 ± 1.03 millimeters, with a median of 1.10 millimeters and a range from 0 to 5 millimeters. This represents a closure percentage of 25.07%.

No significant difference between spontaneous PDA closure and persistent PDA was found in terms of gender, residence, consanguinity, mood of delivery, ABO, causes of NICU admission, and types of respiratory interventions.There was highly statistically significant correlation between spontaneous PDA closure and gestational age. The results showed that duct closure increases with increased gestational age, p-value = 0.009. There was statistically significant relation between spontaneous PDA closure and albumin. The results showed that duct closure increases with high albumin level, p-value = 0.02. The results showed that persistent PDA was associated with a significant lower gestational age, p-value 0.012.

Previous studies have attempted to identify factors at hospital discharge that predict spontaneous closure. The studies by Romagnoli et al. [13] and Tolia et al. [12] showed that higher gestational age and birth weight were associated with an increased likelihood of spontaneous PDA closure.Nielsen et al. [11] did not find differences in gestational age or birth weight between infants with spontaneous closure and those without. However, a large PDA, left atrial enlargement, and pulmonary hypertension were associated with a decreased likelihood of spontaneous closure. This association was less significant in multivariate logistic regression, likely due to the interdependence of these variables.

Tolia et al. [12] reported that moderate-sized PDAs and left ventricular enlargement were common in infants needing assisted PDA closure. Therefore, careful monitoring and follow-up is highly recommended for infants with large PDAs, pulmonary hypertension, and left ventricular enlargement.

This recommendation is consistent with guidelines from the American Heart Association regarding PDA catheterization in non-premature infants. The guidelines suggest ductal closure for moderate or large PDAs with a left-to-right shunt causing congestive heart failure, failure to thrive, pulmonary over circulation, or left atrial or ventricular enlargement [15].

The study has many strengths: The study collected detailed demographic and clinical data from a significant number of neonates, providing a comprehensive overview of the cohort. The inclusion of neonates with various gestational ages, birth weights, and delivery modes enhances the study's generalizability and applicability to different populations. The study employed a variety of analyses, including laboratory tests and clinical assessments, to explore factors associated with spontaneous closure of patent ductus arteriosus, contributing to a nuanced understanding of the condition. By focusing on a clinically relevant outcome—spontaneous closure of patent ductus arteriosus—the study addresses an important aspect of neonatal care and informs clinical decision-making.

### Limitations of the study

While the study included a reasonable number of neonates, a larger sample size would provide greater statistical power and precision in estimating prevalence rates and identifying factors associated with spontaneous closure. The duration of follow-up may have been insufficient to capture long-term outcomes related to patent ductus arteriosus closure, potentially underestimating or overestimating spontaneous closure rates. Echocardiography was not routinely performed on all premature infants, likely underestimating the incidence of PDA. There is also a risk of interobserver variability as multiple doctors conducted the echocardiographic assessments. The accuracy of echocardiography in preterm infants can be influenced by the infant's condition, with factors such as apnea, bradycardia, arterial hypotension, or changes in skin color potentially affecting hemodynamic measurements. This issue of accuracy has been highlighted in other studies.This study's single-center design minimizes the risk of random variation and interobserver variability.

## CONCLUSION

Factors associated with persistence of the duct opened included low gestational age and low albumin levels. Rate of early spontaneous closure of the patent ductus arteriosus in our study is 19.30%, so we concluded giving a chance for spontaneous closure of the duct unless there is clear indication for closure.

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