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Research Paper

Respiratory Outcomes in Hospitalized Infants With Respiratory Distress and Echocardiography Results

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ABSTRACT

Background and Aim: Respiratory distress is the most common cause of hospitalization in neonatal intensive care units (NICU). An immediate distinction between cardiac and non-cardiac causes can influence the treatment process. This study aimed to determine the relationship between respiratory outcomes in hospitalized infants due to respiratory distress and echocardiography results in educational and medical centers in Qom City, Iran.

Materials and Methods: This research was a cross-sectional analytical study. The study population included patients hospitalized at all NICUs in Qom City. This study focused on infants hospitalized for respiratory distress. The sampling method involved a census of all infants on the first, seventh, and fourteenth days. We measured cardiac output, heart rate, tricuspid annular plane systolic excursion (TAPSE), right ventricular ejection fraction (RVEF) and left ventricular ejection fraction (LVEF) in hospitalized infants using echocardiography performed by a pediatric cardiologist. Respiratory conditions and outcomes were carefully recorded during this period based on the respiratory distress syndrome (RDS) score. Subsequently, the respiratory course and ventricular output were compared using echocardiography. In the final step, this information was entered into SPSS software version 22 and analyzed with appropriate statistical tests. The significance level was set at 0.05.

Results: Repeated measures analysis of variance (ANOVA) for TAPSE, ventricular output, and left ventricular output showed a statistically significant difference ($P<0.05$) based on the RDS score.

Conclusion: Early detection of hemodynamic instability in hospitalized infants due to respiratory distress can help improve hemodynamic conditions by enhancing cardiac function, ultimately leading to improved outcomes and a reduced duration of hospitalization.

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Introduction

Respiratory distress syndrome (RDS), transient tachypnea of the newborn, hyaline membrane disease, meconium aspiration syndrome, sepsis, pneumonia, and congenital heart disease are the most common causes of newborn respiratory distress. In addition to protective and supportive measures of the respiratory system, these conditions sometimes require specific treatment [1]. Newborn respiratory distress manifests as rapid breathing, expiratory wheezing, retraction of the intercostal muscles, movement of the nasal flares during inhalation, decreased respiratory sounds, rales, cyanosis, pallor, and apnea. This state is a non-specific response to severe disease. It is caused not only by a disorder in the respiratory system but also by pulmonary, cardiac, infectious, blood, skeletal, and metabolic diseases and may directly and indirectly involve the lungs [2]. Respiratory distress is the most common cause of hospitalization in both term and preterm infants in the (NICU) [3]. Hypoxemia causes deterioration of heart function. Respiratory distress causes hypoxemia, which affects heart function, especially in the right heart (tricuspid regurgitation) [4]. However, congenital heart diseases have a relatively high prevalence in infancy and may manifest with or without cyanosis. Therefore, neonatologists should quickly distinguish between cardiac and non-cardiac causes because cardiac causes are usually related to the ductus arteriosus during infancy, and in most cases, the patient's condition worsens as it narrows [5].

RDS increases pulmonary blood pressure. Often, this increase in right ventricular afterload leads to cardiac dysfunction [6]. Acute respiratory distress syndrome (ARDS) is associated with high mortality and long-term disability. This poor outcome is probably more than just a hypoxemic defect caused by circulatory failure. Septic shock is responsible for circulatory failure in half of ARDS patients. On the other hand, in the other half of patients, hemodynamic instability is directly related to ARDS due to impaired pulmonary circulation, resulting in right ventricular (RV) failure. When a right ventricular defect plays a significant role in ARDS, it is associated with poor prognosis [7]. Respiratory distress disturbs the transition period from fetal to newborn circulation, resulting in hemodynamic instability. Early detection of shock and instability can aid in treatment. Approximately 30% of cases can be diagnosed using clinical studies. Clinical studies include measurements of blood pressure, capillary refill, tachycardia, urine output, arterial blood gas, lactate, and central venous oxygen saturation [8, 9]. Echocardiography is an emerging technology that can be used to measure cardiac output in ill neonates mainly because the clinical estimation of cardiac output is relatively imprecise. In addition, neonatologists who perform echocardiography can inform physicians about the possible pathophysiological mechanisms of circulatory failure and can be used to evaluate the effects of therapeutic interventions [10-13].

Recently, the purpose of echocardiography in the NICU has changed. In the past, almost all echocardiography studies performed in the NICU were for the diagnosis or follow-up of congenital heart disease (CHD) and the examination of patent ductus arteriosus (PDA) [14]. Recently, neonatologists have become interested in using echocardiography to measure hemodynamic instability. The terms functional echocardiography and point-of-care echocardiography are used to describe echocardiography as a supplement to the clinical evaluation of hemodynamic status in infants [15-18]. Cardiac output is classified into three categories: Normal, low, and high (with a normal range of 4-8 L/min). Combining information about blood pressure levels and cardiac output with echocardiographic details regarding the presence of a shunt, myocardial function, pulmonary pressure, and volume status enables the physician to fully assess the hemodynamic status of the newborn and estimate the underlying pathophysiology. Provided that the therapeutic interventions are sufficient, they prevent tissue damage and improve the results [19].

Considering the extent of functional echocardiography, our study was conducted to determine the relationship between the respiratory outcomes of hospitalized infants due to respiratory distress and echocardiography results from 2022 to 2023 in the medical training centers of Qom University of Medical Sciences. If a significant relationship is found between the normal function of the ventricles and the acceleration of recovery from respiratory distress in infants, it may facilitate predicting the disease course, making decisions more quickly as the infant's condition worsens, applying the necessary treatments to improve ventricular output and addressing respiratory problems in newborns more effectively, which can reduce the duration of hospitalization and the complications associated with it. As mentioned above, these studies have primarily focused on CHD. To the best of our knowledge, this is the first time this procedure has been performed in Iran

Table 1. Review of mean echocardiography indices in the studied infants

Variables	RDS Score	Day 14	Day 7	Day 1
Cardiac output	0	3.73±0.5	3.7±0.48	3.39±0.6
	1	3.68±0.46	3.89±0.49	3.41±0.6
	2	3.78±0.47	3.72±0.5	2.79±0.6
TAPSE	0	1.48±0.4	1.38±0.33	1.48±0.37
	1	1.35±0.34	1.48±0.4	1.4±0.3
	2	1.26±0.5	1.56±0.3	1.46±0.3
LVEF	0	56.8±3.41	56.2±2.42	57.6±4.3
	1	55.7±2.63	55.7±1.29	55.7±3.9
	2	56.2±2.9	55.8±2.07	56.2±2.87

Abbreviations: TAPSE: Tricuspid annular plane systolic excursion; LVEF: Left ventricular ejection fraction; RDS: Respiratory distress syndrome.

Materials and Methods

This study was conducted as a longitudinal study and its population included patients hospitalized in all NICUs in Qom City who were admitted with respiratory distress. Sampling was performed as part of a census. The inclusion criterion included all term and preterm infants hospitalized due to respiratory distress. The exclusion criteria included infants who did not consent to participate in the study or did not participate in follow-up treatment due to cardiovascular abnormalities, birth canal trauma, neurological abnormalities, or poisoning.

After receiving the code of ethics from the Vice President of Research of Qom University of Medical Sciences and obtaining approval from the hospital head, the researcher started sampling. In the next step, patients were selected based on the inclusion and exclusion criteria, their initial history was obtained, and their demographic findings were entered into the checklist. All infants were then subjected to echocardiography by a pediatric cardiologist on the first, seventh, and fourteenth days. The aim was to measure cardiac output, heart rate, tricuspid annular plane systolic excursion (TAPSE), right ventricular ejection fraction (RVEF) and left ventricular ejection fraction (LVEF) in hospitalized infants. During this period, the respiratory conditions and outcomes of the newborns, which included intubation, noninvasive positive pressure ventilation, arterial blood oxygen saturation, duration of connection to the ventilator, respiratory rate, tidal volume, and maximum inspiratory pressure, were accurately recorded based on the RDS score. Then, the respiratory course and the results of the ventricles' output on echocardiography were compared to determine whether the respiratory conditions of the infants improved with the enhancement of output, or in other words, heart function. If initiating inotropes to increase cardiac output is required for the aforementioned reasons, we assessed whether the increase in cardiac output positively affects the respiratory course of newborns, whether there is a change when tapering off the medication, and whether it has a temporary or long-term effect.

In the final step, this information was entered into SPSS software version 22 and in line with inferential analyses, default tests (mean echocardiography indices according to RDS score), repeated measure analysis of variance (ANOVA), and Bonferroni post hoc test were used. The significance level was set at 0.05.

Results

A total of 86 male infants (56.2%) and 67 female infants (43.9%) were examined; 75 cases (49%) had a birth rank of 1, 63 cases (41.2%) had a birth rank of 2 and 15 cases (9.8%) had a birth rank of three or more. The type of pregnancy was natural in 139 cases (90.8%) and IVF in 14 cases (9.2%). Table 1 presents the mean echocardiography results on days one, seven, and fourteen.

Factorial ANOVA was used to check the assumption of intra-group repeated measures ANOVA (P>0.05).

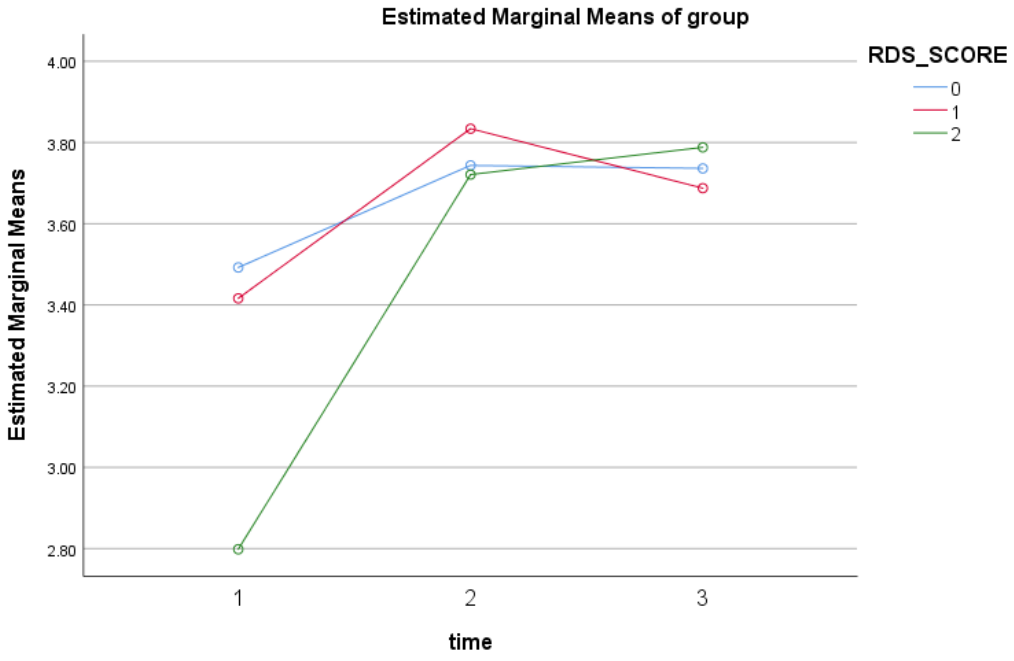

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Figure 1. Comparison of the average output of the ventricles according to RDS score

RDS: Respiratory distress syndrome.

The results of repeated measures ANOVA for three variables—TAPSE, ventricular output and left ventricular output—showed a statistically significant difference (P<0.05) according to the RDS score (Table 2).

The Bonferroni's test results showed a significant statistical difference in the ventricular output per day according to the RDS score (Figure 1).

The results of repeated measures ANOVA regarding left ventricular output showed a statistically significant difference between the RDS score on day one and day fourteen (Table 3 and Figure 2).

The results of repeated measures ANOVA regarding TAPSE showed a statistically significant difference between the RDS score on day seven and day fourteen (Table 4 and Figure 3).

Discussion

The most common causes of newborn respiratory distress are RDS, transient tachypnea of the newborn, hyaline membrane disease, meconium aspiration syndrome, sepsis, pneumonia, and congenital heart disease [20]. Respiratory distress is one of the most common reasons for hospitalization of term and preterm infants in the NICUs [21]. In contrast, hypoxemia causes heart failure, while respiratory distress causes hypoxemia, which affects heart function, especially in the right heart [4, 22]. In contrast, congenital heart disease or a relatively high prevalence occurs in infancy and may manifest with or without cyanosis [23].

The results of our study showed no significant relationship between the normality of the ventricular output function in accelerating the recovery of newborn respiratory distress. Additionally, the frequency of the severity of respiratory outcomes in the follow-up days of the patients, when separating left ventricular output and the TAPSE index, was not significantly different. Poon et al. conducted a cross-sectional study in England to investigate the relationship between premature birth and RDS with pulmonary vascular diseases and myocardial function. In their study, 30 preterm infants diagnosed with RDS, 30 preterm infants without respiratory distress, and 60 term infants were examined as the control group. Echocardiography results were measured and compared within the first 72 hours of birth, at the corrected term, one month later, and one year later. Finally, they concluded that preterm infants diagnosed with respiratory distress had lower systolic and diastolic function of both the right and left ventricles, which improved gradually over time and their respiratory symptoms improved [6]. These results partially confirm the results of our study

Table 2. Repeated measures analysis of variance related to ventricular output

Parameter	Effect Size	P	F Coefficient	Mean Squares	df	Sum of Squares	Source
Ventricular output	0.119	0.001	10.160	2.741	4	10.963	Sphericity Assumed
	0.119	0.001	10.160	2.890	3.793	10.963	Greenhouse- Geisser

Table 3. Repeated measures ANOVA regarding left ventricular output

Parameter	Effect Size	P	F Coefficient	Mean Squares	df	Sum of Squares	Source
LVEF	0.206	0.101	2.021	17.143	4	68.573	Sphericity Assumed
	0.206	0.101	2.021	19.557	3.506	68.573	Greenhouse- Geisser

ANOVA: Analysis of variance; LVEF: Left ventricular ejection fraction.

that in the long-term follow-ups of two weeks and one month, cardiac findings were not significantly related to the severity of respiratory outcomes.

In a cross-sectional study by Arjmandnia et al. in Qom City to evaluate the necessity of echocardiography in evaluating newborns with respiratory distress hospitalized in the NICU, 349 newborns with respiratory distress hospitalized in NICU were examined. Finally, they concluded that when deciding on the need for echocardiography, it is important to consider not only the criteria of prolonged respiratory distress and the presence of murmurs but also the gestational age of the infants i. In addition, 84% of the infants had abnormal echocardiographic findings [24]. Evans et al. conducted a cross-sectional study in Australia to determine the right and left ventricular output in preterm infants undergoing ventilation. They evaluated 120 preterm infants on ventilation within the first 36 hours of birth using Doppler echocardiography to assess the cardiorespiratory effects of right and left ventricular output [25]. Finally, it can be concluded that ventricle output is more commonly associated with the exacerbation of respiratory disease; the output increases on the third day after birth, and the respiratory symptoms of newborns improve.

To examine the effect of RDS on the increase in arterial pressure and the rise in right ventricular afterload and its impact on heart failure in newborn lambs, a study was conducted in the neonatal department of Wilhelmina Hospital in the Netherlands. The function of both ventricles was studied using an experimental model. In this study, RDS was induced by lavages in the lungs of seven lambs, and the other five lambs were used as the control group. Heart function was assessed by indicators that were quantified from end-systolic pressure-volume relationships obtained using pressure-conductance catheters. Right ventricular function improved significantly, as evidenced by a leftward shift and an increase in the end-systolic pressure-volume slope. In the control group, pulmonary artery pressure did not increase and the systolic function of the left and right ventricles remained unaffected. In response to the increase in RV afterload, the neonatal heart could maintain cardiac output, primarily by improving right ventricular function through homeometric resetting [26]. However, it is recommended that when selecting infants hospitalized in the ICU, where echocardiography is indicated for prolonged respiratory distress and wheezing, cardiac causes should be more carefully considered, especially in full-term and near-term infants with respiratory distress.

Also, considering that the average age of babies when heart disease is diagnosed is less than one week, it is recommended to consider most heart problems for babies who experience respiratory distress after the first week

Table 4. Repeated measures ANOVA regarding TAPSE

Environment	Effect Size	P	F Coefficient	Mean Squares	df	Sum of Squares	Source
TAPSE	0.039	0.017	3.080	0.502	4	2.007	Sphericity assumed
	0.039	0.017	3.080	0.510	3.937	2.007	Greenhouse- geisser

ANOVA: Analysis of variance; TAPSE: Tricuspid annular plane systolic excursion.

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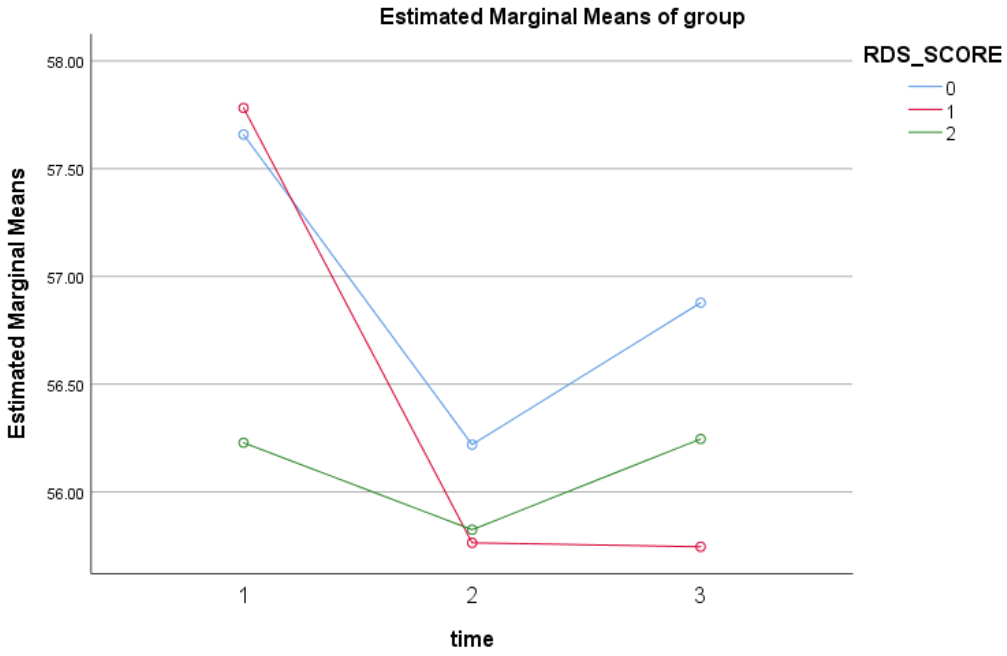

Figure 2. Comparison of the average output of the left ventricle according to RDS score

RDS: Respiratory distress syndrome.

of birth. One of the potential limitations in determining the relationship between respiratory outcomes in hospitalized infants with respiratory distress and echocardiographic results is the complex and multifactorial nature of respiratory distress in infants. Respiratory distress in infants can have various underlying causes, including lung conditions, heart abnormalities, and infections. Therefore, isolating the specific impact of echocardiographic results on respiratory outcomes may be challenging, particularly in a heterogeneous population of

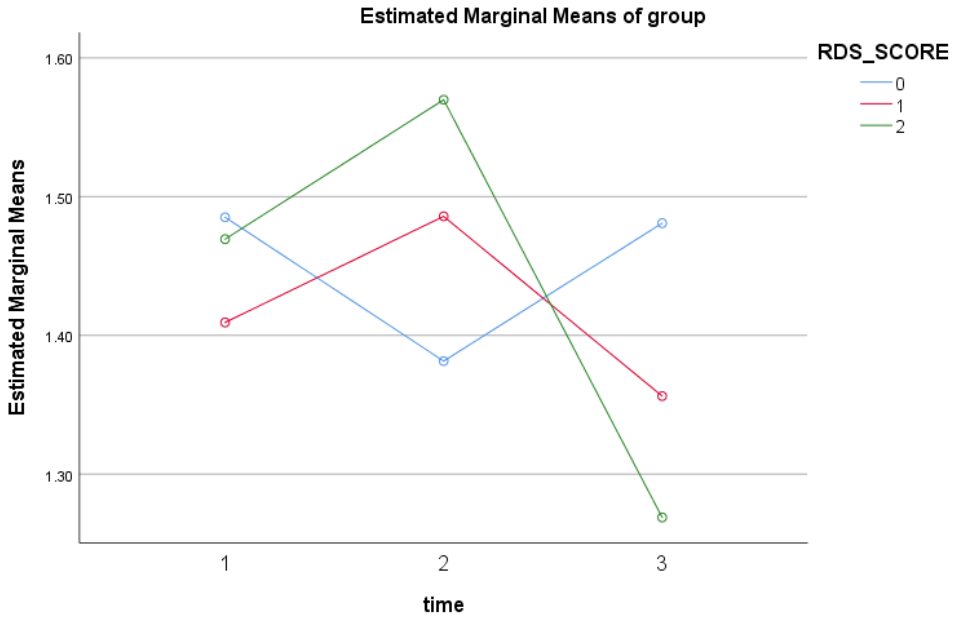

Figure 3. Comparison of average TAPSE according to RDS score

TAPSE: Tricuspid annular plane systolic excursion; RDS: Respiratory distress syndrome.

hospitalized infants with respiratory distress. To address this limitation, it is necessary to develop a comprehensive approach that considers the multifactorial nature of respiratory distress in infants. When evaluating the relationship between echocardiographic results and respiratory outcomes, researchers should control for potential confounding variables, such as gestational age, birth weight, comorbidities, and other clinical factors that may affect respiratory and cardiac function.

Additionally, conducting a longitudinal study that follows infants over time and includes serial echocardiographic assessments with monitoring of respiratory outcomes can provide a stronger understanding of the relationship between cardiac function and respiratory outcomes in hospitalized infants. This longitudinal approach may help elucidate how changes in cardiac function, as assessed by echocardiography, affect respiratory status and clinical outcomes in infants with respiratory distress. By considering these factors and adopting a comprehensive longitudinal study design, researchers can overcome potential limitations and gain valuable insights into the relationship between echocardiographic results and respiratory outcomes in hospitalized infants with respiratory distress. This approach could contribute to a deeper understanding of the complex interplay between cardiovascular and respiratory health in vulnerable populations.

Conclusion

Our study showed that echocardiography results in the follow-up of infants with respiratory distress had a significant relationship with the severity of respiratory consequences on day one, but not on days seven and 14; therefore, it was related to the severity of RDS on the first day. According to the study results, early detection of hemodynamic instability in hospitalized infants due to respiratory distress can help improve hemodynamic conditions by enhancing cardiac function, ultimately leading to improved outcomes and reduced duration of hospitalization.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Qom University of Medical Sciences (Code: IR.MUQ.REC.1402.009).

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Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interception of the results, and manuscript drafting. Each author approved the submission of the final version of the manuscript.

Conflict of interest

The authors declared no conflict of interest.

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