Original Article

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Paediatrics Section

Thymic Size in Preterm Neonates with RDS and its Relation to Survival: A Prospective Observational Study

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ABSTRACT

Introduction: Thymic size in neonates is represented by the Cardiothymic-Thoracic ratio (CT/T) as measured on chest X-ray. Various pre and post natal factors have been shown to affect thymic size in neonates. Respiratory Distress Syndrome (RDS) is an important cause of mortality in preterm neonates and CT/T ratio in infants with RDS may actually be larger, owing to a decrease in serum cortisol levels in them. We therefore intend to find out the thymic size in infants diagnosed with RDS and whether it is related to survival.

Aim: To determine the thymic size in preterm neonates with RDS and their relation to survival and to determine which antenatal and post natal factors have an influence on, or correlation with thymic size.

Materials and Methods: The study was conducted in the NICU of Department of Pediatrics, Himalayan Institute of Medical Sciences, Dehradun, India, over a period of nine months. Premature (<37 weeks gestation) neonates admitted in NICU with clinical evidence of RDS, (Silvermann's score ≥3) and a chest X-ray suggestive of RDS were included in the study. CT:T ratio was determined on chest X-ray and compared between survivors and non-survivors.

Results: Total 42 neonates were enrolled in the study. The mean±SD, CT:T in the study was 0.367±0.026. The CT:T in neonates who survived and those who expired was 0.36 and 0.38 respectively. A neonate with a CT:T of less than 0.403 had a 50% probability of survival. Although, CT:T was higher in the non-survivor group, the result was not statistically significant (p=0.33). Gestational age, sex, mode of delivery, administration of antenatal steroids or presence of birth asphyxia or sepsis did not affect the CT:T ratio.

Conclusion: A large CT:T on X-ray chest can be used as a prognostic marker. Preterms with a CT:T of more than 0.40 have a poorer prognosis in terms of survival.

Keywords: Birth asphyxia, Cardio-thymic thoracic ratio, Cortisol, Thymus

INTRODUCTION

The thymus plays an important role in the development of cell mediated immunity. In the well neonate the thymus is proportionally at its largest when compared with body weight. The thymic size can be calculated on chest X-ray by measuring the CT:T at the level of the carina [1-3]. Various pre and post natal factors such as chorio-amnionitis, Broncho-Pulmonary Dysplasia (BPD), sepsis and Respiratory Distress Syndrome (RDS) have been shown to affect the thymic size in the neonate [4-6]. Neonates with RDS may have a larger thymus probably because of an associated decrease in serum cortisol levels in these patients. In neonates with sepsis, a smaller thymus has been observed [6]. We therefore undertook this study to estimate thymic size in infants diagnosed with RDS and to find out whether it is related to survival. In addition, we aimed to find the relation, if any, between the CT/T ratio and various prenatal and postnatal factors that might have influenced the CT/T ratio.

MATERIALS AND METHODS

This prospective observational study was conducted on 42 neonates admitted with RDS in the NICU of Department of Pediatrics, Himalayan Institute of Medical Sciences, Dehradun, India, over a period of nine months from June 2014 to February 2015.

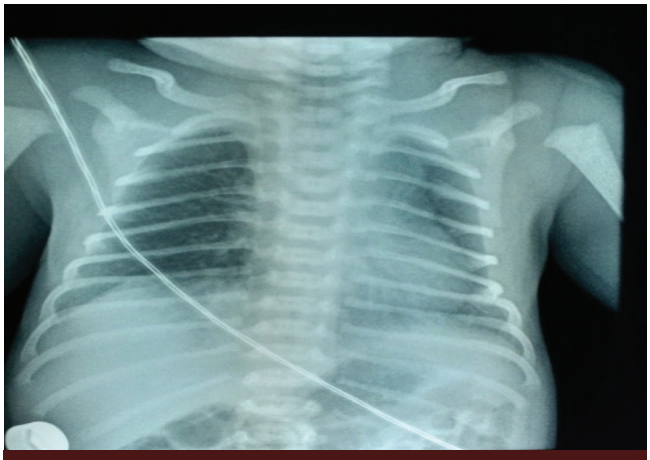
Inclusion Criteria

Premature (<37 weeks gestation) neonates admitted in NICU with clinical evidence of RDS (Silvermann's score ≥3) and a chest X-ray performed within 48 hours of delivery and showing evidence of RDS [7].

Exclusion criteria

1) Congenital cardiac malformations.
2) Multiple congenital anomalies.
3) Infants with a chest X-ray that was excessively rotated or the cardio-thymic shadow could not be differentiated from that of the lungs owing to severe RDS (Grade IV).
4) Neonates who had already received surfactant prior to chest X-ray.

Written and informed consent was taken from the parent/guardian of each patient prior to enrollment. Thymus size was expressed as CT:T by measuring the width of the cardio-thymic shadow at the level of carina and dividing it by the width of the thorax at the costo-phrenic angles by a single radiologist who was blinded to the identity and the clinical course of the patient [Table/Fig-1]. For each X-ray chest, three readings were taken and their average was considered as the final CT:T ratio. For each patient data about the mother's health and pregnancy related history, and the child's birth and postnatal course was recorded on a pre-structured format. The study was approved by the Institutional Ethics Committee.



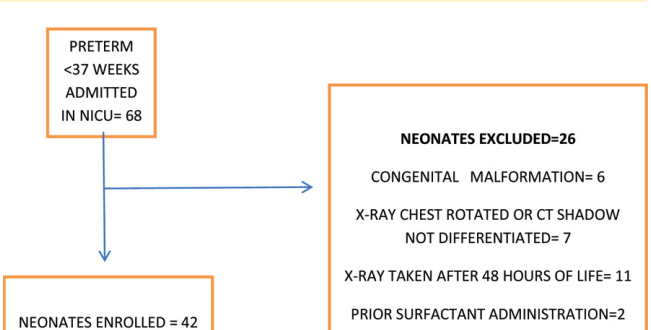
[Table/Fig-1]: X-ray chest of a newborn with RDS. Cardiothymic: thoracic ratio (CT/T) was calculated by measuring the width of the cardio-thymic shadow at the level of carina and dividing it by the width of the thorax at the costo-phrenic angles.

STATISTICAL ANALYSIS

Analysis of continuous data with normal distribution was done by unpaired 't'-test and the data which was not normally distributed was analysed by Mann-Whitney test. One-way-ANOVA and 't'-test were used to compare values between different groups. Mc Fadden R-square and adjusted R-square models were used to find the relation between CT:T ratio and survival. The p-value of less than 0.05 was taken as significant.

RESULT

A total of 42 neonates were enrolled in the study [Table/Fig-2]. The base line characteristics of the study population is given in



[Table/Fig-2]: Showing neonates enrolled in the study.

Parameters	
Birth weight (grams)*	1527±433.44
Gestational Age (Weeks)*	32.83±2.49
Sex#	
Male	24(57.2%)
Female	18(42.8%)
Mode of Delivery#	
Vaginal	19(45.2%)
Caesarian	23(54.8%)
Birth Asphyxia#	18(42.8%)
Pre-eclampsia#	27(64.2%)
Antenatal Steroids#	12(28.5%)

[Table/Fig-3]: Baseline characteristic.
*Mean±SD; # n(%)

[Table/Fig-3]. The mean ±SD of birth weight and gestational age was 1527±433.44 grams and 32.83±2.49 weeks respectively. Only 12 neonates received antenatal steroids.

The mean ±SD cardiothymic thoracic ratio (CT:T) in the study was 0.367 ± 0.026. The CT:T in neonates who survived and those who expired was 0.36 and 0.38 respectively. There was no statistical difference between the two groups (p=0.33). A neonate with a CT:T of less than 0.403 had a 50% probability of survival. The mean CT:T in neonates with a birth weight of less than 1000 grams was higher (0.41) as compared to those with a birth weight of more than 1000 grams with a statistically significant p-value of 0.004 [Table/Fig-4]. There was no statistically significant difference in the CT:T in relation to gestational age, sex, mode of delivery, administration of antenatal steroids or presence of birth asphyxia or sepsis.

DISCUSSION

The mean ±SD cardiothymic thoracic ratio (CT:T) in the study was 0.367 ± 0.026 which is smaller than the mean of 0.40 found by Chen CM et al., [4]. However, Tooke LJ et al., in their study on 49 preterms found a slightly lower CT:T of 0.36 [8]. In neonates small thymus has been associated with infection

Characteristic		n(%)	Mean CT:T	p-value
Birth weight (in grams)	<1000	3(7)	0.41	0.004
	1000-1500	19(45)	0.37	
	>1500	20(47)	0.36	
Gestational Age (in weeks)	<32	10(24)	0.38	0.401
	32-34	20(48)	0.36	
	>34	12(28)	0.37	
Maturity	AGA	27(64)	0.36	0.431
	SGA	15(36)	0.37	
Outcome	Survival	31(74)	0.36	0.33
	Non-Survival	11(26)	0.38	
Sex	Male	24(57)	0.37	0.532
	Female	18(43)	0.36	
Antenatal Steroids	Yes	12(29)	0.36	0.188
	No	30(71)	0.37	
Ventillatory Support	Yes	17(40)	0.38	0.248
	No	25(25)	0.36	
Sepsis Screen	Positive	15(36)	0.36	0.219
	Negative	27(64)	0.37	
Mode of Delivery	Vaginal	19(45)	0.36	0.412
	Caesarian	23(55)	0.37	
Birth Asphyxia/ Delayed Cry	Yes	18(43)	0.37	0.820
	No	24(57)	0.36	

[Table/Fig-4]: CT:T ratio in relation to antenatal and post natal factors.

especially chorioamnionitis. Glavina-Durdov M et al., in their study on preterm neonates found that infection was more often associated with thymic involution than RDS [9]. Although, chorioamnionitis was not proven in any of the mothers in our study, neonates with a positive sepsis screen had a lower CT:T as compared to those with a negative sepsis screen. The difference was however statistically not significant. Although, studies show that post natal administration of glucocorticoids leads to smaller thymic size radiologically in the infant, the effect of antenatal exogenous steroid given to mother on thymic size is not well established. In our study, antenatal administration of steroids to the mother did not affect the CT:T ratio significantly. There was no significant difference in CT:T in relation to sex, mode of delivery or presence of asphyxia. This was similar to the findings of Chen CM et al., [4].

A significant positive correlation was found by Iscan A et al., and Yekelar E et al., between birth weight and thymic size when measured ultrasonographically [5,10]. In our study, similar trend was seen in neonates with gestational age of >32 weeks. However, in neonates with GA of <32 weeks there was a higher CT:T. There were 3 neonates of GA<30 weeks with birth weight <1000 gm. They had a CT:T of 0.41 which was significantly higher than that of those with a birth weight of >1000 gm (p=0.004).

RDS is an important cause of neonatal respiratory failure and deaths and prematurity is the single most important risk factor associated with RDS. Of the 42 neonates studied by us, 11 expired. The mean±SD of CT:T in those who survived was 0.36±0.23 , which was slightly lower than that of those who expired 0.38±0.27 although the difference was not statistically significant. A neonates with a CT:T of less than 0.403 had a 50% probability of survival.

In our study, the severity of RDS was more in non-survivors as compared to survivors. Also the incidence of sepsis was higher in non survivors as compared to survivors. The higher CT:T in neonates with more severe RDS may be due to the decrease in lung volume that is associated with RDS. Prolonged intrauterine stress, such as that seen in pre-eclampsia or chorio-amnionitis has been shown to cause involution of the thymus. This stress related involution appears to be mediated by the activation of hypothalamic-pituitary-adrenal (HPA) axis. The activation of HPA leads to a surge in serum corticosteroids which has been shown to have a thymocytolytic effect [11].

Neonates who are more preterm and are ELBW have a higher mortality rate. X-ray chest is a relatively cheap and easily available mode of investigation. Measurement of CT:T on X-ray chest done within 48 hours of life does not require much expertise and can even be used in the periphery for identification of high risk cases like neonates with larger CT:T having poorer prognosis. This can assist in decision making regarding early referral and help reduce mortality.

LIMITATIONS

The main limitation of our study was the small sample size.

CONCLUSION

Preterm neonates with RDS, who expired, had a larger CT:T ratio as compared to those who survived. X-ray chest being a relatively cheap and easily available investigation, a larger CT:T can be used as a prognostic marker. Preterms with a CT:T ratio of more than 0.40 should be closely observed for any worsening of symptoms and referred early to centers well equipped in managing RDS. This will help in significantly reducing the mortality associated with prematurity and RDS.

REFERENCES

[1] De Felice C, Latini G, Toti P, D'Addario V, Petraglia F, Bagnoli F. Small thymus at birth and gestational age. Eur J Pediatr. 2002;161:362-63.
[2] De Felice C, Latini G, Del Vecchio A, Toti P, Bagnoli F, Petraglia F. Small thymus at birth: A predictive radiological sign of bronchopulmonary dysplasia. Pediatrics. 2002;110(2):386-88.

[3] De Felice C, Toti P, Santopietro R, Stumpo M, Pecciarini L, Bagnoli F. Small thymus in very low birth weight infants born to mothers with subclinical chorioamnionitis. J Pediatr. 1999;135(3):384-86.
[4] Chen CM, Yu KY, Lin HC, Yeh GC, Hsu HH. Thymus size and its relationship to perinatal events. Acta Pediatr. 2000;89:975-78.
[5] Iscan A,Tarhan S, Guven H, Bilgi Y, Yuncu M. Sonographic measurement of the thymus in newborns: close association between thymus size and birth weight. Eur J Pediatr. 2000;159(3):223-24.
[6] Jeppesen DL, Hasselbalch H, Nielsen SD, Sorensen TU, Ersboll AK, Valerius NH et al. Thymic size in preterm neonates: a sonographic study. Acta Pediatr. 2003;92(7):817-22.
[7] Paetzal M. Respiratory distress syndrome (Grade 1-4) of the premature and newborn (IRDS). Ped Rad [Serial online]. Vol 2, no.11. URL: www.PedRad.info/?search=20021110223558.
[8] Tooke LJ, Smith J, Griffith-Richard S, Martz JS. Thymic size at birth in preterm infants with severe respiratory distress syndrome can be used to predict the likelihood of survival: A retrospective cohort study. SA Journal of Child Health. 2010;4(2):50-53.
[9] Glavina-Durdov M, Springer O, Capkun V, Saratlija-Novakovic Z, Rozic D, et al. The grade of acute thymic involution in neonates correlates with the duration of acute illness and with the percentage of lymphocytes in peripheral blood smear. Biol Neonate. 2003;83(4):229-34.
[10] Yekeler E, Tambag A, Tunaci A, Genchellac H, Dursun M. Analysis of thymus in 151 healthy infants from 0-2 yr of age. J Ultrasound Med. 2004;23(10):1321-26.
[11] de Felice C, Toti P, Musarò M, Peruzzi L, Paffetti P, Pasqui L, et al. Early activation of the hypothalamic-pituitary-adrenal axis in very low birth weight infants with small thymus at birth. J Matern Fetal Neonatal Med. 2008;21(4):251-54.

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