Original Research Paper

Volume - 12 | Issue - 11 | November - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Neonatology

COMPARISON OF PERINATAL RISK FACTORS IN NEONATES OF DIFFERENT GESTATIONAL AGE ADMITTED WITH RESPIRATORY MORBIDITY.

Dr Amita Surana	M.D. Ped Associate Professor, Dept of Pediatrics Surat Municipal Institute of Medical education and Research, Surat/India
Dr Nidhi Modi	M.D. Ped Ex PG student, Dept of Pediatrics Surat Municipal Institute of Medical education and Research, Surat/India
Dr Mital Gover	M.B.B.S. JR , Ped, Dept of Pediatrics Surat Municipal Institute of Medical education and Research, Surat/India
Dr. Bhavya Adroja	M.B.B.S. JR , Ped, Dept of Pediatrics Surat Municipal Institute of Medical education and Research, Surat/India

ABSTRACT **Background:** Respiratory disorders are most common cause of neonatal admissions in both term and preterm. Factors associated with neonatal respiratory morbidity (RM) are poorly described. **Objective:** To compare the frequency and risk factors for respiratory morbidity at different gestational age **Methods:** Hospital based cross sectional study over 15 months. Neonates with onset of respiratory distress within 72 hours of birth enrolled and divided into early preterm, late preterm and full term groups. Comparison was done to find the association of RM with neonatal, maternal and pregnancy related factors among three groups. Chi- square/ Annova/ Fisher's exact test was applied for Statistical signifance. **Results:** 150 neonates were analysed. The frequency of respiratory morbidity was 35%, 29% and 25% for group I, II & III respectively. Statistically significant neonatal factors were lower gestational age ($p < 0.001$), lower birth weight ($p < 0.001$), SGA especially late preterm & term SGA ($p<0.001$), male gender ($p=0.043$) especially term male (0.019) and late preterm/ term with low APGAR score (0.0033). Statistically significant maternal factors were young maternal age (< 20 year) in late preterm neonates (p 0.00028) and maternal gestational diabetes in term group (p 0.012). Pregnancy related factor analysis showed PIH ($p =0.01$), Placenta previa ($p =0.02$), Cord Prolapse ($p =0.02$), PROM > 24 hour ($p =0.03$), MSL ($p <0.001$) and LSCS delivery ($p = 0.01$) as significant risk factors for RM. **Conclusion:** Early and late gestation RM differs in term of potential perinatal factors. The gestational age and birth weight had inverse relationship with occurrence of RM. Risk factors such as PROM, placenta previa with early gestation; SGA,PIH, LSCS and young maternal age with late preterm while male gender, gestational DM, MSL and cord prolapse were significantly associated with term gestation RM.

KEYWORDS : Gestation, Morbidity, Neonate, Respiratory, Perinatal, Risk Factor

INTRODUCTION

Respiratory morbidities are the most common cause of neonatal admissions in NICU. [1] The overall prevalence of respiratory morbidities is 7 -8% among live births and respiratory problems are responsible for about 20% of neonatal mortality. [2, 3] The respiratory morbidity is due to pulmonary causes in 80% – 85% of cases while remaining 15% - 20% cases are due to extra-pulmonary causes. [2] Common pulmonary causes include Hyaline membrane disease (HMD), Transient tachypnea of newborn (TTN), Congenital pneumonia, Aspiration syndromes, Pneumothorax & air leaks, Pulmonary edema and pulmonary hemorrhage. [2] The causes and risk factors affecting lung adaptation and thus leading to respiratory distress may be different in late term gestation than in early term gestation. [3, 4] The present study was planned to find the frequency of respiratory morbidity at different gestational age at our centre and to find whether the risk factors for respiratory morbidity vary at different gestational age.

MATERIALS & METHODS:

Study setting, design & duration: this was a hospital based cross sectional observational study conducted among neonates admitted in SNCU of tertiary care centre. The study was conducted over a period of one and half year. Ethical clearance was obtained from institutional ethical committee. Written informed consent was taken from the parent of neonate.

Inclusion & exclusion criteria: study subjects: the study included all neonates having onset of respiratory distress within 72 hours of birth. Diagnosis of respiratory distress was based on presence of any two of the following feature: (1) Tachypnea (Respiratory rate > 60 / min), (2) Intercostal / subcostal retraction / Nasal flaring (3) Grunting . [1]

Neonates were excluded if they were: referred from other hospital, < 500 Gm or < 25 week gestation, had major congenital malformation or whose parents didn't give consent.

Data collection:

The enrolled neonates were divided into 3 groups based on their gestational age. Group I: Early preterm i.e. < 34 weeks gestational age. Group II: Late preterm babies i.e. Gestational age between 34 0/7 to 36 6/7 weeks. Group III: Term babies i.e. Gestational age between 37 0/7 to 41 6/7.

A detailed proforma was filled up regarding maternal, neonatal & delivery information. Maternal information included age, socio economic status, pre pregnancy weight, parity status, booked/ un-booked pregnancy, number of antenatal visits, presence of gestational diabetes, any systemic illness, maternal hemoglobin (Hb) and WBC count at the time of delivery was noted.

Pregnancy related / obstetric information included mode of delivery, type of liquor, intra-partum events such as premature rupture of membrane (PROM), cord prolapse, abruptio placentae, placenta previa and foul smelling liquor.

Neonatal information included gestational age, birth weight, gender, weight for gestation, APGAR score, multiple gestation, age at onset of respiratory symptoms, severity of respiratory distress at admission. Gestational age was estimated based on first day of last menstrual period (LMP). When LMP was not known gestational age was estimated by modified Ballard score. Severity of respiratory distress was assessed by Silverman Anderson score or Downe's score for preterm and term babies respectively. [1]

All the babies were subjected to baseline investigation like complete blood count (CBC), C reactive protein (CRP),X Ray chest, blood culture at admission as per the unit policy. Arterial blood gas (ABG) analysis was done within one hour of admission. Further investigations were done based on clinical condition.

The most likely etiological diagnosis for cause of respiratory distress was made based on history, clinical and radiological finding. Treatment was given as per standard protocols.

Sample size estimation: considering 10% prevalence of respiratory distress [5] with allowable error of 5%, sample size of 138 was determined. However 150 babies were recruited and analyzed during study period.

Statistical analysis: Data were entered in Excel sheet and analyzed using Open Epi software. Qualitative data were represented by percentages and proportions. Statistical significance was determined

by using Pearson's Chi- square test or Fisher's exact test as appropriate. Quantitative data were represented by mean with standard deviation and Statistical significance was determined by using Annova test for 3 groups. Level of significance was set at p value < 0.05.

Results:

Total 150 neonates having respiratory morbidity were included in the study. The point prevalence of respiratory morbidity was 35%, 29% and 25% for group I, II & III respectively. (figure 1)

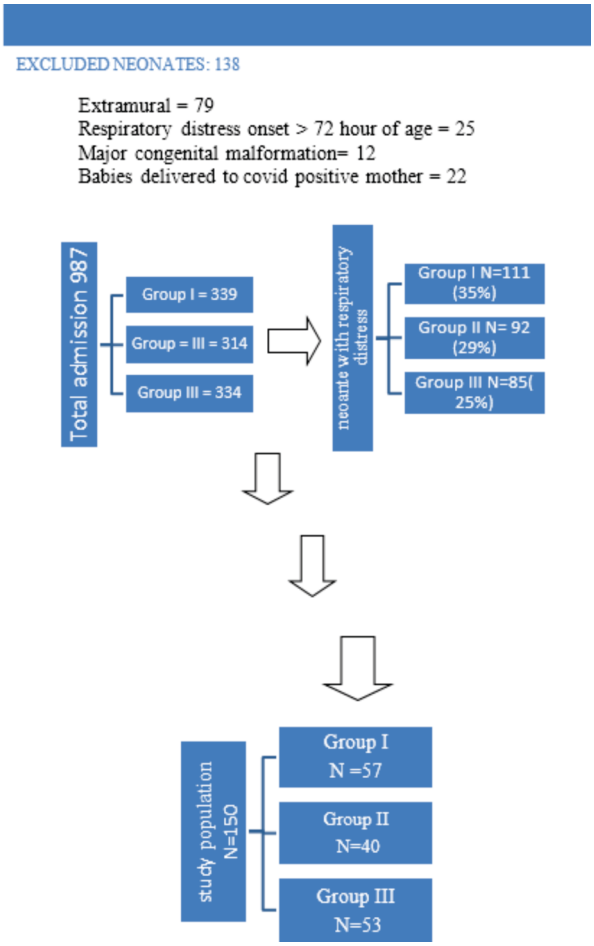

Figure 1: Study Group Enrollment

The common causes for respiratory morbidity noted in our study were HMD (27%), TTN (17%), Perinatal Asphyxia (17%), MAS (13%) and congenital Pneumonia (9%). The remaining 10 – 15% causes noted were CHD (3%), Congenital Diaphragmatic hernia (1%), Tracheo esophageal fistula (3%), Early onset sepsis (6%).

Table 1: Neonatal factors comparison

Variable	Group I N=57	Group II N=40	Group III N=53	P value	P1	P2	P 3
Gestational age(in weeks)							
Mean (S.D.)	30.46 (1.46)	34.96 (0.98)	38.41 (0.98)	< 0. 001	< 0. 001	< 0. 001	< 0. 001
Birth weight (in Kg)							
Mean (s.D.)	1.20 (0.19)	1.68 (0.22)	2.69 (0.49)	< 0. 001	< 0. 001	< 0. 001	< 0. 001
SGA n (%)	18 (32)	12 (30)	26 (49)	< 0. 0001	0. 68	< 0. 0001	< 0. 001
Male gender n(%)	25 (44)	25 (63)	35 (66)	0. 043	0. 07	0. 72	0. 019
Low APGAR score n(%)	6 (11)	5 (13)	19 (36)	0. 0033	0. 46	0. 005	0. 0008

*P1:pvalues between early and late preterm groups.P2:p values between late preterm and term groups.P3:p values between term and early preterm groups.

Table 1. Neonatal factors were compared between three groups. A statistically significant association for occurrence of respiratory morbidity was found between lower gestational age ($p < 0.001$) and lower birth weight ($p < 0.001$).Intergroup comparison was suggestive of inverse relationship of respiratory morbidity with gestational age ($p_1, p_2, p_3 < 0.001$) and birth weight ($p_1, p_2, p_3 < 0.001$).

Also in our study SGA neonates were significantly found to have respiratory morbidity as compared to AGA neonates ($p < 0.0001$). Intergroup comparison showed late preterm SGA had significant association with respiratory morbidity as compared to term SGA ($p < 0.0001$) and term SGA ($p < 0.001$) had significant association with respiratory morbidity as compared to early preterm SGA neonates.

Gender comparison showed male sex as a significant risk factor for respiratory morbidity ($p = 0.043$). Intergroup comparison showed term babies with male gender was significantly associated with respiratory morbidity as compared to preterm male babies. (66% v/s 44% ,$p = 0.019$).

Low APGAR score was significant risk factor for respiratory morbidity in our study (0.0033).Intergroup comparison showed late preterm and term babies with low APGAR score was significant risk factor for respiratory morbidity as compared to early preterm group.

Table 2. Maternal factor comparison

Variable	Group I N=57	Group II N=40	Group III N=53	P value
Maternal age (in years) n (%)				
< 20	5 (9)	15 (38)	5 (9)	0.00028
21 – 30	46 (81)	17 (42)	38 (72)	
>30	6 (10)	8 (20)	10 (19)	
Prepregnancy weight mean (S.D.)	54.70 (5.30)	55.65 (6.20)	54.38 (8.13)	0.8
Parity >= 2 n (%)	40 (70)	28 (70)	38 (72)	0.9
Booked pregnancy. n(%)	53 (93)	38 (95)	52 (98)	0.19
Antinatal visits >= 4 n(%)	46 (81)	37 (92)	46 (87)	0.48
Maternal systemic illness n(%)				
Gestational diabetes	1 (2)	3 (7)	7 (13)	0.04
Asthma	6 (11)	2 (5)	2 (4)	0.13
HIV	3 (5)	0	1 (2)	0.6
Heart disease	2 (4)	1 (2)	0	0.3
Seizure disorder	2 (4)	0	0	0.32

Table 2: Young maternal age (< 20 year) was significantly associated with respiratory morbidity in late preterm neonates as compared to early preterm or term group. Maternal gestational diabetes was significantly associated with respiratory morbidity (p 0.04).

No statistically significant association was found between maternal parity, maternal pre-pregnancy weight and maternal systemic illness other than gestational diabetes with respiratory morbidity in all three groups. Majority of the pregnancy was booked and had adequate antenatal visits in our study.

Table 3: Pregnancy complication & Obstetric intervention comparison

Variable	Group I n=57 n (%)	Group II n=40 n (%)	Group III n=53 n (%)	P value
Pregnancy induced hypertension	10 (18)	14 (35)	6 (11)	0.01
Eclampsia	5 (9)	7 (18)	8 (15)	0.14
Abruptio placenta	8 (14)	2 (5)	4 (8)	0.28
Placenta previa	10 (18)	3 (8)	1 (2)	0.02
Cord prolapse	2 (4)	3 (8)	10 (19)	0.02
PROM > 24 hour	12 (21)	7 (18)	2 (4)	0.03
Multiple pregnancy	11 (19)	3 (8)	6 (11)	0.21
Meconium stained liquor	2 (4)	2 (5)	20 (38)	< 0.001
Mode of delivery				
Vaginal delivery	25 (44)	4 (10)	23 (43)	0.0006
Cesarean section delivery	32 (56)	36 (90)	30 (57)	

Table 3: Pregnancy complication & obstetric intervention factor analysis showed PIH (p =0.01), Placenta previa (p =0.02), Cord Prolapse (p =0.02), PROM > 24 hour (p =0.03), MSL (p <0.001) and LSCS delivery (p = 0.01) as significant risk factors for respiratory morbidity.

DISCUSSION:

The present study was done to evaluate various perinatal factors associated with respiratory distress in early preterm, late preterm & term neonates. Out of 150 neonates admitted with respiratory distress 35% were early preterm, 29% late preterm and 25% were term babies.

Our analysis of neonatal factors showed significant association of respiratory morbidity with early gestation, lower birth weight, male gender and SGA neonates. The study done by V condo et al [6], J Wang et al [7], A Baseer et al [8] noted an inverse relationship of respiratory morbidity with gestational age and birth weight. A little different finding of bimodal incidence pattern by gestational age with a peak incidence at late preterm gestation then declining slightly at 37 weeks and rising again at >= 39 weeks gestation was observed by A Mehrabadi et al [4]. The occurrence of respiratory distress in early preterm babies is due to surfactant deficiency while in late preterm babies who are born in the late saccular stage of development have deficiency of surfactant as well as immature anti-oxidant system. The immature lung structure leads to delayed intrapulmonary fluid absorption, surfactant inefficiency and inefficient gas exchange. [6,9,10]This explains the higher incidence of respiratory morbidity in neonates of lower gestational age as maturity of fetal lung is slower. [6]

Male gender was observed to be a significant risk factor for respiratory morbidity by different studies. [4, 6, 11] This has been explained due to effect of male hormone androgen which delays fetal lung maturation by delaying development of type II alveolar cells. The androgens also delays the release of surfactant. [6,12]

The association of late preterm SGA and term SGA with respiratory morbidity was observed by V Condo et al [6] and A Mehrabadi et al [4] which is similar to our finding. The intrauterine stress which the SGA babies are subjected to may be the reason.

Low APGAR score is suggestive of perinatal asphyxia. The resultant hypoxia leads to respiratory center inhibition resulting in respiratory distress. [6] Our study found association of respiratory distress with term babies having low APGAR score. Similar observation was made by A mehrabadi et al too. [4]

Amongst maternal factors a significant association was found between late gestation respiratory morbidity with young maternal age (< 20 years) and gestational diabetes in our study. Some of the studies reported advanced maternal age (> 30 years) associated with late gestation RDS [8,14], some have reported young maternal age (< 20 years) associated with early gestation RDS [4] while some have reported no such influence of maternal age with occurrence of respiratory morbidity at any gestational age. [6,11,14] It is likely that factors other than direct effect of maternal age may be the reason for respiratory morbidities in these babies. Consistent to our finding of association of maternal gestational diabetes with respiratory morbidity in late preterm & term babies has been noted by other studies. [4,6,13] Similar to other studies we didn't found association of other maternal factors like pre-pregnancy weight, parity or multiple gestation with respiratory morbidity risk at different gestation.[6,7,15]

Amongst the pregnancy complication our study found PIH, MSL and cord prolapse to be associated with respiratory morbidity in late preterm and term neonates which is consistent to the previous findings. [4,6,7,8] The possible explanation for this association is increased susceptibility of fetal central nervous system to serious compromise leading to encephalopathy at later gestation.[4,16,17] Early gestation respiratory morbidity was associated with PROM and placenta previa in our study. J Wang et al [7] and Aynelam et al [13] made similar observation with PROM and early gestation RDS. However no such association was found between placenta previa with RDS. [7,14]

Babies born via cesarean section have been consistently found at increased risk of developing respiratory morbidity in most studies. [5,6,18] Late preterm cesarean delivered babies were found to be at increased risk of RDS as compared to early gestational babies in most studies. [4,6,7,19] Similar finding was observed in our study. Cesarean section influence in causing respiratory morbidity is due to multiple factors like lung fluid retention, less surfactant secretion, insufficient activation of sympathetic nervous system, exposing neonates to increased risk of developing RDS. [7]

Our study included neonates of different gestational age. Limited data available in Indian literature about comparison of perinatal factors in causing respiratory morbidity at different gestation. So our study can help in generating data for further research taking Indian population into consideration. The limitation of our study includes of being hospital based study with relatively small sample size. We would also like to recommend further studies involving neonates of different gestational age with denominator as neonates of different gestational age without respiratory distress.

CONCLUSION

Early and late gestation respiratory morbidity differs in term of potential perinatal factors. The gestational age and birth weight shows an inverse relationship with occurrence of RDS. Risk factors such as PROM, placenta previa with early term; SGA babies, PIH and young maternal age with late preterm while male gender, gestational diabetes mellitus, MSL and cord prolapse were significantly associated with term gestation respiratory morbidity.

Source of Funding: Nil
Conflict of Interest: None

REFERENCES:

1) Singh M. Care of the Newborn. 9th Edi. CBS Publication: New Delhi. 2021. Chapter 19, Respiratory Disorders; p. 358 - 385.
2) Bajad, M., Goyal, S., & Jain, B. (2016). Clinical profile of neonates with respiratory distress. International Journal of Contemporary Pediatrics, 3(3), 1009-1013. doi:http://dx.doi.org/10.18203/2349-3291.ijcp20162382
3) Neonatal morbidity and mortality: Report of the national neonatal perinatal data base. Indian Pediatr. 1997;34:1039-42.
4) Mehrabadi, A., Lisonkova, S. & Joseph, K. Heterogeneity of respiratory distress syndrome: risk factors and morbidity associated with early and late gestation disease. BMC Pregnancy Childbirth 16, 281 (2016). https://doi.org/10.1186/s12884-016-1085-7
5) Anadkat JS, Kuzniewicz MW, Chaudhari BP, Cole FS, Hamvas A. Increased risk for respiratory distress among white, male, late preterm and term infants. J Perinatol. 2012 Oct;32(10):780-5. doi: 10.1038/jp.2011.191. PMID: 22222548; PMCID: PMC3461404.
6) Condò V, Cipriani S, Colnaghi M, Bellù R, Zanini R, Bulfoni C, Parazzini F, Mosca F. Neonatal respiratory distress syndrome: are risk factors the same in preterm and term infants? J Matern Fetal Neonatal Med. 2017 Jun; 30(11):1267-1272. doi: 10.1080/14767058.2016.1210597. PMID: 27399933.
7) Wang J, Liu X, Zhu T, Yan C. Analysis of neonatal respiratory distress syndrome among different gestational segments. Int J Clin Exp Med. 2015 Sep 15;8(9):16273-9. PMID: 26629144; PMCID: PMC4659032.
8) Baseer KAA, Mohamed M, Abd-Elmawgood EA. Risk Factors of Respiratory Diseases Among Neonates in Neonatal Intensive Care Unit of Qena University Hospital, Egypt. Ann Glob Health. 2020 Feb 26;86(1):22. doi: 10.5334/aogh.2739. PMID: 32140431; PMCID: PMC7047767.
9) Ruth CA, Roos N, Hildes-Ripstein E, Brownell M. 'The influence of gestational age and socioeconomic status on neonatal outcomes in late preterm and early term gestation: a population based study'. BMC Pregnancy Childbirth. 2012 Jun 29;12:62. doi: 10.1186/1471-2393-12-62. PMID: 22748037; PMCID: PMC3464782.
10) Cheng YW, Kaimal AJ, Bruckner TA, Halloran DR, Caughey AB. Perinatal morbidity associated with late preterm deliveries compared with deliveries between 37 and 40 weeks of gestation. BJOG. 2011 Nov;118(12):1446-54. doi: 10.1111/j.1471-0528.2011.03045.x. Erratum in: BJOG. 2011 Dec;118(13):1687. Hallaron, D R [corrected to Halloran, D R]. PMID: 21883872; PMCID: PMC3403292.
11) Badran EF, Abdalgani MM, Al-Lawama MA, Al-Ammouri IA, Basha AS, Al Kazaleh FA, Saleh SS, Al-Katib FA, Khader YS. Effects of perinatal risk factors on common neonatal respiratory morbidities beyond 36 weeks of gestation. Saudi Med J. 2012 Dec;33(12):1317-23. PMID: 23232680.
12) Liu J, Yang N, Liu Y. High-risk Factors of Respiratory Distress Syndrome in Term Neonates: A Retrospective Case-control Study. Balkan Med J. 2014 Mar;31(1):64-8. doi: 10.5152/balkanmedj.2014.8733. PMID: 25207170; PMCID: PMC4115996.
13) Aynalem YA, Mekonen H, Akalu TY, Habtewold TD, Endalamaw A, Petrucka PM, Shiferaw WS. Incidence of respiratory distress and its predictors among neonates admitted to the neonatal intensive care unit, Black Lion Specialized Hospital, Addis Ababa, Ethiopia. PLoS One. 2020 Jul 1;15(7): e0235544. doi: 10.1371/journal.pone.0235544. PMID: 32609748; PMCID: PMC7329073.
14) Kuti BP, Mohammed LO, Oladimeji OI, Ologun BG, Kuti DK, Fawale OO. Respiratory distress in nigerian neonates: Prevalence, severity, risk, and etiological factors and outcome. Niger J Basic Clin Sci 2018;15:42-9
15) Bicocca MJ, Blackwell SC, Sibai BM. Does Prepregnancy Weight or Maternal BMI at Betamethasone Administration Impact Late Preterm Respiratory Morbidity? Am J Perinatol. 2020 Mar; 37(4):365-369. doi: 10.1055/s-0039-1696644. PMID: 31529450.
16) Hayes BC, McGarvey C, Mulvany S, Kennedy J, Geary MP, Matthews TG, King MD. A case-control study of hypoxic-ischemic encephalopathy in newborn infants at >36 weeks gestation. Am J Obstet Gynecol. 2013; 209(1):29 e1–e19. DOI: https://doi.org/10.1016/j.ajog.2013.03.023
17) Badawi N, Kurinczuk JJ, Keogh JM, Alessandri LM, O'Sullivan F, Burton PR et al. Antepartum risk factors for newborn encephalopathy: the western Australian case – control study. BMJ 1998; 317: 1549. Doi:10.1136/bmj.317.7172.1549.
18) Hansen AK, Wisborg K, Uldbjerg N, Henriksen TB. Risk of respiratory morbidity in term infants delivered by elective caesarean section: cohort study. BMJ. 2008 Jan 12;336(7635):85-7. doi: 10.1136/bmj.39405.539282. PMID: 18077440; PMCID: PMC2190264.
19) Ghartey K, Coletta J, Lizarraga L, Murphy E, Ananth CV, Gyamfi-Bannerman C. Neonatal respiratory morbidity in the early term delivery. Am J Obstet Gynecol. 2012 Oct; 207(4):292.e1-4. doi: 10.1016/j.ajog.2012.07.022. PMID: 22902075.