



An Investigation on the Incidence and Risk Factors of Respiratory Distress Syndrome, Pneumonia, and Seizures in Newborns

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ABSTRACT

The study was conducted to investigate the incidence of respiratory distress syndrome, pneumonia and seizures in newborns. It was a prospective observational study. Preterm and full term neonates born in NICU were included in the study and totally 658 cases were recruited. The study showed that the incidence of RDS, pneumonia and seizures in preterm newborns was much higher than in term newborns. Comparing c-section and NVD the incidence of RDS, pneumonia and seizures were 4:1, 1.1:1 and 1.44:1 respectively. The incidence of RDS and seizures was higher in male newborns than in female newborns which were 2.67:1 and 1.75:1 respectively. Incidence of RDS in mothers with complications who undergo drug therapy was 5.64%. There was a higher incidence of RDS in newborns with birth weight ranging between 2-3.5 kg and for pneumonia and seizures it was 1.5-3.5 kg. The incidence of RDS and pneumonia was higher in the newborns of mothers in the age group 20-30 years and seizures it was 20-25 years. The incidence of RDS, pneumonia and seizures is considerably higher in Indian rural population, which should be improved by proper education and timely medical care.

Keywords: RDS, Pneumonia, Seizure, Prospective, NICU, incidence.

INTRODUCTION

Respiratory distress syndrome (RDS) is one of the main syndromes occurring in premature newborns (< 37 weeks). It is one of the main life threatening syndromes in newborns if adequate management is not provided. Its rate of incidence is higher in premature newborns compared to term newborns this condition makes the newborn difficult to breathe¹. Globally, RDS has been estimated to occur in 20,000-30,000 newborn infants each year and is a complication in about 1% pregnancies. Approximately 50% of the neonates born at 26-28 weeks gestation develop respiratory distress syndrome, whereas less than 30% of premature neonates born at 30-31 weeks gestation develop the condition².

Pneumonia is the most frequent invasive bacterial infection in newborns, which require prolonged endotracheal intubation because of lung disease. Late-onset pneumonia usually occurs after 7 days of age, most commonly in neonatal ICUs newborns. Neonatal pneumonia is a serious respiratory infectious disease caused by a variety of microorganisms, mainly bacteria, with the potential of high mortality and morbidity³. Worldwide, neonatal pneumonia is estimated to account for up to 10% of childhood mortality, with the highest case fatality rates reported in developing countries. Reported frequencies of neonatal pneumonia range from 1 to 35 %, most commonly 1% for term newborns and 10% for preterm newborns. The incidence varies according to gestational age, intubation status, diagnostic criteria or case definition, the level and standard of neonatal care, race and socioeconomic status.

Neonatal seizures or neonatal convulsions are epileptic fits occurring from birth to the end of the neonatal period. The neonatal period is the most vulnerable of all periods of life for developing seizure, particularly in the first 1–2 days to the first week from birth. They may be short-lived events lasting for a few days only. However, they often signify serious malfunction of or damage to the immature brain and constitute a neurological emergency demanding urgent diagnosis and management. Most neonatal seizure are focal (seizure initially affects only on one hemisphere of the brain), because of the generalization, electrical activity is delayed in neonates by deficiency of myelination and incomplete formation of dendrites and synapses in the brain⁴. The prevalence of seizures is approximately 1.5% and overall incidence approximately 3 per 1000 live births. The incidence in pre-term infants is very high (57–132 per 1000 live births). Most (80%) neonatal seizures occur in the first 1–2 days to the first week of life⁵.

Many researchers have conducted trials to study the incidence of RDS, Pneumonia, and Seizures in newborns. In the year 2015, Keerti Swarnkar *et al* conducted a prospective study on neonatal respiratory distress in early neonatal period⁶. In the year 2003, Ghafoor T and his colleagues performed a prospective study on incidence of respiratory distress syndrome⁷.

In the year 2007, Numan Nafie and his colleagues conducted a case control study on respiratory distress in full term newborns to assess some possible risk factors, types, and short term outcome of RD in full term newborns⁸. In 2006, Ahmad f Bakr *et al* conducted a prospective study on severe respiratory distress in term



infants born electively at high altitude⁹. In 2016, Sayid M Barkiya and his colleagues conducted a prospective study on Clinico-Etiological Profile and Outcome of Neonatal Respiratory Distress¹⁰. In 2015, Maryam Saboute and her colleagues conducted a study on the incidence of respiratory distress syndrome among preterm infants admitted to neonatal intensive care unit: a retrospective study¹¹.

In 1999, Gabriel M. Ronen conducted a study on the epidemiology of clinical neonatal seizures to study the incidence, clinical features, etiologic distribution, and day of seizure onset by etiology in neonates with seizures¹². In 2009, December, Frances E. Jensen, MD conducted a study on Neonatal Seizures: An Update on Mechanisms and Management The lifespan risk of seizures is highest in the neonatal period¹³. In March 2006, Manoel R.R. Holanda conducted a prospective comparative clinical study on preterm and full-term newborn neonatal seizures¹⁴. In 2007, Gabriel M. Ronen, MD, conducted prospective study on Long-term prognosis in children with neonatal seizures. In the year 2002, N.B. Mathur, K. Garg and S. Kumar conducted a prospective descriptive study on respiratory distress in neonates with special reference to pneumonia.

The objective of the study was to calculate the incidence proportion, incidence odds and odds ratio for

1. The number of preterm and term newborns who shows signs of RDS, pneumonia, and seizures.
2. To assess the incidence of RDS, pneumonia, and seizures in male and female newborns.
3. To assess the incidence of RDS, pneumonia, and seizures in newborns of mothers with risk factors.
4. To assess the incidence of RDS, pneumonia, and seizures in relation with body weight of the newborns.
5. To assess the incidence of RDS, pneumonia, and seizures in relation with age of the mother.

Many epidemiological studies and supportive literature state that RDS is one of the important reasons for persistent neonatal morbidity and mortality in developed countries. But in developing countries like India the reported cases of incidence of RDS is less compared to that of developed countries. But studies show that, since much childbirth in India occur at home and villages the incidence of RDS goes unreported and the actual epidemiology of RDS in newborns in India is not well understood.

The study was designed in an attempt to understand the actual incidence of RDS and also convulsion or seizures and pneumonia, which were expected to be reported at hospitals in rural and city suburb regions in Salem district.

The study was conducted enrolling the mothers strictly on the basis of underlying diseases and disorders, age, and medications. So the results were expected to be unbiased and non-confounding.

Since the study was conducted in hospitals located in rural and city/township regions it was expected to give a clear report on the incidence of RDS and also seizures and pneumonia, and the results were expected to be more reliable, repeatable and reproducible.

METHODOLOGY

Study design: Prospective observational.

Study center: Vivekanandha Medical Care Hospital, Tiruchengode.

Study duration: 6 months (180 days)

Ethical clearance: The approval for conducting the study was issued by the Institutional Ethical Committee (IEC) of Vivekanandha Medical Care Hospital. Ref. No. SVCP/ IEC/ JAN/2016/02, dated 17/1/2016. Patient Consent was taken from the participants before the start of the study.

Sample population

Total no. of newborns enrolled: 658

No. of full-term babies: 559

No. of pre-term babies: 99

Inclusion criteria

1. Neonates who were born during the course of the study.
2. Birth weight ≥ 1000 g.
3. Preterm newborns admitted with respiratory distress syndrome, convulsion or seizures, and pneumonia.
4. Full-term newborns admitted with respiratory distress syndrome, convulsion or seizures, and pneumonia.

Exclusion criteria

The following patients were excluded from the study

1. Newborns without respiratory distress syndrome, pneumonia and seizure.
2. Age of mother >40 years.
3. Mothers under cancer chemotherapy.

Formulae used

Incidence Proportion: No. of incidences/Total no. of enrollees; Maximum possible value is 1.

Percentage Risk/Incidence Percentage: Incidence Proportion $\times 100$; Maximum value is 100%.

Incidence Odds: No. of incidences/No. of enrollees without any outcome; Maximum possible value is total no. of enrollees.

Odds Ratio:



No. of incidences/No. of enrollees without any outcome
(Mothers with complications)

No. of incidences/No. of enrollees without any outcome
(Mothers without complications)

RESULTS

Demography

The demography of the study population indicates clearly that complications during pregnancy are more common among Indian population as explained by Table 1.

Table 1: Demography of the study population

NEWBORNS (658)			
Full term (559)		Preterm (99)	
Mothers with complication	Mothers without complication	Mothers with complication	Mothers without complication
421	138	97	2
64%	21%	14.7%	0.3%
85%		15%	

Full term-Preterm ratio was 5.65:1

Full term (mothers) – with complications-without complications ratio was 3.05:1

Preterm (mothers) – with complications-without complications ratio was 48.5:1

Mothers with complications – Full term-preterm ratio was 4.34:1

Mothers without complications – Full term-preterm ratio was 69:1

Incidence of RDS in Newborns

Incidence of RDS in full term newborns based on pathophysiological condition of mother:

Totally there were 13 incidences of RDS. Mothers with gestational diabetes mellitus gave birth to more number of full term babies than others with RDS as shown by Table 2.

Table 2: Incidence of RDS in full term newborns based on pathophysiological condition of mother

Full Term Newborns			
Pathophysiological condition of mother	No. of newborns having RDS		Total
	Male	Female	
Normal	1	0	1
Gestational Diabetes mellitus	4	2	6
Thyroid disorders	1	1	2
Hypertension	2	0	2
Oligohydramnios	1	0	1
Asthma	1	0	1
Total	10	03	13
Percentage	76.7%	23.3%	100%

Incidence Proportion (full term): $13/559=0.0232$

Percentage risk/Incidence percentage: $0.0232 \times 100 = 2.32\%$

Incidence odds: $13/546=0.0238$

Incidence odds (mothers with complications): $12/409 = 0.0293$

Incidence odds (mothers without complications): $1/137 = 0.0072$

Odds Ratio: $0.0293/0.0072 = 4.07$

Incidence of RDS in preterm newborns based on pathophysiological conditions of mother

Totally there were 17 incidences of RDS. Mothers with gestational diabetes mellitus gave birth to more number of full term babies than others with RDS as shown by Table 3. But mothers with thyroid disorders and hypertension also gave birth to newborns with RDS.



Table 3: Incidence of RDS in preterm newborns based on pathophysiological condition of mother

Preterm Newborns			
Pathophysiological condition of mother	No. of newborns having RDS		Total
	Male	Female	
Normal	1	0	1
Gestational Diabetes mellitus	5	2	7
Thyroid disorders	3	1	4
Hypertension	2	1	3
Oligohydramnios	1	0	1
Asthma	0	1	1
Total	12	5	17
Percentage	70.5%	29.5%	100%

Incidence Proportion (Preterm): $17/99=0.1717$

Percentage risk: $0.1717 \times 100 = 17.17\%$

Incidence odds: $17/82 = 0.2073$

Incidence odds (mothers with complications): $16/81 = 0.1975$

Incidence odds (mothers without complications): $1/1 = 1$

Odds Ratio: $0.1975/1 = 0.1975$

Incidence of RDS in newborns of mothers under medication

Of the 30 mothers whose newborns were having RDS 28 were under medication for various Pathological conditions. Table 4 explains it.

Table 4: Effect of mothers' medication on newborns

Mothers' medication	No. of newborns having RDS	Percentage
Methyldopa	3	10.7%
Metformin	4	14.28%
Labetolol	2	7.1%
Bronchodilators	1	3.67%
Thyroxine	2	7.14%
Other Medications:- antidiabetic, antihypertensive drugs, etc.	16	57.2%
Total	28	100%

Incidence Proportion (Mothers under medication): $28/518=0.0540$

Percentage risk: $0.0540 \times 100 = 5.4\%$

Incidence odds: $28/490 = 0.0571$

Incidence odds (mothers under medication): $28/462 = 0.0606$

Incidence odds (mothers not under medication): $2/138 = 0.0144$

Odds ratio: $0.0606/0.0144 = 4.21$

The newborns born of caesarean section had more incidences of RDS than the babies born by normal vaginal delivery. The caesarean - normal vaginal delivery ratio for incidence of RDS was 4:1. Of the 30 newborns who had RDS, 22 were male and 8 were female. The Male – Female ratio of incidence of RDS was 2.75:1. The incidence of RDS was higher in the group with birth weight ranging between 3-3.5 kg and 22.5 kg. The incidence of RDS was

higher with newborns of mothers of the age group 20-25 and 26-30 years.

Incidence of Pneumonia In Newborns

Incidence of pneumonia in full term newborns based on pathophysiological conditions of mother

Only mothers with asthma were reported to be having full term newborns with pneumonia.

Incidence Proportion (full term): $4/559 = 0.0071$

Percentage risk: $0.0071 \times 100 = 0.71\%$

Incidence odds: $4/514 = 0.0077$

Incidence odds (mothers with complications): $4/417 = 0.0095$

Incidence odds (mothers without complications): $0/138 = 0$

Odds ratio: $0.0095/0 = \infty$



Incidence of pneumonia in preterm newborns based on pathophysiological conditions of mother

The mothers of all the 6 preterm babies with pneumonia were reported to be having asthma.

Incidence Proportion (preterm): $6/99 = 0.0606$

Percentage risk: $0.0606 \times 100 = 6.06\%$

Incidence odds: $6/512 = 0.0117$

Incidence odds (mothers with complications): $6/91 = 0.0659$

Incidence odds (mothers without complications): $0/2 = 0$

Odds Ratio: $0.0659/0 = \infty$

The newborns born of caesarean section had slightly more incidence of pneumonia than the babies born by normal vaginal delivery. The caesarean - normal vaginal delivery ratio for incidence of pneumonia was 1.5:1. Of the 10 newborns having pneumonia 6 were male and 4 were female.

The Male – Female ratio of incidence of pneumonia was 1.5:1. The incidence of pneumonia was higher in the group with birth weight ranging between 1.5-3.5 kg. The incidence of RDS was higher with newborns of mothers of the age group 20-25 and 26-30 Years.

Incidence of Seizures in Newborns**Incidence of seizures in full term newborns based on pathophysiological conditions of mother**

Only mothers with gestational diabetes mellitus and hypertension were reported to be having full term newborns who had incidence of seizures.

Incidence Proportion (full term): $4/559 = 0.0071$

Percentage risk: $0.0071 \times 100 = 0.71\%$

Incidence odds: $4/514 = 0.0077$

Incidence odds (mothers with complications): $4/417 = 0.0095$

Incidence odds (mothers without complications): $0/138 = 0$

Odds Ratio: $0.0095/0 = \infty$

Incidence of seizures in preterm newborns based on pathophysiological conditions of mother

The mothers of all the 4 preterm babies with seizures were reported to be having gestational diabetes mellitus and those of the other 3 preterm babies were having hypertension.

Incidence Proportion (preterm): $7/99 = 0.0707$

Percentage risk: $0.0707 \times 100 = 7.07\%$

Incidence odds: $7/511 = 0.0136$

Incidence odds (mothers with complications): $7/90 = 0.0777$

Incidence odds (mothers without complications): $0/2 = 0$

Odds Ratio: $0.0777/0 = \infty$

The newborns born of caesarean section showed more incidences of seizures than the babies born by normal vaginal delivery. The caesarean - normal vaginal delivery ratio for incidence of seizures was 1.75:1. Of the 11 newborns having seizures 7 were male and 4 were female. The Male –Female ratio of incidence of seizures was 1.75:1. The incidence of seizures was higher in the group with birth weight ranging between 1.5-3.5 kg. The incidence of seizures was higher with newborns of mothers of the age group 20-25 years.

INCIDENCE OF RDS, PNEUMONIA, AND SEIZURES

Table 5 shows the entire picture of the incidence of RDS, Pneumonia, and Seizures in newborns with respect to the prevalence of complications in the mother.

Incidence of RDS, Pneumonia, and Seizures With Reference to Mother's Pathological State

Table 6 explains the influence of mother's pathological state on the incidence of RDS, pneumonia, and seizures.

Different Types of Therapy Given to Treat Neonatal RDS

The selection of therapy for neonatal RDS differs from patient to patient and it is decided by the severity of the disease. Table 7 tells about the various treatment options for neonatal RDS.

DISCUSSION

The demography of the study population says that for every 6 full term births there is a possibility for one preterm birth. The prevalence or incidence of complications in mothers was higher even in them who had full term babies. The prevalence or incidence of complications in mothers is even much higher in them who had preterm babies. The complicated mothers gave birth to preterm babies most of the time.

The incidence of RDS in full term newborns was found to be 2.37%, which is supporting the study results of Keerthi Swarnkar *et al* and Numan Nafie *et al*, which were 2.83% and 2.16% respectively.

Our study also shows that for every 9 RDS newborn cases in complicated mothers there is 1 RDS newborn case in uncomplicated mothers. But in preterm newborns there is an incidence of 17.13% RDS cases which is considered high.



Table 5: Incidence of RDS, Pneumonia, and Seizures

Risk of newborns	RDS		Pneumonia		Seizures	
	+ve	-ve	+ve	-ve	+ve	-ve
Mothers with complication	28	490	10	508	11	507
Mothers without complication	2	138	0	140	0	140
Total	30	628	10	648	11	647
Percentage	4.5%	95.4%	1.5%	98.4%	1.6%	98.3%

Table 6: Incidence of RDS, Pneumonia, and Seizures with reference to mother's Pathological state

Underlying diseases or disorders of the mother	RDS		Pneumonia		Seizure	
	+ve	-ve	+ve	-ve	+ve	-ve
Diabetes mellitus	13	20	0	33	7	26
Hypertension	5	53	0	58	4	54
Thyroid disorders	6	23	0	29	0	29
Anaemia	0	354	0	354	0	354
Oligohydramnios	2	32	0	34	0	34
Asthma	2	8	10	0	0	10
Total	28	490	10	508	11	507
Percentage	5%	95%	2%	98%	2.2%	97.8%

Table 7: Different types of therapy given to treat Neonatal RDS

Treatment for RDS	No. of newborns	Percentage
CPAP (Continuous Positive Airway Pressure)	10	33.3%
Surfactant Replacement Therapy	5	16.6%
Mechanical Ventilation	15	50%
Total	30	100%

As per Ghafoor *et al*, the incidence of RDS in full term and preterm newborns were 0.11% and 37.28% respectively. He also states that the incidence of RDS is 3.7% at 36 weeks. Our value (17.13%) for preterm newborns comes within this range between 3.7% and 37.28%. As per Moravedji *et al*, the incidence of RDS in preterm newborns between 34-36 weeks was 16.7%, which is very close to our number 17.13%. Our study shows that for every 4 incidences of RDS in newborns of caesarean section there is 1

Incidence of RDS in newborns of normal vaginal delivery. Also, it shows that the incidence of RDS is higher in male babies than in female babies, which is 2.67:1. There was a 5.64% incidence of RDS in complicated mothers who undergo drug therapy, while the incidence was very rare in newborns of mothers who were not in medication.

There was a higher incidence of RDS in newborns with birth weight ranging between 2-3.5 kg. The incidence of RDS was higher in the newborns of mothers in the age group 20-30 years.

The incidence of Pneumonia is higher, 5.56%, in preterm newborns, than in full term newborns. As per Dr. Michael E Speers the incidence of pneumonia in full term newborns is less than 1%, which is well supported by our study which was 0.74%. Only complicated mothers were noted to be having newborns with pneumonia. There was no incidence of pneumonia in newborns of uncomplicated mothers. The possibility of incidence of pneumonia is 1.1:1 both in newborns of caesarean section and normal vaginal delivery. The incidence of pneumonia is slightly more in male newborns than in females. The incidence of pneumonia was higher in newborns of the weight range between 1.5-3.5 kg. The incidence of pneumonia was higher in the newborns of mothers in the age group 20-30 years.

The incidence of seizures in preterm babies is 6.48% which is higher than that in full term babies which is 0.65%. Our study supports the NCBI sources which tell that the incidence of seizure in preterm newborns is 5.7-13.2%. But as per Frances E Jensen the incidence of seizures in newborns is 3.9% in preterm babies. As per Gabriel M. Ronen *et al*, the incidence of seizures in full term and preterm neonates of Newfoundland are 2% and 11.1% respectively, which were very close to our study



values. This can be justified by that the incidences of neonatal complications are low in developed countries compared to developing countries like India.

However, the incidence of seizures is common in newborns of both complicated and uncomplicated mothers. The possibility of incidence of seizure is 1.44:1 both in newborns of caesarean section and normal vaginal delivery. The incidence of seizures is more (1.75:1) in male newborns than in females. The incidence of seizures was higher in newborns of the weight range between 1.5-3.5 kg. The incidence of seizures was higher in the newborns of mothers in the age group 20-25 years. We conclude that the incidence of RDS in preterm newborns was much higher than in term newborns. This indicates that hospitalization of newborns for RDS has increased.

Most of the neonatal RDS cases reported were of preterm newborns. Newborns born of caesarean section are having the highest risk of having RDS. Moderate exercises can be recommended to pregnant women so that the incidence of c-section can be possibly reduced.

Pregnant women under medications for chronic conditions are having the highest probability of giving birth to newborns with RDS. So, their prescription drugs should be checked frequently to avoid preterm births as well as the incidence of RDS in the newborns.

The incidence of pneumonia and seizure is lower compared to that of RDS. However, the incidence is higher in preterm newborns and mothers with underlying complications. The incidence of RDS is predominant in male than the female newborns. Birth weight of the neonate also has considerable effect over the incidence of RDS, pneumonia and seizure in newborns.

By this we conclude that the incidence of RDS, pneumonia and seizure is considerably higher in Indian rural population, which should be improved by appropriate education and timely medical care.

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