# Respiratory Distress and Its Outcome among Neonates Admitted to Neonatal Intensive Care Unit of Assiut University Children Hospital, Egypt

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## Abstract

**Objective:** To identify proportion and etiology of respiratory distress (RD), its mortalities and associated risk factors among neonates admitted to Neonatal Intensive Care Unit (NICU) of Assiut University Children Hospital. **Methods:** A cross-sectional study design was carried out. All RD neonates admitted to NICU of Assiut University Children Hospital during the study period were included. **Results:** Respiratory distress neonates constituted 52.9% of total admission. Hyaline membrane disease represented 45.8% of RD cases. The majority of hyaline membrane disease cases (RDS) were preterm and low birth weight (96.2% & 93.7% % respectively). The majority of hyaline membrane diseased neonates who were treated by surfactant or Continuous Positive Airway Pressure (CPAP) recovered (75.8%& 66.7% respectively) with significant statistically difference. The most fatal of respiratory distress diseases were persistent pulmonary hypertension (91.2%). Significant independent factors associated with neonatal mortalities due to respiratory distress were residence, causes of RD, birth weight and place of delivery. **Conclusion:** Hyaline membrane disease, pneumonia, transient tachypnea of the newborn (TTN), meconium aspiration syndrome (MAS) were important causes of neonatal respiratory distress. Residence, causes of RD, birth weight and place of delivery were significantly associated with respiratory distress mortalities. **Recommendation:** Development of strategies aiming to reduction of RD among neonates is highly recommended. Moreover, surveillance programs for neonatal mortality should be coupled with preventive measures and interventions for better natal care and postnatal outcome.

**Key words**: *respiratory distress, neonate, Neonatal Care Unit, outcome, Assiut University Children Hospital.*

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## Introduction

The neonatal period (first month of life) conveys the most prominent dangers of death in the human life expectancy. To study neonatal mortality, it is required to know causes of disease, its distribution and transmission cause-of-death and wellbeing intercession.[1]

The causes of early neonatal death (first 24 hours) are different from those that occur later. To improve outcome of interventions programs, it is important to know précised data about timing and causes of death.[2] The most important cause of neonatal morbidity and mortality is respiratory distress (RD). It commonly occurs in premature babies, with an

occurrence and seriousness conversely related to gestational age and birth weight. The incidence of RD is 1% of all births, however increases to 50% at 30 weeks gestation, 75% at 28 weeks and 90% at 26 weeks.[3]

Apnea, cyanosis, inspiratory stridor, snorting nasal flaring, grunting, feeding problem, and tachypnea (over 60 breaths in step with minute) are important signs and symptoms of respiratory distress of neonate. In addition to intercostals and sub costal retractions. Hyaline membrane diseases, transient tachypnea of the neonate (TTN), or meconium aspiration syndrome (MAS) are the most widely recognized reasons for RD. In addition, sever infection as pneumonia, persistent pulmonary hypertension of the newborn, and pneumothorax considered major causes.[4]

In NICU, RD of neonate is significant problem. The important risk factors of RD are: history of maternal smoking, male sex and elective caesarian delivery. Usage of antenatal corticosteroid drugs and holding up delivery until 39 weeks are significant interventions for decreasing RD after elective C/S at term.[5]

RD is an important cause of neonatal mortality globally particularly in developing countries. The fundamental interventions of oxygen and continuous positive airway pressure (CPAP) have the best effect on diminishing RD and its mortality globally.[6]

In Egypt, a study of neonatal mortality in intensive care unit in children's hospital, Cairo University revealed that mortality from RD among neonates comprise 26.7% of all deaths and constitute 9.6% and one of important causes of admission to the NICU.[7]

Decrease morbidity and mortality due to RD in Neonatal Intensive Care Unit of Assiut University Children Hospital, Egypt and improve neonatal health is the main goal of this study. **Objectives:** (1) To identify proportion and etiology of RD among neonates admitted to Neonatal Intensive Care Unit (NICU) of Assiut University Children Hospital. (2) To identify mortalities (case fatalities) from RD and their associated risk factors among neonates admitted to Neonatal Care Unit of Assiut University Children Hospital.

## Methods

***Study population*:** Neonates admitted to the Neonatal Intensive Care Unit of Assiut University Children Hospital who diagnosed as RD. ***Study site:*** Neonatal Intensive Care Unit (NICU) of Assiut University Children Hospital. ***Study design:*** cross sectional study. ***Sampling and sample size:*** Sample size was calculated using EPI INFO VERSION 7 software. Stat-Calc function. Based on the following criteria: Expected frequency of the studied phenomenon: 19.7 %[8] at Confidence level 99%. The calculated sample size was 420 neonates, 487 were included in the present study. About 2000 neonates admitted per year into NICU, so monthly admission about 166 neonates about half of admission neonates were diagnosed as RD, in order to yield sample size the study continue for 6month.

*Sampling technique:* (Total coverage for RD neonates admitted to the neonatal care unit of Assiut University Children Hospital during the period of the study (6 months) between June 2014 to November 2014.

*Data collection:* Data was collected from the patient sheet of NICU with more details of the sheet which includes the following:

*First part: data of the mother:* Personal data as name, age, occupation and consanguinity, Obstetric history: History of stillbirth, abortion and congenital anomalies. History of the present

**Table (1): Characteristics of admitted respiratory distressed neonates in NICU of Assiut University Children Hospital, 2014.**

| | N (N=487) | % |
|---|---|---|
| **Residence** | | |
| • Urban | 170 | 34.9 |
| • Rural | 317 | 65.1 |
| **Sex** | | |
| • Male | 263 | 54.1 |
| • Female | 224 | 45.9 |
| **Type of the neonate** | | |
| • Single | 368 | 75.6 |
| • Twins | 91 | 18.7 |
| • Triplet | 20 | 4.1 |
| • Quadruplet | 8 | 1.6 |
| **Gestational age** | | |
| • Full term* | 152 | 31.2 |
| • Preterm** | 335 | 68.8 |
| **Birth weight** | | |
| • Normal birth weight[a] | 129 | 26.5 |
| • Low birth weight [b] | 149 | 30.6 |
| • Very low birth weight [c] | 142 | 29.2 |
| • Extremely low birth weight [d] | 67 | 13.8 |
| **Place of delivery** | | |
| • Hospital | 428 | 87.9 |
| • Private hospital or clinic | 48 | 9.9 |
| • Home | 11 | 2.3 |
| **Method of delivery** | | |
| • Normal vaginal delivery | 164 | 33.7 |
| • Elective C.S | 110 | 22.6 |
| • Emergency C.S | 213 | 43.7 |

* Full term:gestational age from 37 to 42 weeks. ** Preterm: gestational age less than 37 weeks. a Normal birth weight: more than 2500 gm. b Low birth weight: between 1500 and 2500 gm. c Very low birth weight: between 1000 gm and 1500gm. d Extremely low birth weight : less than 1000 gm. (10)

pregnancy as antepartum hemorrhage, premature rupture of membranes and preeclampsia. Data of delivery as place and method of delivery.

*Second part: data of the neonates:* Personal data as name, age, sex, residence , date of birth and date of admission. Data of examination on admission as weight, length, vital signs, systematic examination and provisional diagnosis. Laboratory flow sheet and investigation sheet. Complications and treatment. Discharge sheet including date of discharge, weight, length and diagnosis at discharge.

***Operational definition:*** Respiratory distress in the neonates is documented as one or more signs of increased effort of breathing, such as nasal flaring, tachypnea, chest retractions, or grunting.[9]

## Results

Out of 919 neonates admitted to NICU of Assiut University Children Hospital during study period 487 of them had RD which constituted 52.9% of total admission.

Table (1) shows the characteristics of admitted neonates of respiratory distress.

A total of 487 neonates were admitted during study period. Majority of neonates were from rural , single born and preterm (65.1%, 75.6% &68.8% respectively).

On the other hand only 26.5% of neonates had normal birth weight.

Moreover, 87.9 % of neonates were delivered at hospital and 43.7%of them were delivered by emergency C.S.

Table (2): shows that majority of cases of hyaline membrane disease were preterm and low Birth weight (96.2% & 93.7% % respectively), with statistical significant difference. While most of cases of meconium aspiration syndrome (88.9% & 66.7%) were full term and normal birth weight with statistical significant difference. Table (3): shows that all cases of meconium aspiration syndrome were delivered single with insignificant statistical difference. Although 91.2% of cases of persistent pulmonary hypertension and 90.4% of cases of congenital anomalies were delivered single with significant statistical difference. In addition, all cases of meconium aspiration syndrome were males, while 64.7% of Persistent pulmonary hypertension cases

**Table (2): Relationship between gestational age, birth weight and causes of RD of neonates admitted to NICU of Assiut University Children Hospita, 2014**

| Causes of RD | Gestational age (% from rows) | | Total (N=487 ) | P-value |
|---|---|---|---|---|
| | Full term (152) N (%) | Preterm (335) N (%) | | |
| **Hyaline membrane disease** | 11(4.9) | 212 (96.2) | 223 | **< 0.0001** |
| **Transient tachypnea of the newborn** | 39 (47) | 44 (53.0) | 83 | **0.001** |
| **Meconium aspiration syndrome** | 8 (88.9) | 1 (11.1) | 9 | **0.001** |
| **Pneumonia** | 36 (41.9) | 50 (58.1) | 86 | 0.019 |
| **Persistent pulmonary hypertension** | 18 (52.9) | 16 (47.1) | 34 | **0.005** |
| **Congenital anomalies*** | 40 (76.9) | 12 (23.1) | 52 | **< 0.0001** |
| **Causes of RD** | **Birth weight (% from rows)** | | **Total (N=487 )** | **P-value** |
| | **Normal (129) N (%)** | **Low (358) N (%)** | | |
| **Hyaline membrane disease** | 14 (6.3) | 209 (93.7) | 223 | **< 0.0001** |
| **Transient tachypnea of the newborn** | 41 (49.4) | 42 (50.6) | 83 | **< 0.0001** |
| **Meconium aspiration syndrome** | 6 (66.7) | 3 (33.3) | 9 | **0.013** |
| **Pneumonia** | 25 (29.1) | 61 (70.9) | 86 | 0.55 |
| **Persistent pulmonary hypertension** | 14 (41.2) | 20 (58.8) | 34 | **0.04** |
| **Congenital anomalies*** | 29 (55.8) | 23 (44.2) | 52 | **< 0.0001** |

**Chi square ($\chi^2$) test was used,** Fisher's exact test. *Congenital anomalies (diaphragmatic hernias, pulmonary hypoplasia., tracheoesophageal fistula, congenital lobar emphysema-- and congenital heart disease)

were females with significant statistically difference.

Table (4): shows that 94.2% of mothers congenital anomalies neonates and 66.8% of mothers of hyaline membrane diseased neonates were multigravida with significant statistical difference .Furthermore, 62.8%of congenital anomalies cases were delivered by Cesarean section with significant statistically difference .

Table (5): shows that majority of hyaline membrane diseased neonates who treated by surfactant or CPAP were recovered (75.8%& 66.7%respectively) with significant statistically difference.

Table (6): shows that the highest case fatality of respiratory distress diseases were persistent pulmonary hypertension (91.2) followed by hyaline membrane disease and congenital anomalies (69.5% & 69.2% respectively). Table (7): shows that hyaline membrane diseased, persistent pulmonary hypertension, congenital anomalies neonates had shorter mean survival time than those did not have (27.32±4.22, 8.03±1.3 and 17.47±2.94 respectively) with significant statistically difference.

Table (8): shows that the only significant independent factors associated with mortalities of neonates of respiratory distress were residence, causes of RD, birth weight and place of delivery. Rural, low birth weight and home delivery neonates were risky of mortalities than others.

Fig (1) shows that hyaline membrane disease was the most important cause of neonatal respiratory distress followed by pneumonia and transient tachypnea of the newborn .

## Discussion

The present study revealed that RD constituted 52.9% of total admission. RD

**Table (3): Relationship between type, sex of neonates and causes of RD among admitted neonates to NICU of Assiut University Children Hospital,2014.**

| Causes of RD | Type of the neonate (% from rows) | | Total (N=487) | P-value |
|---|---|---|---|---|
| | Single (368) N (%) | Multiple (119) N (%) | | |
| **Hyaline membrane disease** | 137 (61.4) | 86 (38.6) | 223 | **< 0.0001** |
| **Transient tachypnea of the newborn** | 76 (91.6) | 7 (8.4) | 83 | **< 0.0001** |
| **Meconium aspiration syndrome** | 9 (100.0) | 0 (0.0) | 9 | 0.122 |
| **Pneumonia** | 68 (79.1) | 18 (20.9) | 86 | 0.40 |
| **Persistent pulmonary hypertension** | 31 (91.2) | 3 (8.8) | 34 | **0.03** |
| **Congenital anomalies** | 47 (90.4) | 5 (9.6) | 52 | **0.009** |
| **Causes of RD** | **Sex (% from rows)** | | **Total (N=487)** | **P-value** |
| | **Male (263) N (%)** | **Female (224) N (%)** | | |
| **Hyaline membrane disease** | 119 (53.4) | 104 (46.6) | 223 | 0.6 |
| **Transient tachypnea of the newborn** | 45 (54.2) | 38 (45.8) | 83 | 0.9 |
| **Meconium aspiration syndrome** | 9 (100.0) | 0 (0.0) | 9 | **0.020** |
| **Pneumonia** | 47 (54.7) | 39 (45.3) | 86 | 0. 9 |
| **Persistent pulmonary hypertension** | 12 (35.3) | 22 (64.7) | 34 | 0.07 |
| **Congenital anomalies** | 31 (59.6) | 21 (39.4) | 52 | **0.009** |

**Chi square($\chi^2$) test was used,** Fisher's exact test.

**Table (4): Relationship between gravidity, method of delivery and Causes of RDS among admitted neonates in NICU of Assiut University Children Hospital, 2014.**

| Causes of RD | Gravidity (% from rows) | | Total (N=487) | P-value |
|---|---|---|---|---|
| | Primi-Gravid (129) N (%) | Multigravida (358) N (%) | | |
| **Hyaline membrane disease** | 74 (33.2) | 149(66.8) | 223 | **0.002** |
| **Transient tachypnea of the newborn** | 18 (21.7) | 65 (78.3) | 83 | 0.3 |
| **Meconium aspiration syndrome** | 4 (44.4) | 5 (55.6) | 9 | 0.2 |
| **Pneumonia** | 22 (25.6) | 64 (74.4) | 86 | 0.8 |
| **Persistent pulmonary hypertension** | 8 (23.5) | 26 (76.5) | 34 | 0.7 |
| **Congenital anomalies** | 3 (5.8) | 49 (94.2) | 52 | **<0.0001** |
| **Causes of RD** | **Method of delivery (% from rows)** | | **Total (N=487)** | **P-value** |
| | **Normal (164) N (%)** | **Cesarean (323) N (%)** | | |
| **Hyaline membrane disease** | 78 (35.0) | 145(65.0) | 223 | 0.6 |
| **Transient tachypnea of the newborn** | 28 (33.7) | 55 (66.3) | 83 | 0.9 |
| **Meconium aspiration syndrome** | 4 (44.4) | 5 (55.6) | 9 | 0.4 |
| **Pneumonia** | 32 (37.2) | 54 (62.8) | 86 | 0.4 |
| **Persistent pulmonary hypertension** | 11(32.3) | 23(67.7) | 34 | 0.9 |
| **Congenital anomalies** | 11 (21.2) | 41 (78.8) | 52 | **0.04** |

**Chi square($\chi^2$) test was used,** Fisher's exact test.

represented 41.03% of admission in Special Care Baby Unit (SCBU) at Gharian Teaching Hospital.[11]

Mohamed et al revealed that respiratory distress was the commonest primary diagnosis (94.5%) among all admitted neonates, to neonatal intensive care unit in pediatric Assiut University Hospital.[12]

On the other hand the incidence of neonates with respiratory distress was (33.3%) in Neonatal Intensive Care Unit, National Institute of Child Health, Karachi.[13]

In addition, respiratory distress comprising 16.37% of all NICU admissions at kamla Nehru hospital, Gandhi medican l college,

**Table (5): Relationship between Hyaline membrane diseased neonates, treatment varieties, and their outcome in NICU of Assiut University Children Hospital, 2014.**

| HMD | Surfactant | | Total | P-value |
|---|---|---|---|---|
| | Yes (33) | No (190) | | |
| Recovery | 25 (75.8) | 43 (22.6) | 68 (30.5) | |
| Death | 8 (24.2) | 147 (77.4) | 155(69.5) | <0.001 |
| **HMD** | **CPAP** | | **Total** | **P-value** |
| | **Yes (42)** | **No (181)** | | |
| Recovery | 28 (66.7) | 40 (22.1 ) | 68 (30.5) | |
| Death | 14 (33.3) | 141(77.9) | 155(69.5) | <0.001 |
| **HMD** | **Mechanical ventilation** | | **Total** | **P-value** |
| | **Yes (140)** | **No (83)** | | |
| Recovery | 20 (14.3) | 48(57.8) | 68 (30.5) | |
| Death | 120 (85.7) | 35 (42.2) | 155(69.5) | <0.001 |

HMD: Hyaline Membrane Disease CPAP: Continuous positive airway pressure.

Bhopal[14] and Prasad etal ,2011 reported that RD constitutes 17 % of common causes of morbidities.[15]

This study showed that hyaline membrane disease constituted 24.3% of total admission. A study was done in United States revealed that hyaline membrane disease was constituted 10.5% among neonates admitted to NICU.[16] Knowledge of the causes of respiratorydistress is essential for planning and provision of basic services for sick neonates especially low birth weight.[17]

The study revealed that hyaline membrane disease was the most important cause of neonatal respiratory distress (45.8%) followed by pneumonia and transient tachypnea of the newborn .This agree with a study that was done in Gharian Teaching Hospital.[11] Parkash et al, 2015 documented that sepsis and pneumonia were the most common causes of respiratory distress in the neonates (18% each).[18]

On the other hand studies revealed that common causes of neonatal RD were transient tachypnea of newborns (TTN) and respiratory distress syndrome (RDS). 14, 19, and 20

**Table (6): Fatality of different diseases that cause RD of admitted respiratory distress in NICU of Assiut University Children Hospital , 2014.**

| Diseases that cause RD | Deaths (276) | Cases | % |
|---|---|---|---|
| Hyaline membrane disease | 155 | 223 | 69.5 |
| Transient tachypnea of the newborn | 0 | 83 | 0 |
| Meconium aspiration syndrome | 6 | 9 | 66.7 |
| Pneumonia | 48 | 86 | 55.8 |
| Persistent pulmonary hypertension | 31 | 34 | 91.2 |
| Congenital anomalies | 36 | 52 | 69.2 |

Case Fatality Rate (CFR) = (No. of deaths due to certain disease/ Total cases from that disease) x100 [(10)].

This result documented that majority of cases of hyaline membrane disease were preterm and low birth weight with statistical significant difference this is conformed to finding from many studies.[12,21,22,23] Ghafoor et al, 2003 reported that RDS is the commonest cause of respiratory distress in the preterm infants.[8] Zhang et al,_2015 pointed to that 50% of RDS neonates were preterm.[24] Caner *et al*. 2015 indicated the incidence of RDS was 40.6% among premature infants who were admitted to the neonatal intensive care unit.[25] This result revealed that slightly more than half of cases of transient tachypnoea of newborn were preterm and low birth weight with statistical significant difference this agreed with many studies.[8,22] Furthermore, the present study reported that high mortality rate (56.7%) compared to other studies reporting mortality at NICUs. This may be contributed to higher percentages of preterm and LBW which are the commonest neonatal mortality. In addition to our study

**Table (7): Survival analysis of different causes of RDS of admitted neonates in NICU of Assiut University Children Hospital ,2014.**

| | Mean survival time | P-value | | |
|---|---|---|---|---|
| | | Log rank test | Breslow test | Tarone-ware test |
| **Hyaline membrane disease** | | | | |
| Yes | 27.32±4.22 | 0.003 | 0.014 | 0.006 |
| No | 34.24±4.30 | | | |
| **Meconium aspiration syndrome** | | | | |
| Yes | 12.39±2.55 | 0.353 | 0.851 | 0.634 |
| No | 32.18±3.95 | | | |
| **Pneumonia** | | | | |
| Yes | 29.15±3.50 | 0.394 | 0.486 | 0.448 |
| No | 32.87±4.09 | | | |
| **Persistent pulmonary hypertension** | | | | |
| Yes | 8.03± 1.3 | 0.000 | 0.000 | 0.000 |
| No | 33.87±4.197 | | | |
| **Congenital anomalies** | | | | |
| Yes | 17.47±2.94 | 0.011 | 0.006 | 0.01 |
| No | 34.18±4.45 | | | |

was conducted in Children University Hospital, which represents the reference center for neonates of high risk pregnancies and complicated deliveries. Mohamed et al revealed also higher high mortality rate of 58.8%.[12] Ghafoor et al, 2003 reported that the mortality due to RDS was 43.61% among studied neonates.[8]

Other studies have documented that mortality rate varying from 23% to 37%.[14, 22, 26, 27 and 28]

**Table (8): Associated factors of mortalities of respiratory distress neonates in Neonatal Care Unit of Assiut University Children Hospital,2014 .**

| | B | S.E. | Wald | Sig. | OR |
|---|---|---|---|---|---|
| **Residence** | 0.447 | 0.220 | 4.130 | **0.042** | **1.564** |
| **Causes of RD** | 0.388 | 0.073 | 28.442 | **<0.001** | **1.475** |
| **Birth Weight** | -0.001 | 0.000 | 11.590 | **0.001** | **0.999** |
| **Place of Delivery** | -0.390 | 0.178 | 4.804 | **0.028** | **0.677** |
| Constant | 4.631 | 1.56 | 8.828 | 0.003 | 102.643 |

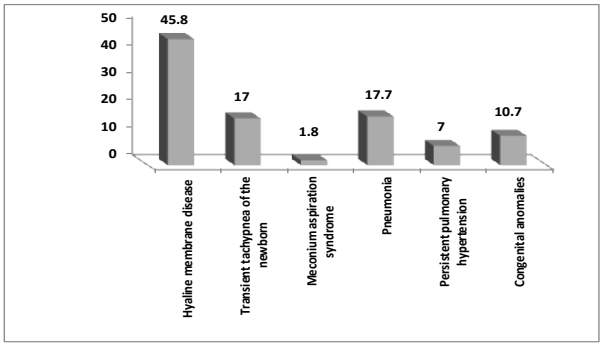


**Fig. (1): Causes of respiratory distress in NICU, Assiut Children University Hospital, 2014.**

Comparison between the causes and their fatalities in the study revealed that hyaline membrane disease has maximum case fatality rate of 69.5 followed by meconium aspiration syndrome **(**66.7%**)**. This result is consistence with many studies.[14, 15, 21, 29] Rajab et al, 2013 reported that mortality rate was high among hyaline membrane disease cases (39.66%).[11]

Introduction of surfactant replacement therapy (SRT) in the management of RD diseases is one of the most important advancements in the field of

neonatology.[30] The present study documented that 75.8% of hyaline membrane diseased neonates who treated by surfactant were cured with significant statistical difference .This result agree with Sanka et al,2016 which revealed SRT is an effective, and feasible management that cause a significant reduction in neonatal mortality of preterm with respiratory distress.[31]

Steven et al, 2007 revealed that surfactant therapy decreased mortality rate of respiratory distress syndrome by just about 50 %. [32]

This study showed that correlates of neonatal mortality were causes of RD, birth weight, type of neonates either single or, multiple and residence. Mohamed et al revealed that the associated risk factors of neonatal mortality in NICU were respiratory distress, twin pregnancy and low birth weight.[12]

## Conclusion

Hyaline membrane disease, TTN, pneumonia, MAS were important causes of neonatal RD in this study. Preterm and low birth weights were common risk of hyaline membrane disease and TT. Hyaline membrane disease followed by MAS had highest case fatality rate. Causes of RD, birth weight, residence and place of delivery were correlates of neonatal mortality.

**Recommendation**

The findings of the present study suggest that development of strategies aiming to reduction of RD among neonates through proper antenatal care to decrease the incidence of premature labor, evaluation of indication of cesarean section encourage hospital delivery. Furthermore, surveillance programs for neonatal mortality should include preventive measures and interventions for better natal care and postnatal care. Finally, improvement of health services quality in the NICU

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