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Outcome of Surfactant Replacement Therapy in Premature Neonates in ICU of Ibn Sina Teaching Hospital of Sirte, Libya in Period Between May – 2019 to May – 2022

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A B S T R A C T

Introduction : Respiratory distress syndrome (RDS) is an acute lung disease of preterm babies caused by surfactant insufficiency . Decreased surfactant results in insufficient surface tension in the alveolus during expiration leading to alveolar collapse , atelectasis , impaired gas exchange , severe hypoxia and acidosis , leading to respiratory failure . Surfactant replacement therapy (SRT) is now accepted as the standard treatment of preterm babies with RDS . **Objective :** The objective of this study was to analyze the incidence and outcome of surfactant replacement therapy in preterm babies with RDS . **Methodology :** This is Quantitative retrospective study , conducted in Neonatal Intensive Care Units (NICU) of Ibn Sina Teaching Hospital , Sirte , Libya . Study duration was of three years period (May – 2019 to May – 2022) . Preterm babies from 24 wks to 36 wks of gestation with RDS received SRT were included in this study . The surfactant was administrated intra- tracheally according to standard procedures . **Results :**In this study of 41 preterm babies with RDS received SRT , 30 (73.2%) were male and 11 (26.8%) were female . The mean gestational age was 33.12 weeks . Among 41 preterm babies with RDS receiving SRT , 21 (51.2%) discharged from the hospital and 20 (48.8%) expired . Maximum survival was seen in the gestational age of ≥32 wks and birth weight ≥ 1500 gms . **Conclusion :** The use of SRT has improved the survival outcome and decreased the associated morbidities in babies with RDS . The maximum impact of survival was seen in the oreterm babies of ≥ 32 weeks with birth weight of ≥ 1500 grams .

1.0 Inroduction

In developing countries , neonatal deaths account for more than one third of all deaths in children under the age of five(1).
Mortality rates are very high in the early neonatal period with 25% - 45% occurring in the first 24 hours of life , and about two third of them accurring during the first week of life(2).
Respiratory Distress Syndrome (RDS) has been recognized as the most common complication of prematurity , with more than half of those occurring with low birth weight and low gestational age(3,4).
Respiratory Distress Syndrome (RDS) of the newborn is an acute lung disease of premature babies caused by insufficient surfactant production in alveolus . Insufficient surfactant results in increased surface tension in the alveolus during expiration leading to alveolar collapse , atelectasis , decreased gas exchange , severe hypoxia with acidosis , leading to respiratory failure . In preterm babies with RDS , exogenous surfactant helps to reduce pulmonary air leaks by 50% and neonatal mortality by 30%(5).
Administration of natural surfactant reduces acute respiratory disease , air leaks , chronic lung diseases , and mortality in preterm infants(6). Surfactant replacement therapy (SRT) is now accepted as the standard treatment protocol for babies with RDS(7). So, the main objective of this study was to analyze the outcome of surfactant replacement therapy in preterm babies with RDS .

2.0 Methodology

1 – Study design:
The study is Quantitative retrospective study, conducted in Neonatal Intensive Care Units (NICU) of Ibn Sina Teaching Hospital, Sirte, Libya.

2 – Study duration:
The study is conducted during the period between May - 2019 to May - 2022.

3 – Study sample:
The study population is all premature neonates (507) , Among them premature neonates received surfactant therapy ,were admitted in Neonatal Intensive Care Units (NICU) of Ibn Sine Teaching Hospital , Sirte , Libya , in period between May – 2019 to May – 2022 **.**

4 – Data collection and analysis:
Data collected in data collection sheet , includes the personal data of the baby (name , file number , phone number , gender , birth weight , gestational age , delivery mode) , diagnosis , date and time of admission (date and time of delivery) , and discharge , date and time of surfactant administration , number of surfactant dose , associated diagnosis , first hemoglobin level Hb reading before surfactant use . Data related to complication (apnea, pneumothorax, pulmonary hemorrhage). Duration of ventilator support when needed and duration of hospitalization. Data related to the mother includes (age, gravidity, mother's job, chronic diseases (DM, HTN), prolonged rupture of membrane, previous affected baby, and antenatal steroids prophylaxis.

5 – Statistical design:
Analyzed data presented in tables and figures. Descriptive data were analyzed as frequency, percentage, mean and std. deviation (SD). The effects of multiple prognostic variables on treatment, effects were evaluated by multivariate logistic regression analyses, for comparison of categorical data; Chi-quare test and Fisher's exact test were used. The computer program, SPSS, was used for statistical evaluation and the level of significance was set at $P < 0.05$.

3. Results

In total, 41 preterm babies with RDS who received SRT were included in this study . Among them, 30 (73.2%) were male and 11 (26.8%) were female . Only one case 1(2.4%) received two dose of SRT . The mean gestational age of preterm babies with RDS receiving SRT was 33.12 weeks , the minimum gestational age included in the study was 24 week gestational by one case 1 (2.4%) , and maximum gestational age was 36 weeks by 5 cases (12.2%) .
1 (2.4%) with birth weight < 1000 gram , and 2 (4.9%) were > 2499 gram . According to time of SRT, 18 (43.9%) were received SRT within first 6 hours of birth, 23 (56.1%) were received SRT after 6 hours of birth .
41 preterm babies with RDS received SRT , Among them, 5 (12.2%) delivered by NVD , while 36 (87.8%) by caesarean section C/S . 37 (90.2%) have APGAR score > 5 at 5 minutes .
After SRT, the mean duration of preterm babies with RDS kept under ventilator support was 4.243 days , there were 12 (29.3%) of preterm neonates as more frequent distribution needed ventilator support for 2 days only, while 1 case only (2.4%) needed ventilator support for 13 days . The mean hospital stay was 9.048 days .
Only 14 (34.15%) of mothers received two doses of antenatal steroid prophylaxis before the delivery of preterm babies , 19 (46.34%) of mothers have previous affected baby with RDS of prematurity , 7 (17%) of mothers have prolonged rupture of membranes before delivery , 1 (2.4%) of mother have diabetes mellitus DM , while 5 (12.2%) of mother have hypertension HTN .
While analyzing the outcome of SRT among 41 preterm babies , 21 (51.2%) of babies were discharged alive from the hospital whereas 13 (31.7%) died within first 3 days of life , and 7 (17.7%) died after first 3 days of the life .
The result showed maximum survival of babies were found with the gestational age ≥ 23 wks , and birth weight ≥ 1500 grams .

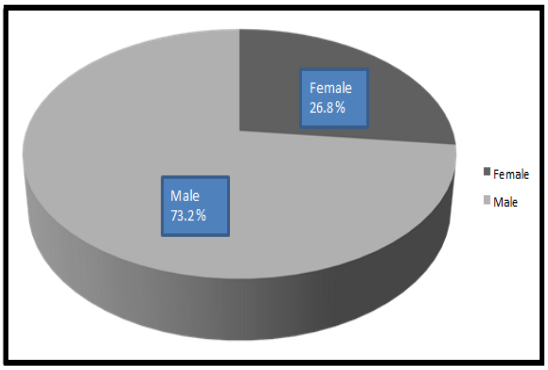

Figure 1: Distribution of gender of premature neonates received surfactant therapy

Table 1: Distribution of gestational age (GA) of premature neonates received surfactant therapy

GA	Number	Percent	Mean	SD	Mix.	Min.
24 wk.	1	2.4%				
30 wk.	6	14.6%				
31 wk.	3	7.3%				
32 wk.	3	7.3%	33.12	2.441	36	24
33 wk.	6	14.6%				
34 wk.	8	19.5%				
35 wk.	9	22%				
36 wk.	5	12.2%				
Total	41	100%				

Table 2: Effect of gestational age groups on outcome of surfactant therapy

GA groups	Surfactant outcome		Total	P value
	alive	Died		
< 26 wk.	0	1	1	
	0%	100%	100%	
26 – 28 wk.	0	0	0	
	0%	0%	0%	
29 – 32 wk.	1	9	10	0.005
	10%	90%	100%	
33 – 36 wk.	20	10	30	
	66.7%	33.3%	100%	
Total	21	20	41	
	51.2%	48.8%	100%	

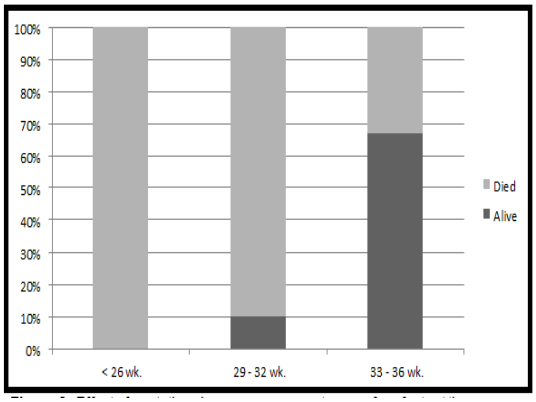

Figure 2: Effect of gestational age groups on outcome of surfactant therapy

Table 3: Distribution of birth weight groups of premature neonates received Surfactant therapy

Birth weight	Number	Percent
< 1000 g	1	2.4%
1000 – 1499 g	13	31.7%
1500 – 1999 g	25	61%
2000-2499 g	2	4.9%
Total	41	100%

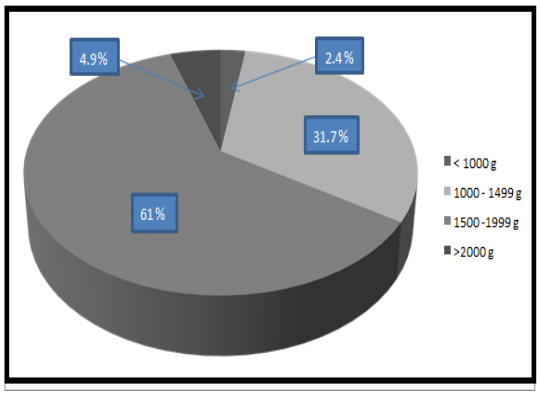

Figure 3: Distribution of birth weight groups of premature neonates received surfactant therapy

Table 4: Effect of birth weight on outcome of surfactant therapy

Birth weight (g)	Surfactant outcome		Total	P value
	alive	Died		
< 1000 g	0	1	1	
	0%	100%	100%	
1000 – 1499 g	23.1 %	10 76.9%	13 100%	
1500 – 2499 g	17 68%	8 32%	25 100%	0.04
> 2499 g	1	1	2	
	50%	50%	100%	
Total	21	20	41	
	51.2%	48.8%	100%	

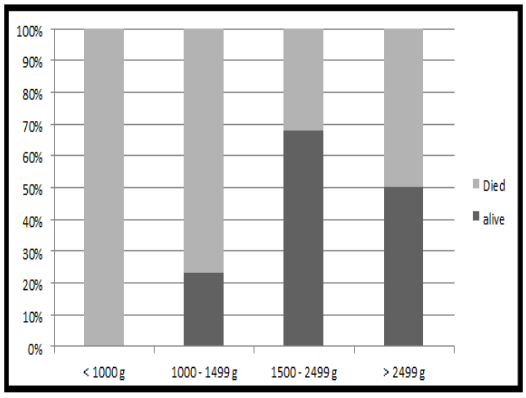

Figure 4: Effect of birth weight on outcome of surfactant therapy

Table 5: Distribution of time of first surfactant dose

Time of surfactant receiving	Number	Percent
≤ 6 h. of age	18	43.9%
7 – 12 h. of age	15	36.6%
> 12 h. of age	8	19.5%
Total	41	100%

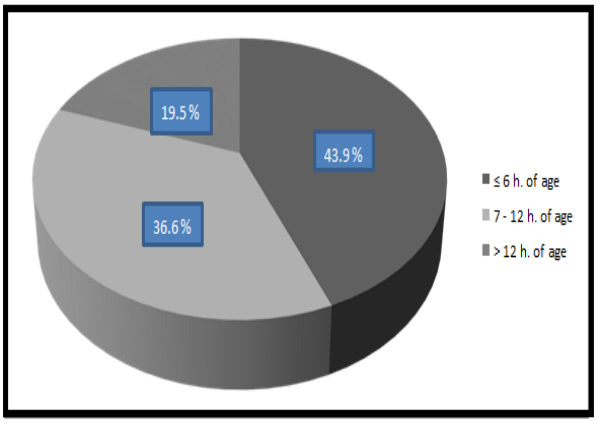

Figure 5: Distribution of time of first surfactant dose

Table 6: Effect of first dose surfactant time on outcome of surfactant therapy

Time of surfactant receiving	Surfactant outcome		Total	P value
	alive	Died		
≤ 6 h. of age	5 27.8%	13 72.2%	18 100%	
7 – 12 h. of age	11 73.3%	4 26.7%	15 100%	0.026
> 12 h. of age	5 62.5%	3 37.5%	8 100%	
Total	21 51.2%	20 48.8%	41 100%	

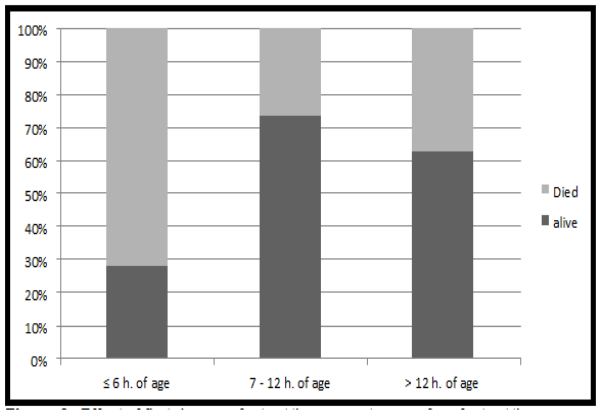

Figure 6: Effect of first dose surfactant time on outcome of surfactant therapy

Table 7: Descriptive statistic of duration of ventilator support / day of

Mean	SD	Median	Mode	Min.	Max.
4.243	3.215	4	1	1 day	13 days

Table 9: Distribution of surfactant therapy outcome

Surfactant outcome	Number	Percent
alive	21	51.2%
Died within 3 days of life	13	31.7%
Died after 3 days of life	7	17.7%
Total	41	100%

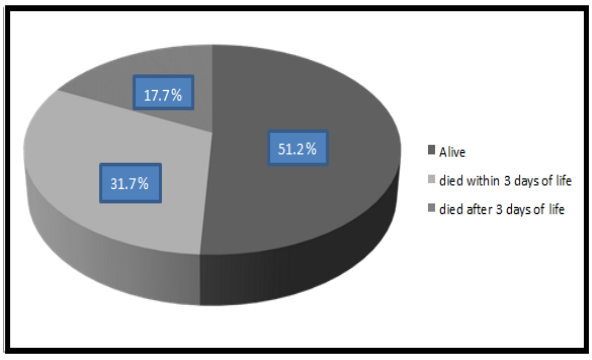

Figure 7: Distribution of surfactant therapy outcome

Table 10: Neonatal parameters

S.N.	Variables	Surfactant outcome		Total	P value
		Alive	Died		
1	Delivery mode				0.675
	NVD	3(60%)	2(40%)	5(100%)	
	C/S	18(50%)	18(50%)	36(100%)	
	Total	21(51.2%)	20(48.8%)	41(100%)	
2	APGAR at 5 min.				0.959
	> 5	19(51.4%)	18(48.6%)	37(100%)	
	≤ 5	2(50%)	2(50%)	4 (100%)	
	Total	21(51.2%)	20(48.8%)	41 (100%)	
3	Steroid prophylaxis				0.046
	Yes	11(78.6%)	3(21.4%)	14(100%)	
	No	10(37%)	17(63%)		
	Total	21(51.2%)	20(48.8%)	41(100%)	
4	Prolonged mm. rupture				0.240
	Yes	5(71.4%)	2(28.6%)	7(100%)	
	No	16(47.1%)	18(52.9%)	34(100%)	
	Total	21(51.2%)	20(48.8%)	41(100%)	
5	Previous affected baby				0.003
	Yes	5(26.3%)	14(73.7%)	19(100%)	
	No	16(72.7%)	6(27.3%)	22(100%)	
	Total	21(51.2%)	20(48.8%)	41(100%)	
6	Chronic diseases				0.448
	DM	0(0%)	1(100%)	1(100%)	
	HTN	2(40%)	3(60%)	5(100%)	
	No chronic disease	19(54.3%)	16(45.7%)	35(100%)	
	Total	21(51.2%)	20(48.8%)	41(100%)	

4.0 Discussion

RDS is an acute illness in preterm babies due to surfactant insufficiency in lung alveoli. RDS is a major cause of morbidity and mortality in preterm babies. EuroNeoStat Annual Report for Very Low Gestational Age Infants

2010 showed a prevalence of 92% for RDS in newborn babies with a gestational age of 24 – 25 weeks , 88% at 26 – 27 weeks , 76% at 28 – 29 weeks and 57% at 30 – 31 weeks suggesting RDS incidence is inversely proportional to gestational age , as less gestational age , more chance of RDS(8). Surfactant is necessary for inflation of lung alveoli by reducing its surface tension. Clinical trials have confirmed that SRT is effective in improving the immediate need for respiratory support and the clinical outcome of premature newborns.

In another study by Narang A et al in postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, received 88 preterm babies with surfactant replacement therapy. The mean gestational age was 30.7 wks and mean birth weight was 1387 gms with survival rate was 75% and mean hospital stay was 14.5 days (9).

In the current study, 30(73.2%) of them were male, and 11(26.8%) were female, so male gender had under gone more surfactant replacement therapy.

According to GA of premature neonates received surfactant therapy was 1(2.4%) of prematures neonates for 24 weeks gestation, 6(14.6%) for 30 weeks gestation , 3(7.3%) for 31 weeks gestation , 3(7.3%) for 32 weeks gestation , 6(14.6%) for 33 weeks gestation , 8(19.5%) for 34 weeks gestation , 9(22%) for 35 weeks gestation , and 5(12.2%) for 36 weeks gestation , So maximum GA included in this study was 36 weeks and minimum GA was 24 weeks .

According to birth weight, distribution of premature neonates received surfactant was one(2.4%) of premature neonates for birth weight group < 1000 g, 13(31.7%) for birth weight group 1000 – 1499 g, 25(61%) for birth weight group 1500 – 2499 g, and 2(4.9%) for birth weight group > 2499 g. Since exogenous surfactant replacement therapy was first used for respiratory distress syndrome (RDS), it has become the main method for treatment of RDS. However, in some infants, death is inevitable despite intensive care and surfactant replacement therapy, the main purpose of this study was to compare the therapeutic effect of pulmonary surfactant for infants at different gestational ages and different birth weight.

According to gestational age, the subjects were classified into 4 groups outcome of surfactant was affected mainly by GA. birth weight, and time of surfactant administration, so after exogenous surfactant received, 1(100%) of premature neonates for GA group < 26 weeks was died, 9(90%) for GA group 29 – 32 weeks were died, and 10(33.3%) for GA group 33 – 36 weeks were died (P = 0.000), according to birth weight, 1(100%) of premature neonates received surfactant therapy for birth weight group < 1000 g was died, 10(76.9%) for birth weight group 1000 – 1499 g were died, 8(32%) for birth weight group 1500 – 2499 g were died, and 1(50%) for birth weight group > 2499 g was died (P = 0.000).

Infant who are at significant risk of RDS should receive surfactant therapy as soon as they are stable within minutes after intubation , because earlier the surfactant therapy is introduced , the higher the survival rate .

In this study, 5(27.8%) of premature neonates received exogenous surfactant within first 6 h. were alive, low survival rate in this group because included low GA and low birth weight , So that effect on outcome in this group , 11(73.3%) of premature neonates received exogenous surfactant at age between 7 – 12 h. Were alive and 5(62.5%) of premature neonates received exogenous surfactant after 12 h. from birth were alive (P < 0.05). were alive, and 5(62.5%) of premature neonates received exogenous surfactant after 12 h. from birth were alive (P < 0.05) .

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In this study, the maximum impact of survival was seen among the preterm

Babies of ≥ 32 weeks' gestation and ≥ 1500 g birth weight.

In this study show no more significant difference between the gender on outcome of surfactant therapy (P > 0.05), five(45%) of female received surfactant therapy were alive, and 16(53.3%) of male received surfactant therapy were alive.

The 5-minutes APGAR score is clinically used as a screening tool to assess how the newborn has reacted to previous care, remaining relevant for predicting neonatal survival. This study aimed to analyze the determinants of the 5-minutes APGAR score , and its effect on outcome of surfactant

replacement therapy , In this study , 19(51.4%) of alive , 18(48.6%) died of premature neonates received surfactant were for APGAR score at 5-min. > 5 , and 2(50%) alive , 2(50%) died for APGAR score ≤ 5 (P > 0.05) .
Outcome of surfactant replacement therapy according to delivery mode was 3(60%) alive, 2(40%) died of premature neonates received surfactant are produced by normal vaginal delivery, and 18(50%) alive, 18(50%) died are produced by caesarean section (P > 0.05) .
In this study, focused on mother had DM and/or HTN and its effect on surfactant replacement therapy outcome, show 19(54.3%) alive and 16(45.7%) died of premature neonates received surfactant therapy were for mother without chronic diseases association , 1 (100%) died were for mother had DM and 2 (40%) alive and 3 (60%) died were for mother had HTN , So show improve in survival rate in group of mother without chronic diseases association than another groups (P > 0.05) .
Babies of mothers with history of prolonged rupture of membrane had increase risk of RDS , but its effect on surfactant therapy outcome was different , because this study show improve survival rate in premature neonates of mother with history of prolonged rupture of membrane during pregnancy , 5(71.5%) alive and 2 (28.6%) died of premature neonates received surfactant were for mother with prolonged rupture of membrane , 16(47.1%) alive and 18(52.9%) died of premature neonates received surfactant of mother without prolonged rupture of membrane (P > 0.05) .

Mother with previous affected baby had increased risk of RDS in next pregnancy , also had significant effect on surfactant therapy outcome , In this study , 16(72.7%) alive and 6(27.3%) died of premature neonates received surfactant were for mother without history of previous affected baby , 5(26.3%) alive and 14(73.7%) died were for mother with history of previous Affected baby (P < 0.05) .
In the course of investigating the initiation of parturition in sheep in 1969, Liggins observed that lambs born preterm after exposure of corticosteroids in utero survived longer than control lambs, subsequently a randomized, placebo-controlled trial of betamethasone administration in women.
In this study, after confirm that antenatal steroids reduce risk of RDS, also show improve survival rate and surfactant therapy outcome, 11(78.6%) alive and three (21.4%) died of premature neonates received surfactant were for mother received antenatal steroids prophylaxis, 10(37%) alive and 17(63%) died were for mother not receive antenatal steroids (P = 0.000).

Current practice guidelines recommend administration of surfactant at or soon after birth in preterm infants with RDS. However, recent multicenter randomized controlled trials indicate that early use of continuous positive airway pressure (CPAP) with subsequent selection surfactant administration in preterm infants results in improve survival rate. Continuous positive airway pressure started at or soon after birth may be considered as an alternative to routine intubation.
In this study, descriptive statistics of duration of ventilator support / Days of premature neonates received surfactant therapy was mean = 4.243, SD = 3.215, median = four, minimum = 1 days and maximum = 13 days (P < 0.05). Descriptive statistics of duration of hospitalization of premature neonates received surfactant therapy was mean = 9.048, SD = 7.273, median = seven, minimum = 1 day and maximum = 36 days (P = 0.000).
In this study, outcome of surfactant replacement therapy was 21(51.2%) of premature neonates received surfactant therapy discharged alive from hospital, 13(31.7%) were died within first 3 days of life, and 7(17.7%) were died after first 3 days of life

5.0 Conclusion

The use of SRT has improved the survival outcome and decreased the associated morbidities in babies with RDS. Benefit of SRT in RDS, which can shorter the duration of ventilation and hospitalization. The maximum impact of survival was seen among the preterm babies of 32 weeks gestation and more and birth weight ≥ 1500 grams.

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