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# Impact of the use of surfactant and Nasal CPAP in the reduction of mortality among very low birth weight preterm babies in Ile-Ife, south western Nigeria

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**Abstract:** *Background:* Respiratory distress syndrome causes significant morbidity and death especially among very low birth weight babies. Though the use of CPAP and surfactant have been shown to improve survival, these interventions were scarcely available in the past. This study aimed at comparing the clinical outcomes of preterm babies with RDS delivered at the Ife Hospital Unit of the Obafemi Awolowo University Teaching Hospitals Complex at two different periods.

*Objective:* To compare the birth weight specific mortality rates and overall mortality rates of preterm babies with RDS between two periods in the neonatal ward of the Ife Hospital Unit of OAUTHC.

*Methods:* A retrospective study comparing outcomes of 92 babies with RDS at GA 26 to 33<sup>+6</sup> weeks between January 2015 and May 2016 and managed with intranasal oxygen alone to 104 babies of same gestational age characteris-

tics between January 2019 and May 2020 who were managed with CPAP/surfactant.

*Results:* The mean weight and gestational age of the babies respectively were 1.36 ( $\pm 0.37$ ) kg and 31.14 ( $\pm 2.3$ ) weeks in 2015/2016 and 1.35 ( $\pm 0.322$ ) kg and 30.95 ( $\pm 2.24$ ) weeks in 2019/2020. The overall case fatality rate and birth-weight specific mortality rates for ELBW, VLBW and LBW were 33.7%, 62.5%, 35.2% and 9.1% in 2015/2016 and 18.3%, 58.3%, 15.5% and 9.7% respectively in 2019/2020.

*Conclusion:* While the use of CPAP and the administration of surfactant clearly show improved survival among very low birth weight babies who are at increased risk of death from RDS, this was not the case for extreme low birth weight babies.

**Keywords** Very low birth weight, surfactant, CPAP, preterm mortality, respiratory distress syndrome, low-cost

## Introduction

Neonatal mortality contributed about 47% of under-5 mortality in 2019 and about 6700 babies died every day in the same year.<sup>1</sup> Premature and low birth weight babies account for 35% of neonatal mortality, therefore survival of this vulnerable group of babies remains a priority of stakeholders.<sup>2</sup> Respiratory distress syndrome, birth asphyxia and sepsis are common causes of death among preterm low birth weight babies.<sup>3-5</sup> In a study by Ochoga *et al*<sup>3</sup> in northern Nigeria, respiratory distress and sepsis accounted for 38.5% and 26.9% of mortality among preterm babies respectively. Similarly, Diala *et al*<sup>4</sup> reported that 20.7%, 28.9% and 9.9% of the deaths among preterm babies were due to respiratory distress syndrome, sepsis and asphyxia respectively. Ugochukwu *et al*<sup>5</sup> in southern Nigeria also reported that

respiratory distress syndrome was implicated in 40% of preterm mortality with severe birth asphyxia and neonatal sepsis contributing to 33.4% and 13.3% of deaths respectively. Overall, 91.6% of deaths occurred among extreme and very low birth weight babies.<sup>5</sup>

Studies in Nigeria have reported mortality rate of preterm babies to be between 24.6% to 41.6% of neonatal admissions.<sup>6-8</sup> Sadly, due to the lack of up-to-date neonatal intensive care facilities across low-income countries, deaths of fragile babies still occur.<sup>9</sup> Therefore, efforts must be geared towards preterm survival as a strategy to reduce neonatal mortality. Globally, the use of CPAP and surfactant have proven very useful in reducing mortality among preterm babies with respiratory distress syndrome.<sup>9</sup> Low-cost interventions have become popular and have shown to be very helpful.<sup>10</sup>

Just as in most low-income countries, our newborn unit

in Ile-Ife, South-western Nigeria has been limited in the use of interventions such as administration of surfactant and the use of CPAP in the past. Over the last three years, nasal CPAP has been used routinely as respiratory support for spontaneously breathing preterm babies suspected to have respiratory distress syndrome in our hospital. The CPAP used is a low-cost one, built as a modified oxygen concentrator that supplies blended humidified oxygen.<sup>11</sup> Also, as part of the unit protocol, surfactant is given to preterm babies with symptoms and signs of respiratory distress syndrome who show increased oxygen requirements on CPAP. Prompt administration of exogenous surfactant to preterm babies with clinical signs of RDS has been shown to improve survival.<sup>12</sup> We found it necessary to compare the mortality rates in the neonatal unit over two periods; before and shortly after we began the routine use of nasal CPAP and surfactant to assess the impact of these interventions on mortality. The objectives therefore were to compare the birth weight specific mortality rates and overall mortality rates of preterm babies with RDS between two periods (2015/2016 and 2019/2020) in the neonatal ward of the Ife Hospital Unit (IHU) of OAUTHC. We believe that the information derived from this study will be of benefit to other low-income settings such as ours and encourage investment into neonatal intensive care.

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## Subjects and Methods

The study was retrospective and descriptive in design. The periods covered in the study were January 2015 to May 2016 and January 2019 to May 2020. Data of all preterm infants born in the IHU of the OAUTHC with gestational age 26 to 33<sup>+6</sup> weeks with respiratory distress syndrome was obtained retrospectively from the hospital records. Institutional permission was obtained before data was retrieved. The case definition for respiratory distress syndrome according to the unit protocol is the occurrence of respiratory distress immediately after delivery or within the first few hours of life characterized by one or more of the following: tachypnea, nasal flaring, grunting, subcostal and intercostal recession or cyanosis occurring in a preterm neonate.<sup>13</sup>

Data obtained also included sex, gestational age, birth weight and outcome (dead or alive). Gestational age was determined using the first day of the mother's last normal menstrual period. Weight was sub-classified into extreme low birth weight (ELBW), very low birth weight (VLBW) and low birth weight (LBW). Only babies delivered in the IHU (inborn) with a clinical diagnosis of respiratory distress syndrome within the time periods were included in the study. Inborn babies were selected so as to eliminate the confounding factor of death from late presentation and ineffective resuscitation at birth. Gestational age 26 to 33<sup>+6</sup> weeks was also chosen because of the high prevalence of RDS in this age group.<sup>12</sup> Post mortem analysis or examination was not done for the cases.

Prior to the advent of CPAP and surfactant, the unit protocol for the management of preterm babies with respiratory distress syndrome involved the commencement of intranasal oxygen and its continuous use with intermittent oxygen saturation monitoring until signs of respiratory distress resolved. However, from January 2019, a protocol for management of RDS was developed. Immediately after birth, spontaneously breathing preterm babies with features of respiratory distress syndrome are commenced on CPAP at FiO<sub>2</sub> (Fraction of inspired oxygen) of 0.5 with a positive end expiratory pressure of 5cm H<sub>2</sub>O.<sup>14</sup> Surfactant is administered only to babies that show increased oxygen requirement while on CPAP characterized by the need of an FiO<sub>2</sub> greater than 0.5 to maintain oxygen saturation above 90%.<sup>14</sup> Also, for preterm babies without spontaneous respiratory effort at birth, resuscitation is carried out and upon resumption of spontaneous breathing, CPAP is commenced and surfactant subsequently administered.<sup>14</sup> The less invasive surfactant administration (LISA) or minimally invasive surfactant therapy (MIST) technique is routinely used in our unit.<sup>15</sup> Babies are weaned off CPAP when saturation is above 90% at FiO<sub>2</sub> of 0.28.<sup>14</sup>

## Statistical Analysis

Means and standard deviation were calculated for weight and gestational age and comparison of the mean birth weight and gestational age was made using student t-test. The proportion of deaths in the two periods were compared using Chi square and *p* value less than 0.05 was regarded as significant.

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## Results

A total of 997 babies were admitted into the neonatal unit during the January 2015 to May 2016 period with 154 (15.4%) delivered preterm. Sixty-two babies were excluded because they were 34 weeks and above. A total of 92 babies less than 34 weeks gestation with respiratory distress who were managed with intranasal oxygen were then reviewed. On the other hand, in the 2019/2020 period, a total of 1180 babies were admitted in the neonatal unit between January 2019 and May 2020 with 206 (17.4%) babies delivered preterm. One hundred and two babies were excluded because they were above 34 weeks of gestation while 104 infants were subsequently reviewed. All 104 babies with features of RDS had CPAP administered after birth as part of the unit protocol, whether surfactant was administered or not. A total of 56 (53.8%) of the 104 babies with RDS were administered surfactant. The proportion of ELBW, VLBW and LBW were 17.4%, 58.6% and 24.0% in 2015/2016 and 11.5%, 55.8% and 32.7% in 2019/2020. The mean birth weight and gestational age were similar in both periods under review (Table I).

**Table 1:** Comparison of birth weight and gestational age of the babies

Clinical Parameters	2015/2016	2019/2020	Statistics T test	p value
Total number of neonates	92	104		
Mean (SD) Gestational age	31.14 (±2.3) weeks	30.95 (±2.24)	-0.589	0.556
Mean (SD) birth weight	1.36 (±0.37) kg	1.35 (±0.322)	-0.203	0.839

The overall mortality rates were 33.7% and 18.3% respectively and this was statistically significant ( $p=0.013$ ). Table II shows the comparative birth weight specific mortality rates for the two periods under review. The mortality rates were inversely proportional to the birth weights for both periods. The VLBW category showed a mortality rate of 15.5% in the 2019/2020 period compared to a mortality rate of 35.2% in the 2015/2016 period.

**Table 2:** Comparison of birth weight specific mortality rates in the two periods

Birth weight categories	2015/2016		2019/2020		P value
	N=92	Dead N (MR %)	N=104	Dead N(MR%)	
< 1kg	6 (37.5)	10 (62.5)	5 (41.7)	7 (58.3)	6.113 0.013
1kg-1.49kg	35 (64.8)	19 (35.2)	49 (84.5)	9 (15.5)	
>1.5kg	20 (90.9)	2 (9.1)	31 (90.3)	3 (9.7)	
Total	61(66.3)	31(33.7)	85 (81.7)	19(18.3)	

**Discussion**

Very low birth weight (VLBW) and extreme low birth weight (ELBW) babies constitute a high-risk group and previous studies in Nigeria have demonstrated higher mortality rates compared to larger sized counterparts especially in the absence of assisted ventilation and surfactant replacement.<sup>16,17</sup> The mortality rates for the ELBW and VLBW babies recorded in the 2019/2020 period of the present study were lower than reported figures of 83.8% and 39.3% found by Owa *et al* in Ilesa,<sup>16</sup> 70.6% and 31.7% reported by Oluwafemi and Abiodun<sup>17</sup> in Akure, both in south-western Nigeria, and a mortality rate of 80% and 41% respectively, found by Chidiebere *et al* in Enugu.<sup>18</sup> These studies were all carried out earlier than the present study and reflect the challenges encountered by health workers in battling preterm mortality. Our findings in 2019/2020 were however comparable to that of Ntuli<sup>19</sup> *et al* in South Africa where the birthweight specific mortality was 48.0% for ELBW and 16.3% for VLBW, and babies with RDS were managed with CPAP, surfactant and mechanical ventilation. Sadly, mortality indices among preterm babies in low-income countries are still much higher than reported figures in the more advanced regions of the world.

The difference in the mortality pattern among VLBW babies from the periods reviewed is reflective of some improvement in neonatal care services in the unit, notably the use of CPAP and surfactant which were not available before.<sup>16</sup> Furthermore, facilities for continuous

monitoring of oxygen saturation have also allowed care givers to become proactive in the early detection of danger signs of bradycardia and hypoxia in preterm babies. Availability of neonatal intensive care equipment remains a challenge in our environment due to high-cost implications. Nevertheless, we must remain determined to rise above the challenges in the improvement of outcome for small and vulnerable babies. The routine use of CPAP and availability of surfactant and monitoring devices can go a long way in reduction of mortality.<sup>12</sup> Furthermore, the acquisition of technology will ensure that doctors and nurses become familiar with such facilities and they can be trained while subsequent transfer of knowledge can also occur.

In the current study, though there was some improvement in outcome among babies in the ELBW category when compared to the past, it was not as marked as seen in the VLBW category. Reports of the survival rate of preterm ELBW managed with CPAP varies. Kalimba and Ballot<sup>20</sup> in a tertiary facility in South Africa reported a 26.5% survival rate among 382 preterm ELBW babies while Luthuli and Mckerrow<sup>21</sup> reported a survival rate of 49.5% among 105 neonates less than 1000g. Only preterm babies weighing between 750g and 800g were offered CPAP in the Kalimba and Ballot,<sup>20</sup> and Luthuli and Mckerrow<sup>21</sup> studies respectively. In both studies, administration of surfactant was at the discretion of the clinician. While the Kalimba and Ballot<sup>20</sup> study did not find the use of CPAP associated with increased survival, the Luthuli and Mckerrow study found a relationship, although only 54 % of the 105 babies had CPAP administered. Just as in the current study, there was no mechanical ventilator routinely available for babies that did not improve on CPAP in the Kalimba

and Ballot study.<sup>20</sup>

However, other studies have shown that with the use of nasal CPAP and further use of invasive mechanical ventilation for ELBW infants who do not improve on CPAP, survival is improved.<sup>22,23</sup> Kirsten *et al*<sup>22</sup> reported that 74.8% of ELBW babies who had surfactant and back-up mechanical ventilation survived until discharge. In the Marlow *et al*<sup>23</sup> prospective study across hospitals in England where facilities for invasive mechanical ventilation and life support were available, ELBW babies aged 22-26 weeks were followed up and the overall survival rate was 62.9%, higher than 41.7% in the surfactant and CPAP era of the current study despite having a lower gestational age range. The marked immaturity of the respiratory system in ELBW babies is better managed with invasive ventilation.<sup>24,25</sup> Therefore, it can be argued that if invasive ventilatory techniques were utilized in the latter period in the current study, the chances of survival of babies in the extreme low birth weight category may have improved.<sup>22,23</sup> Mechanical ventilation inflates atelectatic lung and keeps blood gases at an acceptable range although its use may be associated with air leak syndrome and chronic lung disease.<sup>25,26</sup> This is why the European Consensus Guidelines recommend early weaning off invasive ventilation with improvement in respiratory effort.<sup>12</sup>

Although this study clearly shows that preterm mortality can be improved through life-saving measures such as the administration of exogenous surfactant and CPAP, prevention of preterm death is not limited to these interventions alone. Other proven measures include maternal antenatal administration of corticosteroids, prevention of hypothermia, early initiation of breastmilk, effective prevention and management of sepsis as well as the practice of Kangaroo Mother Care.<sup>27</sup> Even though RDS can be diagnosed clinically, a major limitation of this study is that other co-morbidities such as intraventricular hemorrhage and congenital malfor-

mations of the respiratory and cardiovascular systems may have mimicked respiratory distress syndrome. This posed a challenge because routine ultrasound scanning and echocardiography for all preterm VLBW and ELBW babies for the diagnosis of possible intraventricular bleeding and congenital heart diseases respectively, were not done for the babies in both study periods. Also, because the outcome of the current study was birth weight specific mortality, and factors such as sepsis, necrotizing enterocolitis and recurrent apnea may have contributed further to unfavorable outcomes, it may be difficult to attribute these deaths to respiratory distress syndrome alone. Furthermore, autopsies which may have revealed other pathologies were also not carried out. Nevertheless, this comparison of outcomes is considered worthwhile and informative because among other risk factors, RDS still remains a leading cause of mortality among preterm babies and active intervention can improve survival in resource restricted regions.<sup>3-5,28</sup>

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### Conclusion

In conclusion, the study showed that there was about a 50% decline in mortality among very low birth weight babies managed in the period where the routine use of nasal CPAP and surfactant was introduced into our unit compared to an earlier period. This effect was not replicated among extreme low birth weight babies probably due to the absence of more invasive ventilatory techniques for further respiratory support. Notwithstanding, the findings from this study revealed that early respiratory management with CPAP for babies with RDS contributes significantly, or in part, to reducing mortality among preterm very low birth weight babies.

**Conflict of interests:** None

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