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Understanding Low Birth Weight and Beyond: Insights from the Sri Lanka Low Birth Weight Study

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Introduction

Low birth weight (LBW), defined as birth weight less than 2500g, continues to pose significant challenges to healthcare systems worldwide1. It is estimated that nearly 20 million babies are born annually with LBW worldwide2. The global prevalence of LBW is reported as 15% with relatively lower prevalence in developed European and North American countries and higher prevalence in developing low and middle-income countries (LMICs) in South and Southeast Asia3.

The prevalence of LBW is one of the core health indicators of the World Health Organisation (WHO) as it reflects the long-term maternal nutritional status and health care during pregnancy. Reduction in the prevalence of LBW is an indicator of improvement in maternal health and nutritional status in a country. In 2012, the WHO and UNICEF jointly set a target to reduce the global prevalence of LBW by 30% between 2012 and 2025[4]. However, many countries, especially LMICs in Asia, struggle to achieve this target and are expected to fall far behind the goal5.

LBW is further classified into three categories based on severity. Newborns with a birth weight between 1500-2499g are termed 'Low birth weight'; those with a birth weight between 1000-1499g are termed 'very LBW'; and those with a birth weight less than 1000g are referred to as 'extremely LBW'.

Irrespective of the severity, LBW in neonates results from two main causes. They are prematurity and small for gestational age (SGA6. Prematurity is defined as neonates born before 37 completed weeks of gestation, whereas SGA is defined based on the birth weight in relation to the gestational age and sex at birth. Newborns whose birth weight lies below the 10^{th} percentile for the gestational age based on sex-specific growth charts are defined as SGA7. In many countries, including Sri Lanka, the relative contribution of prematurity and SGA to the prevalence of LBW is not known8.

Sri Lanka is a unique country in South Asia with a well-developed healthcare structure and improved health indices compared to many other LMICs9. Over 99% of deliveries occur in hospitals with trained medical and nursing staff, and birth weights are measured accurately immediately after birth in every hospital[10]. This contrasts with other South Asian countries, such as Bangladesh, Nepal, and Pakistan, where only 40-70% of deliveries are reported to be institutional11-13. However, similar to other LMICs, the LBW prevalence has not decreased significantly over the last decade in Sri Lanka. The reasons behind this stagnant rate of LBW are unexplained and understudied.

One major obstacle in reducing the prevalence of LBW to achieve the WHO-UNICEF target for Sri Lanka is the limited understanding and lack of accurate data on the composition and risk factors of LBW. There are no published data from Sri Lanka regarding the relative contribution of prematurity and SGA to the LBW.

Similarly, only a few studies have examined the risk factors associated with LBW in Sri Lanka. Most of these studies are either conducted through secondary analysis of Demographic and Health Survey (DHS) data or done in small, selected areas. There were no prospective island wide studies evaluating the risk factors and determinants of LBW in Sri Lanka.

To address this knowledge gap, the Perinatal Society of Sri Lanka initiated a comprehensive study on low birth weight in Sri Lanka in 2023. Under the guidance of Dr Susie Perera, then President of the PSSL, and co-leadership of Dr Himali Hearath and myself, a subcommittee was appointed to design and conduct an islandwide multicenter study - the Sri Lanka Low Birth Weight Study - to address the outstanding issues related to LBW.

In this oration, I aim to present the results of the primary and subsequent secondary analysis of data from the Sri Lanka Low Birth Weight Study. Firstly, as primary analysis, I present the composition, determinants, and risk factors of LBW in Sri Lanka. Then, as secondary analysis, I present two studies conducted to understand the two factors directly relevant to perinatal outcomes. I.e. the pregnancy and neonatal outcomes of deliveries at different gestations within 'term' and the pregnancy and neonatal outcomes of assisted pregnancies in Sri Lanka.

Methodology of the Sri Lanka Low Birth Weight Study

The Sri Lanka Low Birth Weight Study was a countrywide, multicentre study conducted from 1st August to 30th September 2023. Thirteen hospitals were purposively selected to represent all nine provinces and all tiers of specialist hospitals in Sri Lanka. The selection was made to cover 20% of all neonates born in the country during the study period. One or more hospitals from each province were selected, as shown in this map, to represent at least 15% of births in each province. Additionally, the selection was made to represent different tiers of hospitals where deliveries are carried out. We included Teaching Hospitals, Provincial General Hospitals, District General Hospitals, and Base Hospitals to capture the varied contexts of healthcare delivery within the country.

All live-born neonates born at the thirteen study sites during the study period were recruited. Stillbirths and neonates transferred after birth from other hospitals were excluded. Data were collected by trained medical graduate research assistants using an interviewer-administered questionnaire, which involved interviewing mothers and reviewing patient records.

Birth weights were measured immediately after birth by trained healthcare personnel attending the delivery. The measurements were taken to the nearest 5g. Prematurity was defined as birth before 37 completed weeks of gestation. SGA was defined as a birth weight below the 10th percentile for the sex- and gestational age-specific international growth standards developed in the INTERGROWTH-21 study[18, 19].

The distribution of birth weight

A total of 9130 live births were recorded from 13 study sites over the two months. The median birth weight of the cohort was 2860g, and the birth weight ranged from 410g to 4820g. The mean birth weight of male neonates was higher than that of female neonates.

Overall, 1865 babies in our cohort had birth weight below 2500g, giving a LBW prevalence of 20.4%. This was considerably higher than the LBW rates reported in Sri Lanka between 2020 and 2022, which were around 15%. Our study was the first study to indicate that the prevalence of LBW was rising in Sri Lanka after the COVID-19 and economic crisis. The prevalence of very

LBW in our cohort was 1.1% and that of extremely LBW was 0.8%.

The highest prevalence of LBW, at 27%, was observed at DGH Nuwara Eliya, while TH Jaffna reported the lowest prevalence at 15%. Overall, a higher prevalence of LBW was observed in study sites in the Central, Sabaragamuwa and Western provinces of Sri Lanka. In comparison, a lower prevalence of LBW was reported from study sites in the Northern, North-Western, and North-Central provinces of the country, showing a geographical segregation of LBW neonates.

In our study population, 10.9% of neonates were born preterm. A majority of premature neonates were born between 34 and 36 weeks and were late preterm. 1.2% each were moderate and very preterm, and 0.6% of this cohort were born extremely preterm before 28 weeks of gestation. The prevalence of prematurity was relatively similar across all geographical areas of the country.

Overall, 1819 babies, i.e., 20% of the study population, were born SGA. The highest prevalence of SGA, at 34%, was reported from DGH Nuwara Eliya, while the lowest prevalence, at 16%, was observed in TH Jaffna. Overall, a higher prevalence of SGA was observed in study sites in the Central, Uva, and Eastern Provinces, while a relatively lower prevalence was reported in study sites in the Northern and North Central provinces.

Composition of low birth weight

Next, we evaluated the composition of LBW. I.e. what proportion of LBW is due to prematurity and what proportion is due to SGA. Out of all LBW babies, 63% were SGA, and 37% were premature. 11.5% of neonates were both SGA and premature. Notably, there were 200 neonates, i.e. 10.7% of LBW babies, who were neither premature nor SGA. All these babies were born at 37 weeks of gestation. The reason for this is that the 10^{th} percentile cut-off value for SGA at 37 weeks is 2380g for males and 2330g for females, which are lower than the 2500g cut-off for LBW. Thus, a baby born at 37 weeks with a birth weight of 2400g would not be small for gestational age nor premature despite having LBW.

A very recent commissioned series published in *The Lancet* introduced the concept of Small Vulnerable Newborns[5]. Here, the three groups of high-risk neonates, i.e. LBW, premature and SGA, were collectively referred to as ‘Small vulnerable newborns’ as they have increased risk of morbidity and mortality. In our cohort, 214 of the premature neonates were SGA. Notably, 304 premature neonates, i.e., 30.5% of the total, had a normal birth weight. Similarly, a large proportion, i.e., 637 or 35% of SGA newborns, had a normal birth weight of more than 2500g. Overall, only 69% of the neonates were born at term with a normal birth weight for the gestational age and did not belong to any of the risk groups. Thus, 31% of neonates of our cohort were small vulnerable newborns with one or more risk factors of prematurity, LBW or SGA.

Next, we examined the birth weight distribution of neonates born at each gestation in our cohort. The median birth weight increased by approximately 150g for each week of gestation after 37 weeks until 40 weeks. This clearly shows that significant fetal weight gain is achieved during the last few weeks of gestation, even after reaching term. Therefore, continuing pregnancies beyond 37 weeks of gestation when the fetus is healthy would significantly increase the birth weight and reduce the prevalence of LBW in Sri Lankan newborns.

Risk factors for LBW

Our next objective was to identify the risk factors for different components of LBW. Thus, using multivariable logistic regression analysis, we examined the risk factors for SGA and prematurity separately.

We examined several socio-demographic and clinical factors of mothers to identify modifiable and non-modifiable independent risk factors for SGA. Multiple pregnancy and teenage pregnancy were significant risk factors for SGA. Importantly, mothers of the Indian Tamil Ethnicity had a higher risk of delivering babies with SGA. This could at least partly explain the high prevalence of SGA observed in Central and Uva Provinces. Also, maternal underweight with pre-pregnancy BMI <18.5kg/m^2, maternal short stature, inadequate weight gain during pregnancy, and anaemia at delivery were all independent risk factors for SGA. This indicates the importance of pre-pregnancy and intra-pregnancy nutritional status of the mother for the birth weight of their offspring.

Finally, we assessed the risk factors associated with prematurity. Our analysis confirmed several traditional risk factors, including multiple pregnancy, chronic diabetes, chronic hypertension, and pregnancy-induced hypertension, as risk factors for prematurity. In addition, as with SGA, many nutritional factors that include maternal underweight, maternal short stature, and inadequate weight gain during pregnancy were risk factors for prematurity. This again emphasises the impact of female and maternal nutrition on the birth weights of their babies.

Based on the findings of our study, we recommend improving pre- and intra-pregnancy nutritional indicators, minimising teenage and elderly pregnancies, and preventing chronic diabetes, hypertension, and anaemia during pregnancy as evidence-based targeted interventions to reduce LBW prevalence in Sri Lanka. In addition, continuing pregnancies beyond 37 weeks when the foetus is healthy would significantly improve the birth weight and reduce the prevalence of LBW. These findings were published in our paper in *Plos One* 20.

Perinatal outcomes of deliveries at different gestations at term

Our primary analysis of the Sri Lanka Low Birth Weight Study revealed that the birth weight of newborns increased significantly with increasing gestation, even after reaching term. Therefore, we were curious to find out about other significant differences in the outcome of neonates born at different gestations at 'term'.

The period between 37 and 41 weeks of gestation, conventionally classified as the 'term', is often perceived as a low-risk phase for both the mother and the neonate. The outcomes of newborns born at any gestation within 'term' are perceived not to be significantly different. However, the 'term' period spans a full five weeks. Therefore, we hypothesised that there could be significant differences in the characteristics and outcome of neonates born at different gestations within 'term'.

Previous studies that compared pregnancy and neonatal outcomes of deliveries at different gestations at 'term' in developing countries are rare. Our search did not reveal a single study from Sri Lanka that compared the outcomes of neonates born at different 'term' gestations. Therefore, we performed a secondary analysis of the data from the Sri Lanka Low Birth Weight Study to evaluate the perinatal outcomes of births at different gestational ages within the 'term' range. Only data of singleton pregnancies were included to minimise confounders.

There were 8053 'term' singleton deliveries in our birth cohort. 22% of them were delivered at 37 weeks, 29% at 38 weeks, 26% at 39 weeks, 22% at 40 weeks and 0.4% at 41 weeks. 61% of neonates born at 37 weeks were delivered by Caesarean section (CS), which was significantly higher than the CS rates of later gestations. Notably, the elective CS rate at 37 weeks was 43%, which was significantly higher compared to 31% at 38 weeks, 6% at 39 weeks, and 4% at 40 weeks. In fact, 46% of all elective CSs done at term were performed at 37 weeks.

Then we analysed the modes of delivery of pregnancies without medical or obstetric complications. Among uncomplicated pregnancies, 44% of neonates born at 37 weeks were delivered by elective CS. Even among uncomplicated pregnancies, 40% of elective CSs performed at term were done at 37 weeks.

The prevalence of LBW was significantly higher among neonates born at 37 weeks compared to later gestations. 29% of neonates born at 37 weeks had LBW compared to 15% babies born at 38 weeks or 7% born at 39 weeks. Nearly half of the 'term' LBW babies were delivered at 37 weeks.

Neonates born at 38 weeks of gestation showed the best immediate neonatal outcome among all 'term' neonates, with lower proportions of them having perinatal asphyxia, requiring resuscitation at birth and needing neonatal intensive care unit (NICU) admission. Delivery at 37 weeks was associated with a significantly higher risk of having perinatal asphyxia, requiring resuscitation at birth and admission to the NICU, compared to birth at 38 weeks of gestation. There was no significant difference in adverse neonatal outcomes between neonates born at 38 and 39 weeks of gestation.

These findings suggest that when elective delivery is necessary, planning it at 38 weeks, rather than 37 weeks, would have a significant positive impact on neonatal outcomes with lower risk of LBW, perinatal asphyxia, needing resuscitation at birth and admitting to the NICU. A manuscript describing these findings was published in *Lancet Regional Health - Southeast Asia* 21.

Perinatal outcomes of assisted pregnancies

Next, using the data of the Sri Lanka Low Birth Weight Study, we examined another understudied area of perinatal medicine in Sri Lanka, the outcomes of assisted pregnancies and assisted reproductive techniques.

Assisted reproductive techniques that include intra-uterine insemination (IUI) and *in-vitro fertilisation* (IVF) are increasingly used to achieve fertility in developing countries like Sri Lanka. However, the data on the outcome of assisted pregnancies in LMIC like Sri Lanka are sparse. Therefore, we performed a secondary analysis of the Sri Lanka Low Birth Weight Study to evaluate the obstetric and neonatal outcomes of assisted pregnancies.

Of the 8,992 pregnancies in our cohort, 92 were assisted pregnancies, resulting in an assisted pregnancy rate of 1.0%. Fifty-two pregnancies were following IUI, and 40 were following IVF. The prevalence of gestational diabetes and urinary tract infection was significantly higher among mothers who had assisted pregnancies compared to spontaneous conceptions. When considering IUI and IVF separately, gestational diabetes was higher in IVF pregnancies, and urinary tract infections were higher in IUI pregnancies.

As expected, multiple births were higher following assisted reproductive methods. 1.9% IUI pregnancies and 5.0% IVF pregnancies were twin pregnancies, compared to 1.2% spontaneous conceptions that end up having twins. Neonates born following assisted pregnancies reported significantly higher adverse outcomes. The prevalence of prematurity and LBW were significantly higher in assisted pregnancies. Also, a significantly higher proportion of neonates born following assisted pregnancies were admitted to the NICU and died within the first day of life.

Based on the above findings, we recommended that assisted pregnancies should be considered a high-risk group to provide more intense antenatal follow-up and be delivered at specialised centres with adequate neonatal facilities. These findings were published in our paper in *BMC Pregnancy and Childbirth*22.

Conclusions and Recommendations

Here, I presented the results of one of the most extensive countrywide studies evaluating LBW in Sri Lanka. This study was conducted through the prospective collection of data from 13 hospitals across Sri Lanka, covering all nine provinces and various tiers of hospitals, which represent over 20% of births in the country during the study period.

We derived the following conclusions and recommendations based on the findings of our study.

- The prevalence of LBW in our cohort was 20.4% showing an increase in the LBW rates in Sri Lanka.
- The prevalence of prematurity and SGA were 10.9% and 20.0% respectively.
- SGA accounts for approximately two-thirds, while prematurity accounts for one-third of the LBW burden in Sri Lanka.
- 31% of neonates born in our birth cohort had LBW, prematurity, or SGA, making them small vulnerable newborns
- Several modifiable risk factors were identified for SGA and prematurity. Poor pre- and intra-pregnancy nutritional indicators, namely maternal undernutrition and inadequate pregnancy weight gain, were risk factors for both prematurity and SGA.
- Teenage pregnancy and maternal anaemia at delivery were risk factors for SGA, and elderly pregnancy, chronic diabetes and chronic hypertension were modifiable risk factors for prematurity.
- Therefore, improving pre- and intra-pregnancy nutritional indicators, minimising teenage and elderly pregnancies, and preventing chronic diabetes, hypertension and anaemia during pregnancy are evidence-based targeted interventions to reduce LBW prevalence in Sri Lanka.
- From the secondary analysis, we concluded that the assisted pregnancy rate in our cohort is 1%.
- Assisted pregnancies were significantly associated with adverse neonatal outcomes of prematurity, LBW, admission to NICU and death within the first day of life.
- Therefore, assisted pregnancies should be identified as a high-risk group to provide more intense antenatal follow-up and arrange delivery at specialised centres with adequate neonatal facilities.
- Further, we conclude that over one-fifth of term neonates were delivered at 37 weeks, and over 40% of them were delivered by elective CS. Nearly half of the elective CS done at term were performed at 37 weeks.
- The mean birth weight of neonates steadily increased even after reaching term from 37 to 41 weeks.
- The LBW prevalence was significantly higher among neonates born at 37 weeks compared to later gestations.
- Neonates born at 38 weeks of gestation showed the best immediate neonatal outcome among all ‘term’ neonates.
- Delivery at 37 weeks was associated with a significantly higher risk of having

perinatal asphyxia, requiring resuscitation at birth and admission to the NICU, compared to birth at 38 weeks of gestation.

- There was no difference in adverse outcomes between neonates born at 38 and 39 weeks.
- Therefore, when elective delivery is indeed necessary, performing it at or after 38 weeks, rather than at 37 weeks, would have a significant positive impact on birth weights and outcomes of newborns.

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