



USE OF BIRTH WEIGHT IN SCREENING FOR RETINOPATHY OF PREMATURITY IN SRI LANKA. DO WE NEED A CHANGE IN CUT-OFF BIRTH WEIGHT?

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ABSTRACT

Background - Constant revision of screening guidelines for retinopathy of prematurity(ROP) resulted in birth weight cut-off being lowered in some western centres. However, countries with limited neonatal care reports that more mature, bigger babies being detected with significant ROP.

Objectives - To find whether lowered cut-off birth weight criterion in screening for ROP are safe to be applied in Sri Lanka and whether current cut-off limit needs revision.

Methods - A retrospective study was carried out on babies screened during a one year period in a tertiary care ophthalmology centre. Gestational age less than 32 weeks and / or birth weight less than 1500 grams were used as primary screening criteria. Some older and heavier babies were also screened due to exposure to risk factors.

Results - ROP was diagnosed in 89 (31.6%) out of 282 babies studied. Severe ROP was detected in 52 babies. Mean birth weight for those needing treatment was 1209 ± 282 grams. six infants(6.5%) older than 32 weeks and heavier than 1250 grams(a lowered cut-off used in some units) received treatment. Four of them(5%) were heavier than 1500 grams. Of the babies born heavier than 1250 grams, those born before 32 weeks of gestation had a higher chance of developing ROP.($p < 0.0006$)

Conclusion - ROP still occurs in heavier and older babies in Sri Lanka. A reduction in birth weight cut-off limit is not advisable. Current guidelines need revision as some babies heavier than current cut-off had treatable ROP.

Key Words - Retinopathy of prematurity, screening criteria, birth weight, Sri Lanka

INTRODUCTION

Retinopathy of prematurity (ROP) is a disorder of the developing retinal blood vessels of a preterm infant that can give rise to poor visual outcome including blindness if left untreated or detected at a later stage(Repka et al. 2011). Prematurity and low birth weight are direct risk factors for ROP and exposure to supplementary oxygen ,hypoxia, acidosis, apnoea and sepsis have been identified as contributory factors(Wheatley et al. 2002). Screening for retinopathy of prematurity has resulted in early detection of progressive disease and timely retinal ablative therapy which led to a decrease in the likelihood of a poor visual outcome (Ng et al. 2002). On

the other hand screening programs are time-consuming, labour-intensive and uncomfortable to the infants. In one study an average of 39 screening examinations and 19 hours of an ophthalmologist's time was necessary to detect one single case of threshold ROP(Reynolds et al. 2002). All these factors have to be weighed against missing a child with treatable ROP.

At the time of this study, the College of Paediatricians in Sri Lanka adopted the widely accepted American Academy of Paediatrics screening criteria (Vedantham 2007) for retinopathy of prematurity. These criteria were:

1. Gestation age of less than 32 weeks at birth
2. Birth weight less than 1500 grams
3. babies beyond these criteria but exposed to risk factors as decided by a neonatologist

The screening criteria for ROP have been revised worldwide over the years. The cut-off gestational age at birth has been modified slightly over the past years but the cut off birth weight as a criterion for ROP has been in use with a wide variation, ranging from 1250 grams in countries such as Canada to 1750 grams in regions such as Latin America (Ells et al. 2005). Most countries select 1500 grams as a safe cut-off criterion.

Recent studies carried out in countries with advanced neonatal care have proven that ROP requiring treatment is extremely rare in premature infants born beyond 31+6 weeks with a birth weight more than 1250 grams. The 2008 United Kingdom guideline development group reviewed 23 articles involving 10,481 screened babies and found only one infant requiring treatment who weighed more than 1250 grams at birth. A similar finding was noted in a study done on data obtained from the Canadian Neonatal Network(Jefferies 2010).

While countries with advanced neonatal intensive care are moving towards a lowered birth weight criterion, studies carried out in countries with less advanced neonatal care have revealed different results. A research from post graduate institute of Chandigarh has revealed a significant percentage of severe ROP in babies weighing more than 1250 grams at birth(Vinekar et al. 2007), while some centres in south India has extended the cut-off weight up to 2000 grams. Researchers from a study concluded in Saudi Arabia, have also recommended that their current guidelines of screening babies with birth weight below 1500 grams should not be changed(Ammar et al. 2012). In a research carried out in China in year 2005 revealed similar findings and alarmingly 27.3% of babies treated for severe retinopathy had birth weights exceeding 1500 grams(Chen and Li 2006), the cut-off taken as a safe value in current practice.

New evidence constantly emerge from different parts of the world regarding birth weight for screening for ROP , but surprisingly, there are no published studies in Sri Lanka on this aspect. All centres providing ROP screening facilities in Sri Lanka use 1500g as the cut-off birth weight but we do not have data to indicate whether this is the ideal cut-off for Sri Lankan babies. This type of data are needed during revision of guidelines in order to decide whether to continue with the current cut-off birth weight or to lower it considering research evidence. On the other hand we may be missing babies heavier than 1500g with treatable ROP as shown in some of the studies done in neighbouring countries. Therefore this study was designed to gather information regarding the relationship between birth weight and ROP in Sri Lankan babies, which can be used in revising the existing guidelines.

MATERIALS AND METHODS

This study was conducted at the ophthalmology unit(Centre for Sight) of Teaching Hospital Kandy, Central Province, Sri Lanka. This centre provides screening facilities for all neonatal

units in Kandy district as well as specialized management for babies referred from other districts. The study was approved by ethical review committee of Faculty of Medicine, University of Peradeniya. The study period was from 1st September 2012 to 31st August 2013. This was a retrospective analysis of data collected from the patient notes maintained at the ophthalmology unit.

Infants for screening were dilated with two drops of 1.25% phenylephrine and 0.5% cyclopentolate, 15 min apart 1 h before examination. Infants were examined by binocular indirect ophthalmoscopy and scleral indentation. ROP was classified according to international classification for ROP and laser photocoagulation treatment initiated according to ETROP guidelines. Follow-up examinations were conducted according to the results of the first examination. Follow up was continued at least until the baby reached 42 weeks of post menstrual age. Babies with ROP were followed up further until the condition resolved. Examination and treatment (by laser photocoagulation under general anaesthesia) was carried out by a vitreo retinal surgeon.

Neonates with significant cranio-facial abnormalities, babies who presented after the screening window (delayed referrals) or babies transferred from hospitals outside the Kandy district for specialized management were excluded from the study.

Data collected for each neonate included: Gestational age at birth, birth weight, post menstrual age at first referral, type and duration of oxygen therapy, duration of antibiotic therapy, findings of first visit and subsequent visits, treatment received and final outcome. Any infant who developed stage 1 ROP or higher was labelled as having ROP and anyone who was treated was labelled as a ROP treated patient.

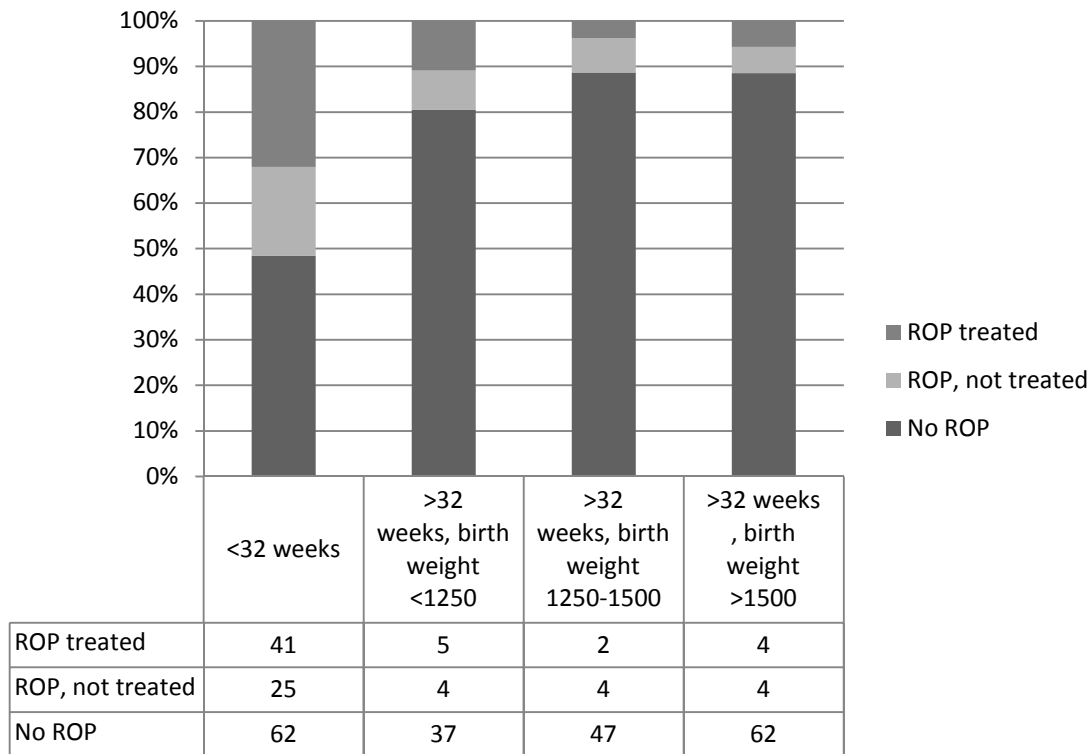
RESULTS

A total of four hundred and nine (409) babies were examined during the study period and 127 were excluded from the study. (109 transfers from hospitals outside Kandy district, 15 delayed referrals and 3 babies with severe craniofacial anomalies). Two hundred and eighty two (282) babies were included in the study.

One hundred and twenty eight neonates (45.4%) were screened by the gestational age criterion (born before 32 weeks of gestation). 84 babies (29.8%) were screened by birth weight criterion of less than 1500 grams (but born beyond 32 weeks of gestation). 70 babies (24.8%) did not qualify by either criterion but underwent screening as they were exposed to risk factors.

Retinopathy of prematurity was diagnosed in 89 neonates (31.6%). 52 neonates (18.4%) had severe ROP which needed treatment while 37 (13.2%) had mild ROP which regressed without intervention. Stage 3 ROP with plus disease was the worst finding on first examination but during follow up two babies developed stage 4 disease despite aggressive therapy. The impact of gestational age and birth weight on ROP is depicted in figure 1.

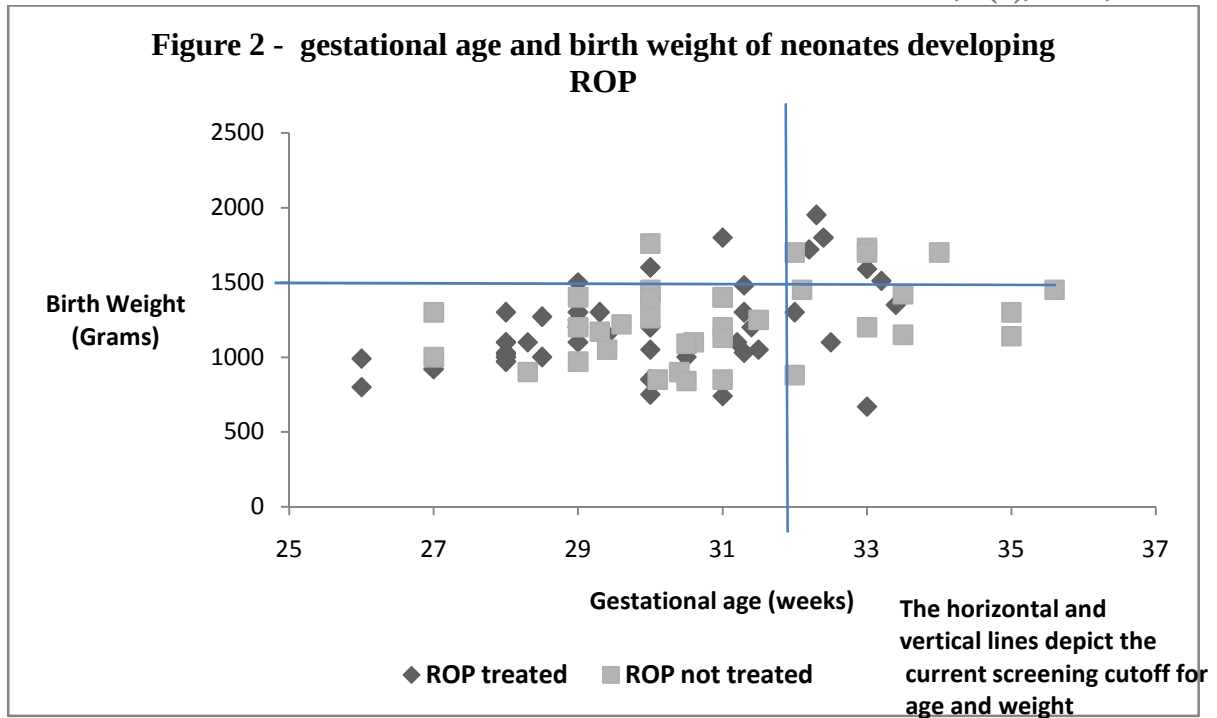
Figure 1 - prevalence of ROP in neonates of different gestational age and birth weight categories.



The mean birth weight for the babies included in the study was 1430 ± 389 grams. The mean birth weight for a baby developing ROP was 1220 ± 274 grams while the treatment group had a mean birth weight of 1209 ± 282 grams. For babies fulfilling one or both criteria for ROP (born less than 32 weeks and/or birth weight less than 1500 grams), the mean birth weight of babies developing ROP was 1171 ± 231 grams while in the same group, babies without ROP had a significantly higher mean birth weight of 1345 ± 267 grams ($p < 0.00001$)

Neonates diagnosed as having ROP had a gestational age ranging from 26 weeks to 35 weeks+6 days. The birth weight for these neonates ranged from 670 to 1950 grams. All infants who received treatment for ROP were born before 34 weeks of gestation. (figure 2)

Of the neonates who developed ROP, 14 neonates (15.7%) were born after 32 weeks and had a birth weight of more than 1250 grams. 8 babies out of these 14 neonates had a birth weight above 1500 grams. 4 (4.5%) of them had to undergo treatment for severe disease. Therefore the current criteria of gestational age and birth weight cut-offs failed to capture 8 babies (9%) with retinopathy of prematurity and 4 (4.5%) required treatment for severe disease. (figure 2)



Babies with a birth weight of more than 1250 grams, a cut-off used in some western countries, were further analyzed. In this weight category, there were 67 babies who were born before 32 weeks of gestation and 117 babies whose gestational age at birth was 32 weeks or more. The occurrence of treatable ROP was significantly higher in babies born before 32 weeks. ($P = 0.0005$).

There were 70 neonates referred by a neonatologist as they had risk factors for ROP but not fulfilling the age and/or weight criteria. Using the available data of these babies maintained at the study centre, we were able to study some of the risk factors known to cause ROP (table 1). All 8 babies who developed ROP in this group had respiratory distress syndrome. 5 of them were exposed to oxygen for more than one week, out of which 4 required treatment for ROP.

Table 1 - Exposure to risk factors in babies with >32 weeks gestation and birth weight >1500 grams

	Number of babies	Babies with ROP treatment not needed	Babies with ROP, treated
Respiratory distress syndrome + oxygen given for > 1 week + sepsis	13	1	2
Respiratory distress syndrome + Oxygen given for < 1 week + sepsis	8	1	0
Respiratory distress syndrome + oxygen given for > 1 week , No sepsis	6	0	2
Respiratory distress syndrome + Oxygen given for < 1 week , No sepsis	24	2	0
Congenital pneumonia and secondary sepsis	5	0	0
Congenital pneumonia with no secondary sepsis	6	0	0
Sepsis only	6	0	0
Prematurity only(32-36 weeks+6 days)	2	0	0
TOTAL	70	4	4

DISCUSSION

Our study reported a 31.6% incidence of retinopathy of prematurity with 18.4% developing severe disease needing treatment. This is somewhat similar to findings from neighbouring countries with similar neonatal care. Biswas et al (2011) reports an incidence of 38.06% in Eastern India, while Karkhaneh et al(2008) reports a value of 34.5% from Iran. But the incidence of ROP in our study is considerably high when compared with studies from western countries. Studies from Netherlands(Hoogerwerf et al. 2010) and Germany(Schwarz et al 2011) report an incidence of 23.3%(1.2% for severe ROP) and 15.1%respectively in recent studies.

Our data confirms that the current weight criterion for screening ROP in Sri Lanka cannot be lowered to 1250 grams, a cut-off increasingly utilized in the western world. Fourteen cases(15.7%) among 89 babies with ROP were mature than the current gestational age criterion and were heavier than 1250 grams. 8(9%) cases were beyond the current birth weight criterion of 1500 grams. Furthermore 4 of these babies (4.5%) had severe disease requiring laser photocoagulation therapy.

Studies from countries such as India and China reveals similar findings of mature and heavier neonates developing ROP. The screening criteria used in these studies were identical to our study. In the study done by Biswas et al(2011) in Eastern India, 19.6 % neonates with ROP were found to be beyond the current screening criteria and 12.9% had severe disease. Vinekar et al(2007), also from India, reports that 17.7% of babies with ROP would have been missed using the same criteria. A larger study from China done by Gu et al(2011), identified 54(9.8%) cases of ROP among 553 babies with a birth weight of 1501 - 2000 grams.

Among the babies who fulfilled gestational age and/or birth weight criteria, the group of babies developing ROP had a significantly lower mean birth weight(1171 ± 231 grams) than the babies not having ROP($p < 0.00005$). Yet, the mean birth weight of the above group developing ROP was considerably higher than their western counterparts. Schwarz et al(2011) from Germany, reported a mean birth weight of 822.3 ± 215.3 g for ROP in babies with birth weight < 1500 grams while similar findings were reported from Canada(Isaza et al 2013). Armer et al(2012) from Saudi Arabia, a country with a higher human development index than Sri Lanka, and rapidly advancing neonatal care also reports lower mean birth weight of 961 ± 237.4 , but even they did not recommended lowering the cut-off birth weight of 1500 grams as heavier babies with ROP were still encountered.

Birth weight has been in use as a second criterion to screen retinopathy of prematurity as gestational age calculation is not reliable all the time. This is important to a country such as Sri Lanka where all mothers do not undergo ideal antenatal dating scans. In many instances, gestational age is calculated using scans done at an age beyond the ideal date scan screening window or using last regular menstrual period as recalled by the mother, hence miscalculations are common. Therefore, having a higher birth weight criterion such as 1500 grams is safer in order to avoid missing premature babies due to over-calculation of gestational age, who have a higher risk of having ROP. This fact is further proven in this study by the finding that of the babies with birth weight above 1250 grams, babies born less than 32 weeks had a significantly higher chance of having ROP than babies born beyond 32 weeks ($p < 0.0005$).

70 neonates who did not fulfil any criteria for ROP were referred due to exposure to known risk factors. As mentioned above 8 babies developed ROP while 4 needing treatment. The data available regarding the exposure to risk factors in these neonates were limited, therefore a thorough statistical analysis was not possible. Yet, available data revealed respiratory distress syndrome being present in all 8 infants with ROP while prolonged exposure to oxygen was

common to those needing treatment. All 4 babies who needed treatment were born less than 34 weeks. Gu et al(2011) reported similar findings from a cohort of Chinese babies with birth weight between 1500 - 2000 grams.

CONCLUSION AND RECOMMENDATIONS

Sri Lanka is a rapidly developing nation and neonatal care has been improving consistently. But we have not reached standards set by developed nations yet. Hence applying western guidelines directly to our set up could be inappropriate. Our study reveals that applying recent guidelines for ROP with lowered birth weight criteria would lead to missing babies with treatable ROP. The findings of the study hints that even the existing criteria may not be ideal as 4 babies with severe disease were lying outside the current criteria.

But findings of a single study are not enough to revise guidelines. Therefore it is time for multi centred trials to be carried out in Sri Lanka in order to formulate our own guidelines which contains safer cut-off limits.

LIMITATIONS

The study was conducted using data gathered from a single screening unit in Kandy district, therefore the study population does not represent the country as a whole. The ROP findings can significantly vary from one district to another depending on the available facilities of neonatal care. Therefore data from different districts will be needed before a final conclusion can be drawn on ROP findings of neonates in Sri Lanka and the applicability of current screening guidelines.

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CONFLICT OF INTEREST

None

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