Characteristics of babies referred to a tertiary eye hospital of Bangladesh for retinopathy of prematurity screening and management, a database analysis

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ABSTRACT

Background: IspahaniIslamia Eye Institute and Hospital (IIEIH) is a not for profit hospital and a leading Retinopathy of Prematurity (ROP) screening center in Bangladesh.

Objective: The study had an aim to analyze the characteristics of referred babies and identify possible bottlenecks in the referral system.

Methods: Electronic records of babies referred to IIEIH for a period of three years (2016-2018) were analyzed retrospectively. All the babies registered in the electronic file were screened by any of the three consultants with a keen interest in ROP. Variables of interest were ROP stage, gestational age, birth weight, time to screening, referring institution and treatment modalities (laser, Anti-VEGF, retina surgery or combination). Data was exported to SPSS version 23 for Mac for descriptive and correlation analysis. A P-value of less than 0.05 was considered statistically significant.

Results: Eight hundred and eighty seven babies with ROP stage 1 or above were registered over the 3 years period, a large majority were referred mostly by neighbouring private institutions (75%), 60% of babies were moderate pre-terms according to WHO classification, the mean birth weight was 1563±397.1 grams. ROP stage 2 was dominant (37%) and 61% of any stage ROP babies had at least one treatment modality. There was an obvious delay in screening since only 55% of babies were screened within a period of less than 8 weeks. The younger the gestational age and the lower the birth weight, the higher the risk of presenting with ROP with advanced stage. (P-value<0.001).

Conclusions: The majority of babies with ROP came from private institutions and more than half of them needed at least one treatment modality. The delay in screening was a key bottleneck and needs to be addressed. We recommend more NICUS and more ROP services in public hospitals.

Keywords: Retinopathy of prematurity, Screening, Treatment options, Referrals

INTRODUCTION

In 2014, Bangladesh ranked fourth in the top ten countries with the highest incidence of the pre-terms population behind India, China, and Nigeria. The same report showed an estimate of 19% of 3 152 549 live births were pre-terms, representing 4% of the global population of pre-terms1.

ROP screening in Dhaka started in 2010, IIEIH and National Institute of Ophthalmology (NIO) were the only screening centers by then. They offered limited services for a period of 2 years. In 2013, Orbis International joined the centers and supported the human resources empowerment and raising awareness on ROP2.

In a local press release, the ROP team at Ispahani Islamia Eye Institute and Hospital (IIEIH) in partnership with Orbis international warned there was rising incidence of blindness secondary to ROP thought to be linked to low rate of detection of ROP in the Neonatal Intensive Care Units (NICU) of the country or a late screening of babies who are already at advanced stage of the disease3.

Besides these concerns, there was an international concern over the rising incidence of ROP in the developing countries referred to as “the third epidemic” of blindness directly linked to ROP4.

It is now known that low gestational age, low birth weight, exposure to a high concentration of oxygen and neonatal sepsis are high-risk factors for ROP. WHO categorizes prematurity in 3 stages: extreme preterm <28 weeks, very preterm 28 to less than 32 weeks and late preterm between 32 and 37 weeks5.

Some efforts have been deployed to improve the ROP screening in Dhaka and IIEIH is one leading referral center for ROP screening. At least 20 NICUs (only 3 are public) in the town of Dhaka are referring babies to IIEIH who either meet the objective criteria (gestational age <33 weeks or birth weight <2000 grams) or assumed to be at higher risk at the discretion of the neonatologists. Some babies may come from other centers, these are usually seen lately and may already have advanced disease.

In 2017, a study presented an overview of the screening program at IIEIH with a focus on the pattern...
of ROP in the screened population. The major conclusion lines highlighted the significant public concern brought in by ROP morbidity and the need for a stronger government response. This study objective was to analyze the characteristics of babies referred for ROP screening.

MATERIALS AND METHODS

This was a retrospective study conducted at IIEIH, an urban tertiary eye hospital of Dhaka, Bangladesh. The study period covered January 2016 till December 2018. The data was retrieved in the ROP screening electronic database an excel folder that stores patients’ medical records numbers, gestational age, birth weight, ROP stage, time to screening, referring institution (private, public, not for profit or self-referrals) and treatment modalities (laser, Anti-VEGF, retina surgery or combination). Data was broken down monthly. Since the database was specifically designed for ROP, all the stored data was included in the study. There were no exclusion criteria.

The investigator did not get access to the whole database but was granted a copy of the data for the specific period of the study by the Head of the Department. To process the data, the investigator checked the data sheet for completeness before they were exported to SPSS version 23 for Mac for descriptive and correlation analysis. A one-sample t-test was used to test for correlation. Results were presented using tables, pie-charts, bar charts. A P-value of less than 0.05 was considered statistically significant. The study was approved by Ispahani Islamia Eye Institute and Hospital Ethical Research Committee (IIEIH-ERC) and no patient consent forms were needed since the researchers used a database and did not involve any human or photography.

RESULTS

ROP in numbers and treatment modalities: We retrieved 2540 babies screened for the three years period in the database among which 887 had ROP of any stage. The ROP incidence was 34.9%. Demographics and some clinical data were not available in the database. The summary of the numbers of babies screened and treated are presented in Table 1.

More than half (53%) of the screened babies were eligible for at least one treatment modality. Laser is the most commonly prescribed and performed procedure. Cumulatively, 382(43%) babies underwent laser photocoagulation over the 3 years. Trends analysis for the same period shows there is a sharp increase in use of anti-VEGF(from 5 (2%) cases in 2016, 49 (17%)in 2017 to 68(13%) in 2018) and a shy decrease in numbers of babies who need vitreoretinal surgeries (from 19 (7%) surgeries in 2016, 19(6.5%) in 2017 to 16 (4.5%)in 2018). Some babies required a combination of 2 or 3 treatment options.

Table 1: Incidence of ROP and treatment needs

<table>
<thead>
<tr>
<th></th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screened babies</td>
<td>953</td>
<td>778</td>
<td>809</td>
<td>2540</td>
</tr>
<tr>
<td>ROP(Incidence)</td>
<td>246(25.8%)</td>
<td>292(37.5%)</td>
<td>349(43.1%)</td>
<td>887(34.9%)</td>
</tr>
<tr>
<td>No treatment</td>
<td>121</td>
<td>137</td>
<td>159</td>
<td>417</td>
</tr>
<tr>
<td>Laser treatment</td>
<td>102</td>
<td>89</td>
<td>118</td>
<td>309</td>
</tr>
<tr>
<td>Anti-VEGF injections</td>
<td>1</td>
<td>26</td>
<td>22</td>
<td>49</td>
</tr>
<tr>
<td>VR surgeries</td>
<td>18</td>
<td>13</td>
<td>11</td>
<td>32</td>
</tr>
<tr>
<td>Laser +Anti-VEGF</td>
<td>3</td>
<td>21</td>
<td>44</td>
<td>68</td>
</tr>
<tr>
<td>Laser +VR surgery</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Laser +Anti-VEGF+VR surgery</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

Gestational age: The gestational age is presented in Figure 1. Five hundred twenty-eight babies (60%) were moderate or late preterm according to WHO classification. Of note, 216 babies were older than 33 weeks (24%) and 14 babies (2%) did not fit in any WHO category of prematurity although diagnosed to have various stages of ROP. The mean gestational age was 31.9± 2.3 weeks, with a range of 23 to 40 weeks.

Figure 1: Gestational age according to WHO categories
Birth weight: The mean birth weight was 1563 ± 397 grams, with a range of 600 to 3700 grams. The birth weight subcategories commonly used in ROP studies are summarized in Figure 2. Babies weighing 1501-2000 grams represented 34.6% of the total number of ROP babies, followed by babies weighing 1251-1500 grams (32.6%). Thirteen babies (1.5%) had birth weight exceeding 2500 grams.

![Birth weight categorized](image)

**Figure 2:** Birth weight subcategories

ROP staging: Stage 2 ROP was the most prevalent (37.1%) among babies seen. Stages 3 and 1 have almost a similar prevalence. Of note, the aggressive posterior ROP (APROP) prevalence was as high as 10.5%. Details are shown in Figure 3. Trend analysis over the period shows exponential increase of ROP stage 2 and a decrease of stages 4 & 5 (prone to surgical management).

![ROP staging](image)

**Figure 3:** ROP staging

Chronological age and time to screening: Barely half of the babies (55.3%) were screened before age 2 months corroborating the widely recommended 4–6 weeks screening period, the mean time to screening was 1.7 ± 1.19 months, with a range of 1 to 10 months. More details are presented in Figure 5.

![Chronological age at time of screening](image)

**Figure 5:** Chronological age at time of screening

Origin of referrals: The majority of babies are referred by private practitioners (75.4%) mostly from Dhaka the main city. Public hospitals referred 18.4%. Note that almost 3% of babies came directly from the community (self-referred) (Figure 6).

![Origin of referrals](image)

**Figure 6:** Origin of referrals

Correlation analysis between ROP stages and risk factors: There is a negative correlation between the gestational age, birth weight, and ROP stage, the lower the parameter, the higher the risk for severe ROP stage (P-value < 0.001). Conversely, the babies who delayed coming to the hospital were likely to have a higher ROP stage (P-value < 0.001). Values are displayed in Table 2.

Subset analysis: There were 14 babies older than 37 weeks of gestational age in the database. Four of these babies were treated. Three had a low birth weight of 1300 grams each, the fourth was seen later after 2 months and the weight was already 3000 grams. One baby had a stage 5 ROP, no surgical intervention was possible.

![Trend analysis of ROP stages over time](image)

**Figure 4:** Trend analysis of ROP stages over time
DISCUSSION

Ispahani Islamia Eye Institute and Hospital (IIEIH) screened more than 800 babies yearly and therefore the institute can be regarded as one of the most important ROP centers in the world. This is an important dataset for ROP screening compared to the numbers seen in the literature.

IIEH ROP experience shows how ROP screening and management services can be scaled up in a given hospital; from 50 ROP cases screened in year 2012 to a yearly average of 296 cases in the last 3 years is a giant step made forward.

The incidence of ROP among the referrals was 34.9%. Incidences reported in the literature vary and often depend on the screening guidelines of each country. In this study, although the screening guidelines targeted preterm babies younger than 33 weeks of gestational age or babies with a birth weight lower than 1500 grams, there was a big number of babies (24%) older than that GA. Elsewhere, reported incidence was calculated at 32 weeks of GA and there is clear difference between developed and developing countries whereby ROP incidence appears to be lower in the former and higher in the latter: France (22.3%), Sweden (25.5%), United Kingdom (19.2%), India (37.2%), Kenya (40%), Saudi Arabia (41%), Iran (47.3%), Turkey (50.9%) and Istanbul (52.7%).

Among the babies screened to have any ROP stage, 53% needed at least one treatment modality. As reported and supported by other researchers in this field, photocoagulation laser remains the most common treatment modality for ROP and was performed in 389 (43.8%) cases alone or combined with other treatment options. Trends analysis for the 3 years period shows there is a shy but steady increase in use of anti-VEGF (from 5(2%) cases in 2016, 49(17%) in 2017 to 68(13%) in 2018) and a decrease in numbers of babies who were admitted for vitreoretinal surgeries (from 19(7%) surgeries in 2016, 19 (6.5%) in 2017 to 16 (4.5%) in 2018). This was in keeping with the decreasing numbers of surgical cases as observed in the trend analysis.

Table 2: Correlation analysis

<table>
<thead>
<tr>
<th></th>
<th>Stage</th>
<th>Time to screening</th>
<th>Birth Weight</th>
<th>Gestational age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Pearson’s r</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Time to screening</td>
<td>Pearson’s r</td>
<td>0.219</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt; .001</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Birth Weight</td>
<td>Pearson’s r</td>
<td>—</td>
<td>-0.110</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt; .001</td>
<td>0.001</td>
<td>—</td>
</tr>
<tr>
<td>Gestational age</td>
<td>Pearson’s r</td>
<td>—</td>
<td>-0.229</td>
<td>0.519</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>&lt; .001</td>
<td>&lt; .001</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

*Correlation is significant at 0.01 level (2-tailed)
The mean gestational age in this study is higher than those usually reported elsewhere, and some 14 babies were not preterm as they exceeded 37 weeks. Some of the babies had low birth weight or had other risk factors including but not limited to admission in a NICU for sepsis or anaemia necessitating transfusion. Among this sub-group, nine babies did not need any treatment, three had 1300 grams of birth weight and were treated by laser and one who reported lately after 8 weeks in NICU needed retinal detachment surgery. Other researchers have postulated ROP incidence was found to be more associated with low birth weight rather than gestational age17.

Although ROP in big babies has been reported in India, the authors still put a caveat on the accuracy of the reported gestational age and recommended an emphasis on younger preterm rather than big babies so as not to waste man-hours15,18.

The birth weight analysis shows a mean of 1563 ± 397 grams, this was comparable to the findings of Açıkgöz et al19 in their study on ROP screening in a tertiary eye hospital in Istanbul where the birth weight mean was 1,549.4 ± 512.9 grams. Al-Amroet al9 in Saudi Arabia had a completely different scenario where ROP was only diagnosed in babies aged less than 32 weeks and who had a birth weight less than 1250 grams. IIEIH cut-off for screening is 32 weeks and is a referral center as opposed to other research centers that report data obtained from their hospitals’ NICUs. Moreover, some babies were not referred by a health professional, which means they decided to consult when parents noted obvious symptoms like poor or no fixation or leukocoria. A subset analysis of ‘self-referred’ group showed 7 babies (26%) were classified ROP stage 5 of whom only one baby was admitted for surgery. This is a clue that these babies come very late to the hospital.

The time (postnatal age) to screening is also following the same trend as the gestational age and birth weight as it is longer than what we would expect. It is worth noting that 9% of babies came after 3 to 10 months of chronological age. Delayed screening is a matter of concern as it is an important prognostic factor for the successful management of ROP. Many clinicians and researchers report there is a short window for screening between symptoms appearance and complications occurrence. However, this has been a debate and may change from population to population9.

The socioeconomic status of the families was not available in our database and such a piece of valuable information may shed more light on the issue of a delayed screening.

Our finding on ROP staging is in agreement with other researchers’ reports as stage 2 was the most prevalent in our case series. Aggressive posterior ROP was 10.5% of the cases. Other authors reported a similar incidence of APROP in India (13.2%)20. The classification in zones was not available in the database and should be included in the future.

The referring institutions were private in the majority of cases. This is partly explained by the large number of private NICUs in Dhaka. We could not ascertain whether the babies were necessarily born in the referring hospitals or whether they consulted in a private institution after birth. In the first hypothesis, two scenarios are possible; either ROP screening is effectively happening in the public hospitals and there is no need to refer or parents of babies born in public hospitals do not get to know about ROP screening. The former is less likely based on the previous studies2,3.

In the second hypothesis, it would mean many parents trust private pediatricians and still visit them even after the babies were born in public hospitals. Whichever hypothesis is considered, public hospitals need their mother and child health strategy reinforced to bridge the gaps noted in ROP screening for a timely management.

**CONCLUSIONS**

IIEIH is an important ROP screening center given the numbers seen yearly and has achieved a great deal in scaling up services over the last few years. A database is an excellent tool that helps to monitor the progress, however socio-economic status, ROP zones, “plus disease” occurrence data are yet to be included. The delay in screening was evident. Babies with ROP risk factors are referred late and some have advanced disease that requires vitreo-retinal surgeries. The public hospitals need to increase the number and capacity of NICUs with ROP screening staff for a large public access.

**Ethics approval and consent to participate:** This is a database analysis; however, consent was taken from babies’ parents before screening and treatment and agreed their data to be used for research purposes. The study was approved by IIEIH –ERC.

**Consent for publication:** The study was approved by the relevant authority (IIEIH-ERC).

**Competing interests:** None of the authors has competing interest to declare

**Funding:** None was received,

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