Retinopathy of Prematurity in Louisiana

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ABSTRACT

OBJECTIVE: To describe the burden and distribution of disease from retinopathy of prematurity (ROP) in infants in the state of Louisiana. To emphasize current concepts of ROP.

SOURCE OF DATA: A review of hospital discharge data from years 1999 – 2003. The current literature was searched using both Pubmed and OVID.

SUMMARY OF THE FINDINGS: ROP is a common, preventable cause of irreversible impaired vision in children. Although ROP risk factors are known, consensus is weak concerning when to screen for disease or how to define a study case. In Louisiana, there is no trend the overall incidence of ROP throughout the study period. However, the condition is more common in African American infants than in Caucasian infants. There is no difference in incidence between female and male infants.

CONCLUSIONS: The ability to further describe ROP is limited by the case-data available. ROP risk factors include low birth weight and premature birth. For this reason, the study recommends screening of all infants of birth weight < 1,500g and/or all infants of gestational age < 32 weeks.

INTRODUCTION

This study was conducted to describe the burden and distribution of retinopathy of prematurity (ROP), formerly known as retrolental fibroplasia, in infants in the state of Louisiana, and to emphasize current concepts of ROP.

ROP is a disorder of retinal vascularization and is common in premature and/or low birth weight infants. ROP is one of the most common causes of irreversible childhood blindness, and can also lead to myopia, loss of visual field, and strabismus.

The history of ROP is brief, because only following improvement of the last 50 years have newborns at risk for ROP regularly survived. However, the pathogenesis of ROP is now well understood. Retinal vascularization begins at the posterior eye during gestational week eight. Progressing anteriorly, vascularization is complete by week thirty-seven. Premature birth can disrupt the normal vascularization process, resulting in the growth of irregular blood vessels, scarring, and retinal traction.

Treatment for ROP depends upon disease severity and can range from observation to laser surgery.

BACKGROUND

A review of current literature reveals that that there is consensus concerning the pathogenesis of ROP, its major risk factors, and thresholds for treatment. However, there are divergent ideas concerning ROP incidence and thresholds for screening. It is difficult to compare rates of ROP from different centers due to differing selection and exclusion criteria.

Clearly identified risk factors for ROP include the following: birth weight <1,500 g (3.3 lbs), gestation < 31 – 32 weeks, and the prolonged administration of supplemental oxygen.

Munoz and West describe the contribution of ROP in the prevalence of severe visual impairment throughout The Americas. They conclude that ROP mortality is the greatest where the survival of...
premature infants has increased but neonatal technology lags, especially middle income nations. They report ROP-related visual losses account for 8%-19% of all severe visual loss in the United States.4.

In their review of ophthalmologic problems faced by preterm infants, Graziano and Leone characterize at-risk infants as those with birth weights less than 1,500 grams and/or those born at 31 weeks or less gestational age. They conclude that 5%-10% of at-risk infants will develop stage 3 plus disease.2.

Aggarwal et al. characterize trends in ROP incidence at an academic institution in New Delhi, India. They find that although the overall incidence of ROP is not changing, the average severity of the cases is declining. So, the number of cases requiring treatment has declined. Defining “at-risk” as birth weight <1,500g and/or gestational age <32 weeks, their data suggests that 27%-32% of at-risk babies eventually develop ROP.3.

In their review of ROP, Stout and Stout define “at-risk” as birth weight <750g (1.7 lbs) and/or gestational age <28 weeks. However, the review confirms established risk factors and treatment thresholds.1.

Termote, Shalij-Delfos et al. use similar methods as Aggarwal et al., but find in an increase in the incidence of severe ROP with steady overall ROP incidence. They report that 37% of at-risk babies eventually develop ROP.5.

Termote, Donders et al. examine ROP screening criteria, confirming that both gestational age and birth weight are independently significant risk factors for ROP. However, they also suggest that the number of erythrocyte transfusions is also a significant risk factor. They concluded that ROP screening is not necessary if the following relationship is true:7:

If \( b + 2*(g - 20) - 6*e \geq 34 \)

\( b = \) birth weight (decigrams)
\( g = \) gestational age (weeks)
\( e = 0 \) if transfusions < 4
\( e = 1 \) if transfusions \( \geq 4 \)

**METHODS**

The published literature is searched using PubMed and OVID using the following keywords: retinopathy of prematurity, retrolental fibroplasia, and ophthalmology descriptive study. Relevant articles are reviewed, relevant references of these articles are also reviewed.4

The incidence of ROP is estimated using identifier-removed human hospital discharge data, provided by the Louisiana Department of Health and Hospitals. Study patient population includes all live births recorded by Louisiana Department of Health and Hospitals Vital statistics department for the years 1999 – 2003. Cases are identified by ICD-9 (International Classification of Diseases, version 9) code 362.21 (retrolental fibroplasia).3

This study is concerned with the incidence of ROP in newborns. However, the data contain 28 cases which are not newborns. These cases are removed from the data set. See Table 1 for a summary of the removed cases.

The relevant data concerning race, gender, and birth weight are compiled and summarized in Table 2. Statistical analysis with these data include \( \chi^2 \) tests for the following:

1. Differences in incidence by race (Table 3)
2. Trends in incidence by race (Table 4)
3. Differences in incidence by newborn gender (Table 5)

**RESULTS**

From 1999 to 2003, there are 1,572 cases of ROP in the study population. These cases represent 0.51% of all births in the study population (Table 2).

Concerning differences in race, the data support comparison between the incidence in Caucasian and African American infants, but not Caucasian versus Other, and not...
African American versus Other. The data show that there is a statistically significant difference between the incidence in the Caucasian and African American populations, $\chi^2 = 42.73$, $p$-value = 0.000 (Table 3). The data show neither an increasing nor a decreasing trend in ROP incidence for both the Caucasian and African American populations, $\chi^2 = 0.899$ and 0.01, $p$-values = 0.34 and 0.91, respectively (Table 4).

Analysis of incidence in males infants versus female infants shows no significant difference in incidence between the sexes, $\chi^2 = 1.62$, $p$-value = 0.2 (Table 5).

**DISCUSSION AND CONCLUSIONS**

The incidence of ROP in Louisiana is stable throughout the study period. This means that any improvement in survival of low birth weight and/or very premature infants may offset by improved neonatal management.

There is no clear explanation for the difference in ROP incidence between races. The difference may be the result of location, pre and post-natal care, or many other factors.

There is no datum in this study to support changes in accepted treatment and threshold for treatment protocols. Although the literature has not reached consensus, it is widely accepted that ROP risk factors include low birth weight and premature birth. For this reason, the study recommends screening of all infants of birth weight <1,500g and/or all infants of gestational age < 32 weeks.

Limitations to this study are numerous. Foremost, the data are not well suited to evaluate ROP. The data are not sufficient to link at-risk newborns (birth weight < 1,500 and/or < 999g) with cases of ROP.

Therefore, it is not possible to compare the incidence of ROP amongst Louisiana’s at-risk newborns with the incidence in other locations in a statistically significant manner. However, if one postulates that all observed ROP cases occur at-risk newborns, then the incidence would be roughly 15%. This is within the range suggested by the literature. Figure 1 shows that there is likely a relationship between the number of at-risk births in Louisiana and the incidence of ROP within that population.

This study is also limited, because it can not identify one of the two major ROP risk factors, gestational age. A future description of ROP should discover or collect data linking ROP with gestational age, exact birth weight, race, and prolonged administration of supplemental oxygen.

Only more severe (stage 3 of 5, and higher) ROP is of significant health concern. However, all severities (stages 1 – 5 plus) of ROP share the same ICD-9 code. Therefore, any future attempt to retrospectively characterize ROP in Louisiana cannot rely solely on hospital discharge data alone and will likely require chart review.

It is difficult to compare ROP incidence between centers. The few studies available are not consistent in their screening criteria, selection, and exclusion criteria. Some authors report increasing trends, but others report flat, or decreasing trends in incidence. Perhaps the most powerful reviews available aim to establish clear screening rules.

The results imply that policy should focus upon improved data collection as a norm. Much of the information needed for improved analysis is already collected as a matter of everyday business; however, data are compiled in a manner that nullifies the relationships amongst birth weight, ROP disease, gestational age, and administration of supplemental oxygen.
ACKNOWLEDGMENTS

Dr. Raoult Ratard, State Epidemiologist, Louisiana Department of Health and Hospitals guided and assisted this study at every step.

REFERENCES


### Table 1

**Summary of ROP Cases Removed from Data**

<table>
<thead>
<tr>
<th>Race</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>African American</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Other Race</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Unknown Race</td>
<td>9</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Missing Race</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>19</strong></td>
<td><strong>9</strong></td>
<td><strong>28</strong></td>
</tr>
</tbody>
</table>
### Table 2

**Summary of Births in Data Population**

<table>
<thead>
<tr>
<th></th>
<th>Birth Year</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Live Births</strong></td>
<td></td>
<td>67034</td>
<td>67843</td>
<td>65193</td>
<td>64755</td>
<td>64689</td>
<td>65903</td>
</tr>
<tr>
<td>Total Caucasian Births</td>
<td></td>
<td>38350 (57.2)</td>
<td>37946 (55.9)</td>
<td>36740 (56.4)</td>
<td>36605 (56.5)</td>
<td>37066 (57.3)</td>
<td>37341 (56.7)</td>
</tr>
<tr>
<td>Total African American Births</td>
<td></td>
<td>27234 (40.6)</td>
<td>28335 (41.8)</td>
<td>26988 (41.4)</td>
<td>26608 (41.1)</td>
<td>25024 (38.7)</td>
<td>26838 (40.7)</td>
</tr>
<tr>
<td>Total Other Race Births</td>
<td></td>
<td>1450 (2.2)</td>
<td>1562 (2.3)</td>
<td>1465 (2.2)</td>
<td>1542 (2.4)</td>
<td>2599 (4.0)</td>
<td>1724 (2.6)</td>
</tr>
<tr>
<td>Total Male Births</td>
<td></td>
<td>34297 (51.2)</td>
<td>34451 (50.8)</td>
<td>33533 (51.4)</td>
<td>33181 (51.2)</td>
<td>33072 (51.1)</td>
<td>33707 (51.1)</td>
</tr>
<tr>
<td>Total Female Births</td>
<td></td>
<td>32737 (48.8)</td>
<td>33392 (49.2)</td>
<td>31660 (48.6)</td>
<td>31574 (48.8)</td>
<td>31617 (48.9)</td>
<td>32196 (48.9)</td>
</tr>
<tr>
<td>Total ROP Incidence</td>
<td></td>
<td>316 (0.47)</td>
<td>392 (0.58)</td>
<td>426 (0.65)</td>
<td>410 (0.63)</td>
<td>207 (0.32)</td>
<td>1752 (0.51)</td>
</tr>
<tr>
<td>Total Birth Weight &lt; 1500g*</td>
<td></td>
<td>1407 (2.1)</td>
<td>1628 (2.4)</td>
<td>149 (2.3)</td>
<td>1295 (2.0)</td>
<td>1423 (2.2)</td>
<td>1451 (2.6)</td>
</tr>
<tr>
<td>Total Birth Weight &lt; 999g**</td>
<td></td>
<td>761 (1.1)</td>
<td>972 (1.4)</td>
<td>798 (1.2)</td>
<td>692 (1.1)</td>
<td>752 (1.2)</td>
<td>795 (1.2)</td>
</tr>
</tbody>
</table>

* 1,500g = 3.3 lbs  ** 999g = 2.2 lbs  (% of total live births)
Table 3

$\chi^2$ Test for Difference in Incidence by Race

<table>
<thead>
<tr>
<th>Race</th>
<th>ROP (%)</th>
<th>No ROP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>196 (0.105)</td>
<td>186,511 (99.895)</td>
</tr>
<tr>
<td>African American</td>
<td>259 (0.193)</td>
<td>133,930 (99.807)</td>
</tr>
</tbody>
</table>

$\chi^2 = 42.73$

p-value = 0.000
### Table 4

χ² Test for Trend in Incidence by Race

<table>
<thead>
<tr>
<th>Race</th>
<th>Expected Annual Incidence (%)</th>
<th>χ² For Trend</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>39 (0.105)</td>
<td>0.899</td>
<td>0.34</td>
</tr>
<tr>
<td>African American</td>
<td>52 (0.193)</td>
<td>0.01</td>
<td>0.91</td>
</tr>
<tr>
<td>Gender</td>
<td>Birth Year</td>
<td>1999</td>
<td>2000</td>
</tr>
<tr>
<td>------------</td>
<td>------------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Total Affected</td>
<td></td>
<td>121</td>
<td>122</td>
</tr>
<tr>
<td>Male (% of total)</td>
<td></td>
<td>53 (43.8)</td>
<td>66 (54.1)</td>
</tr>
<tr>
<td>Female (% of total)</td>
<td></td>
<td>68 (56.2)</td>
<td>56 (45.9)</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 1.62 \]

p-value = 0.2

**Table 5**

\( \chi^2 \) Test for Difference in Incidence by Infant Gender
Figure 1: At-Risk Births and ROP

ROP Incidence

- births < 999g
- births < 1500g

Year

1999 2000 2001 2002 2003

1800 1600 1400 1200 1000 800 600 400 200 0