# Local Validation of WINROP, an Online Screening Tool for Retinopathy of Prematurity

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## ABSTRACT

**Objective:** To validate WINROP, a web-based screening tool for retinopathy of prematurity (ROP), in the detection of any-stage ROP or treatment-requiring ROP among Filipino preterm infants screened for ROP from January 2013 to April 2017.

**Methods:** Charts of preterm infants who were screened for ROP at a tertiary hospital from January 2013 to April 2017 were reviewed. Birth date, gestational age, birth weight, and weekly postnatal weight measurements were collected and entered into WINROP. The number of infants that were tagged by WINROP with alarm signals for any-stage ROP or treatment-requiring ROP were noted and compared with actual ROP screening findings. The sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) of the WINROP application in predicting any-stage ROP and treatment-requiring ROP were computed.

**Results:** Charts of 138 preterm infants were included in the study. Sixty-four (64) had a chart diagnosis of any-stage ROP and 13 had treatment-requiring ROP. WINROP tagged 77 and 10 preterm infants with any-stage ROP and treatment-requiring ROP, respectively. The sensitivity and specificity rates of WINROP for detecting any-stage ROP were 63.5% (95% CI: 51.5% - 74.2%) and 78.1% (95% CI: 65.7% - 87.1%), respectively. While the sensitivity and specificity rates at identifying treatment-requiring ROP were 76.9% (95% CI: 45.9% - 93.8%) and 46.4% (95% CI: 37.5% - 55.5%), respectively.

**Conclusion:** WINROP is fairly sensitive and specific in predicting any-stage ROP but has fair sensitivity and poor specificity in predicting treatment-requiring ROP. WINROP may aid in ROP prediction, but regular screening of preterm infants at risk for ROP based on current criteria remains to be the standard of care.

**Keywords:** retinopathy of prematurity, ROP, WINROP, preterm, postnatal weight gain

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Retinopathy of prematurity (ROP) remains to be a common cause of preventable blindness in children all over the world.[1] Sight-threatening disease develops in approximately 10-15% of babies with ROP. Early detection of preterm infants at risk for ROP through timely screening cannot be overemphasized.[2]

While prematurity and low birth weight are widely-accepted risk factors for developing ROP, poor postnatal weight gain has been implicated in the development and progression of ROP. An online monitoring tool, WINROP (**W**eight, **I**nsulin-like growth factor, **N**eonatal **ROP**) was recently developed to identify infants at high-risk for developing ROP based on weekly postnatal weight measurements. The web-based software calculates a preterm infant's risk for developing any-stage or sight-threatening ROP based on his/her actual weekly weight gain. When the calculated risk exceeds the high-risk level, an alarm is triggered by the software.[4]

Initial studies have reported varying sensitivity rates of the WINROP tool in detecting high-risk ROP infants, ranging from 50% to 100%.[4,6-10] Given the wide variances in study results, it is important to conduct a local validation of the WINROP online tool. The objective of this study is to validate the WINROP online tool in predicting the development of any-stage ROP and treatment-requiring ROP among Filipino preterm infants in a single institution.

## METHODOLOGY

Medical records of preterm infants admitted at the neonatal intensive care unit (ICU) of the East Avenue Medical Center, who underwent ROP screening, from January 2013 to April 2017 were reviewed. Patient confidentiality was strictly maintained in the course of the study with adherence to the standards set forth by the Declaration of Helsinki and ICH-GCP. Charts of preterm infants born with gestational age of 32 weeks or less and who were admitted at the neonatal ICU for at least 2 weeks were included. Charts that were incomplete or belonging to infants who died during the course of ROP screening or who did not complete the ROP screening due to other reasons, or who had non-physiologic weight gain (i.e. hydrocephalus) were excluded.

Screening, diagnosis, and treatment of ROP were performed by a pediatric ophthalmology fellow; findings and diagnoses were confirmed by a pediatric ophthalmology consultant. ROP classification was based on the International Committee on the Classification of Acute ROP. Treatment was carried out based on the criteria of the Early Treatment for Retinopathy of Prematurity (ETROP) study which included zone I, any stage ROP with plus disease; zone I, stage 3 ROP without plus disease; zone II, stage 2 or 3 with plus disease; and aggressive posterior ROP. Weights obtained from the charts were measured using a digital scale.

Anonymized data such as sex, gestational age at birth, birth weight, weekly weight, most severe ROP stage in the worse eye, and treatment type, if done, were collected and entered on the free online screening tool WINROP. Weekly weights were entered in the online tool until 36 weeks gestational age, as recommended by the WINROP study.

WINROP results were then compared with the actual ROP diagnoses derived from the medical chart. The sensitivity and specificity rates of WINROP to detect ROP were calculated. In addition, the positive predictive values (PPV) and negative predictive values (NPV) were also calculated. Stata v13 were used in data processing and statistical analysis. A *P*-value less than 0.05 was considered significant.

## RESULTS

### Demographics

Medical records of 138 preterm infants were included in the study. Half of preterm infants were male (51.4%). The median gestational age was 31 weeks (range: 26 to 32 weeks). Median birth weight was 1,285 grams (range: 800 to 1,935 grams) (Table 1). Sixty-four (64) of 138 (46.4%) of preterm infants had ROP. Nine infants (14.1%) had ROP type I, while 51 (79.7%) had ROP type II. Aggressive posterior retinopathy of prematurity (APROP) was observed in 4 (6.2%) preterm newborns.

### Agreement Between WINROP Results and Chart Diagnosis

The agreement between WINROP results and actual chart diagnosis is plotted in Table 2. WINROP flagged 77 preterm infants (55.8%). Of the 77 infants who were tagged high-risk for ROP, 50 had ROP.

**Table 1: Demographic Characteristics of Preterm Infants**

| Characteristics | n = 138 |
|---|---|
| Gender, n (%) | |
| Male | 71 (51.4%) |
| Female | 67 (48.6%) |
| Gestational age in weeks | |
| Min - Max | 26 - 32 |
| Mean ± SD | 30.16 ± 1.67 |
| Median (IQR) | 31 (2) |
| Birth weight in grams | |
| Min - Max | 800 – 1,935 |
| Mean ± SD | 1,296.77 ± 262.25 |
| Median (IQR) | 1,285 (341) |

SD: standard deviation, IQR: interquartile range

**Table 2: Agreement Between WINROP and Chart Diagnosis on Any-stage ROP**

| | | Chart Diagnosis | | |
|---|---|---|---|---|
| | | With ROP n=64 | No ROP n=74 | *P*-value |
| WINROP | With ROP | 50 (78.1%) | 27 (36.5%) | <0.0001 |
| | No ROP | 14 (21.9%) | 47 (63.5%) | |

Sixty-one (61) infants did not trigger an alarm. Out of which, 47 did not have ROP. Calculated PPV and NPV were 64.9% and 77.0%, respectively (Table 3).

The sensitivity and specificity rates of WINROP to detect any-stage ROP is also plotted in Table 3. Out of the 64 infants who had a chart diagnosis of ROP, 50 were flagged correctly by WINROP to be high-risk for ROP. Sensitivity of WINROP tool in detection of ROP was 78.1%. Of the 74 infants who did not develop ROP, 47 were not flagged by WINROP. Calculated specificity is 63.5%.

**Table 3: Sensitivity, Specificity, Positive and Negative Predictive Values of WINROP in Predicting Any ROP**

| | % | 95% CI |
|---|---|---|
| Sensitivity | 78.1 | 65.7 – 87.1 |
| Specificity | 63.5 | 51.4 – 74.2 |
| Positive Predictive Value | 64.9 | 53.1 – 75.2 |
| Negative Predictive Value | 77.0 | 64.2 – 86.4 |

Table 4 shows the agreement between WINROP results and chart diagnosis based on treatment-requiring ROP. Seventy-seven (77) infants were flagged by WINROP to have treatment-requiring ROP. Only 10 of these 77 infants had treatment-requiring ROP from chart review. WINROP did not tag 60 infants with treatment-requiring ROP. Fifty-seven (57) of whom truly did not have treatment-requiring disease by chart review. The PPV and NPV values of WINROP for detecting treatment-requiring ROP were 13% and 95.1%, respectively (Table 5).

**Table 4: Agreement Between WINROP and Chart Diagnosis on Treatment-requiring ROP**

| | | Chart Diagnosis | | |
|---|---|---|---|---|
| | | With TR-ROP n=13 | No TR-ROP n=125 | *P*-value |
| WINROP | With TR-ROP | 10 (76.9%) | 67 (53.6%) | <0.0001 |
| | No TR-ROP | 3 (23.1%) | 57 (46.4%) | |

TR-ROP: treatment-requiring ROP

**Table 5: Sensitivity, Specificity, Positive and Negative Predictive Values of WINROP in Predicting Treatment-requiring ROP**

| | % | 95% CI |
|---|---|---|
| Sensitivity | 76.9 | 46.0 – 93.8 |
| Specificity | 46.4 | 37.5 – 55.5 |
| Positive Predictive Value | 13.0 | 6.7 – 23.0 |
| Negative Predictive Value | 95.1 | 85.4 – 98.7 |

Among the 13 infants who truly had treatment-requiring ROP, 10 were correctly identified by WINROP. Sensitivity of WINROP in detecting treatment-requiring ROP in this cohort was 76.9%. Out of 125 who did not have treatment-requiring ROP, 58 preterm infants were not flagged correctly by WINROP. Specificity was 46.4%.

Lastly, among preterm infants with treatment-requiring ROP, the mean advanced alarm time, or interval between WINROP alarm to actual development of treatment-requiring ROP, was 5 weeks.

## DISCUSSION

In this study, the online ROP surveillance system, WINROP, had fair sensitivity and specificity (78.1 and 63.5%, respectively) in predicting any-stage ROP among preterm infants from a single institution. Additionally, the sensitivity and specificity rates in detecting treatment-requiring ROP were 76.9% and 46.4%, respectively. These numbers are lower compared to previous studies done in other countries.[4,7-9] Discrepancies in the results may be due to the presence of other postnatal factors in this cohort of premature infants. WINROP only takes into account postnatal weight gain when in fact ROP development and progression is multifactorial. Other postnatal factors including sepsis, respiratory distress

syndrome, hyperbilirubinemia may contribute to development and progression of ROP.

WINROP is a free, online tool. However, the poor to fair sensitivity and specificity rates from this study limit its application in the local setting. WINROP may aid ROP prediction, but regular screening of preterm infants at risk for ROP based on current criteria remains to be the standard of care.

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