·Clinical Research·

Screening for retinopathy of prematurity: a report from upper Egypt

Mahmoud M. Nassar

Department of Ophthalmology, Minia University Hospital, Al-Minia 61111, Egypt

Correspondence to: Mahmoud M. Nassar. Department of Ophthalmology, Faculty of Medicine, Minia University, Al-Minia 61111, Egypt. m.nassar@doctors.org.uk

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Abstract

• AIM: To detect the incidence of retinopathy of prematurity (ROP) in a tertiary referral neonatal intensive care unit in upper Egypt and to describe the obstacles faced during implementing the screening protocol for the first time.

• METHODS: Consecutive infants were enrolled at birth and screened for ROP. We used the UK ROP guideline (May 2008) for infant selection, follow up and treatment. Repeat examinations were performed until retinal vascularisation was complete.

• RESULTS: Fifty–two infants were enrolled: 24 males and 28 females. Mean gestational age was 31.3wk (±2.8 SD) and mean birth weight was 1234.6 g (±221.1 SD). Incidence of ROP was 36.5% (stages 1, 2, 3 and 4a were 9.6%, 9.6%, 15.4% and 1.9% respectively), no stages 4b or 5 were found in this series. Six infants (11.5%) died during screening without ROP, 25 infants (48.1%) were discharged from screening with retinal vascularisation reaching zone III, 5 infants (9.6%) were treated with indirect diode with or without additional cryotherapy and 16 infants (30.8%) were lost to follow up. In this series gestational age rather than birth weight was found significantly correlated and predictive (P<0.05) with ROP stages.

• CONCLUSION: ROP in a single site in upper Egypt appears to have comparable incidence to other areas worldwide. The main screening obstacle was missing cases due to the absence of a national ROP screening protocol.

• **KEYWORDS:** retinopathy of prematurity; incidence in Egypt; neonatal screening

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INTRODUCTION

Retinopathy of prematurity (ROP) has been described as a possibly avoidable cause of blindness in children, particularly in middle income countries [1]. ROP is a potentially blinding condition where abnormal vascularisation develops in the retina of premature infants. These abnormal vessels are liable to bleeding and scarring. This may cause tractional retinal detachment, which is the main cause of visual impairment in ROP. The stages of ROP describe findings at the interface between the vascularised and non-vascularised retina using an ophthalmoscope: stage 1 is a demarcation line, stage 2 is an elevated ridge, stage 3 is an extraretinal fibrovascular proliferation, stage 4 is subtotal retinal detachment, whereas stage 5 is a total retinal detachment. In addition, plus disease, indicates dilatation and tortuiousity of blood vessels in the posterior pole[2]. Whereas, the use of unmonitored supplemental oxygen in the 1940's and 1950's was considered the dominant risk factor for the "first epidemic" of ROP in industrialized countries, the second epidemic of ROP was triggered by the survival of smaller and less mature babies caused by increasingly accurate methods of monitoring oxygen supplementation and improved management of neonatal and perinatal complications. In industrialized countries blindness from ROP is now largely restricted to infants in the extremely low birth weight group[3].

The third epidemic of ROP is used to describe the increasing frequency of ROP blindness in middle income countries and urban areas of low income countries where neonatal care is rapidly improving with survival of less mature and smaller babies. The reason for this epidemic is variable; on one hand low birth weight and very premature birth in nurseries in which care is similar to that found in developed countries and on the other hand, the inadequacy of neonatal care is likely the major contributor to the development of ROP in nurseries with more limited human and equipment resources[4]. Reports from China, Southeast and South Asia, Latin America and Eastern Europe have shown that ROP is becoming an important cause of blindness especially in urban centres in newly industrializing countries[3].

The prevalence of ROP in Minia Governorate is unknown. The current study aims to find out where we stand in terms of incidence and severity of ROP in a tertiary referral intensive care unit (ICU) and to describe the obstacles faced during implementing the ROP screening protocol for the first time.

SUBJECTS AND METHODS

Fifty-two premature babies born between January 2010 and March 2011 and admitted to the neonatal ICU at Maternity and Paediatrics University Hospital, Al-Minia, Egypt (a

facility with 18 incubators and receives nearly 420 neonates per year); were subject to ROP screening. Criteria for inclusion onto ROP screening were: surviving for more than 28d, gestational age (GA) <32wk and or/ a birth weight (BW) <1500 g. The screening protocol was based on the recommendations provided by the UK ROP guideline May 2008 [5] with no modifications to our unit. Ocular fundus examination was performed under pharmacological mydriasis with 2.5% phenylephrine (Phenylephrine® -Misr Co.) and 1% cyclopentolate (Cycloplegico® -Alcon) eye drops. An indirect binocular ophthalmoscope (Keeler Vantage®), 28 D magnifier (double aspheric-Volk), an infantile blepharostat and a scleral indentation were routinely used under topical anaesthesia.

The first ophthalmological examination was performed between the 4th and the 5th weeks of postpartum age, with reviews every 1-2wk until the retinal vascularisation was well into zone III. Every child was designated according to the maximum degree of retinopathy detected, following the international classification of retinopathy of prematurity (ICROP) [6].

Treatment with diode laser (IRIS Medical Diode OcuLight SLx 810 nm) and/or cryotherapy (DORC cryostar 1500-III) was indicated for patients with stage 3 acute retinopathy, as defined by ICROP [6], qualifying for pre-threshold disease, as defined by the early treatment for ROP randomized trial [7]. Surgical treatment was not indicated in this study. Informed consent from parents was obtained for all patients requiring treatment.

The collected data included: GA; BW; gender; multiple or single; maximum stage of retinopathy; presence or absence of plus disease; pre-threshold reached; number of examinations; result of screening (discharged, treated, missed or died).

Descriptive statistics (means, standard deviation and frequencies), comparison of means (Mann-Whitney U) and correlation statistics (Spearman correlation) was performed using SPSS software version 17.0.

This study has gained approval from the Local Research and Ethics Committee, Faculty of medicine, Al-Minia University and has been conducted in accordance to the Declaration of Helsinki.

RESULTS

This study presents the results of 16mo of ROP screening from January 2010 to April 2011. Fifty-two infants were enrolled, born January 2010-March 2011. Twenty-four were males and 28 females. Forty-eight were single births and 4 were multiple. Mean GA was 31.3wk (±2.8 SD) and mean BW was 1234.6 g (±221.1 SD) (Figures 1, 2). Regarding the workload the number of visits ranged from 1-10 (mean 2.24± 2.1) (Table 1).

Infants included in this study fulfilled either one or both inclusion criteria. Nineteen infants (36.5%) had ROP, 13/19 fulfilled both screening criteria and 6/19 fulfilled only one criterion for ROP screening. ROP stages 1, 2, 3 and 4a were

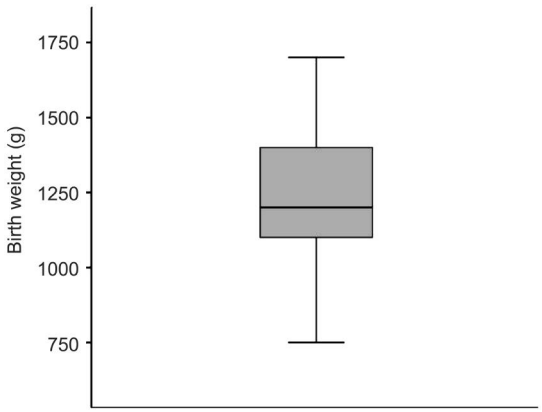

Figure 1 BW box and whiskers showing median, quartiles and extent.

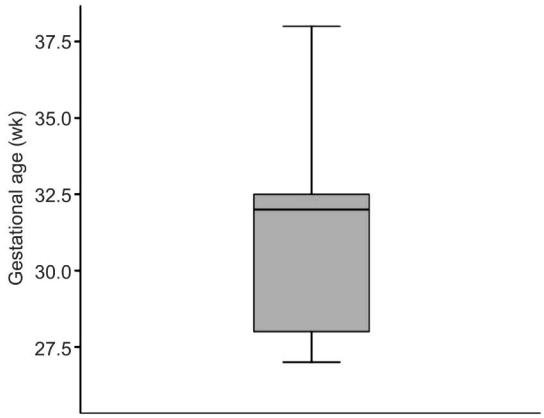

Figure 2 GA box and whiskers showing median, quartiles and extent.

Table 1 Demography in relation to ROP staging

Max ROP stage	GA (wk)		BW (g)		No. of visits	
	Mean	SD	Mean	SD	Mean	SD
0	32.1	3.1	1255	234	1	0
1	30.2	2.0	1280	295	3	1
2	29.4	1.7	1130	84	3	2
3	30.5	1.7	1206	194	5	3
4	28.0		1100		3	

9.6%, 9.6%, 15.4% and 1.9% respectively, no stages 4b or 5 were found in this series (Table 2), 42.1% (8/19) had pre-plus disease and 26.3% (5/19) had plus disease.

The outcomes of this case series were: 25 infants (48.1%) were discharged from screening with retinal vascularisation reaching zone III, 6 infants (11.5%) died during screening without ROP, 5 infants (9.6%) were treated with indirect diode with or without additional cryotherapy and 16 infants (30.8%) were lost to follow up. Table 2 presents outcomes in relation to maximum ROP stage.

In this series GA rather than BW was found significantly different (Mann-Whitney U) between the ROP group and non-ROP group (Table 3), furthermore, a significant inverse correlation (Spearman correlation) was found between GA and the maximum ROP stage (r_s=-0.343; P=0.013, 2-tailed).

DISCUSSION

Prior to our initiation of ROP screening protocol in January

Table 2 Outcomes *n*

Parameters	Maximum ROP stage					Total
	0	1	2	3	4	
Outcome						
Discharged	19	1	1	4	0	25
Treated	0	0	1	3	1	5
Missed	8	4	3	1	0	16
Died	6	0	0	0	0	6
Total	33	5	5	8	1	52

Table 3 Demography of Non-ROP group *vs* ROP group (ROP stage, 1-4) $\bar{x} \pm s$

Parameters	Non-ROP	ROP	[a]*P*
Mean BW (g)	1254.55±233.97	1200±179.9	0.276
Mean GA (wk)	32.06±3.09	30±1.67	0.012

[a]Statistical significance (2-tailed).

2010 high risk infants were referred to ophthalmologist following discharge from the neonatal ICU. Initiating screening was received very well by paediatricians; unfortunately, this was not followed by change in the overall administrative process of the neonatal ICU. This obstacle was partially overcome by weekly phone calls from the author to include new admissions and to ensure timely eye drop instillation prior to examination.

Pre-screening parent counselling was difficult due to mismatching of the authors time table and the parent visiting hours, nevertheless, pre-operative counselling and consenting was a must.

To the author's opinion the main screening obstacle is infants who were lost to follow up (30.8%). As there are no designated notes for screened infants, a liability for accidental discharge from ICU is always present, additionally, the insufficient contact between the author and parents during the screening process has lead to the accidental discharge of infants and no further ophthalmic follow up. Additionally, as screening was conducted purely from the ophthalmology point of view, there was strict adherence to the inclusion criteria of ROP screening and no additional neonates were screened based on other risk factors.

Looking into missing cases (Figure 3) all but one infant were considered high risk of developing pre-threshold disease hence this is considered a major flow in our screening that is yet to be resolved. Whereas many published studies do not specify the rates of cases lost to follow-up studies from India[8], Pretoria[9] and Saudi Arabia[10] reported the incidence of lost to follow up cases as 17%, 20% and 20% respectively. Our study had a 36.5% incidence of ROP in upper Egypt. Table 4 compares other population based studies to ours.

In this study the mean BW and GA were 1234.6±221.1 g and 31.3±2.8wk. Hakeem *et al*[2] report heavier and more mature babies (BW 1510±245 g and GA 33.02±1.72wk). Amer *et al*[19] had comparable BW (1245.4±348.8 g) and GA (30±2.5wk) and Karkhaneh *et al*[12] had comparable BW (1256±389 g) and lower GA (28.8±2.4wk). Whereas Al-Amro *et al*[11] and Al Hazzani *et al*[17] reported smaller and more immature babies (BW 1103±302 and 1062±302 g respectively and GA 28.4±2.4 and 29±2.9wk respectively).

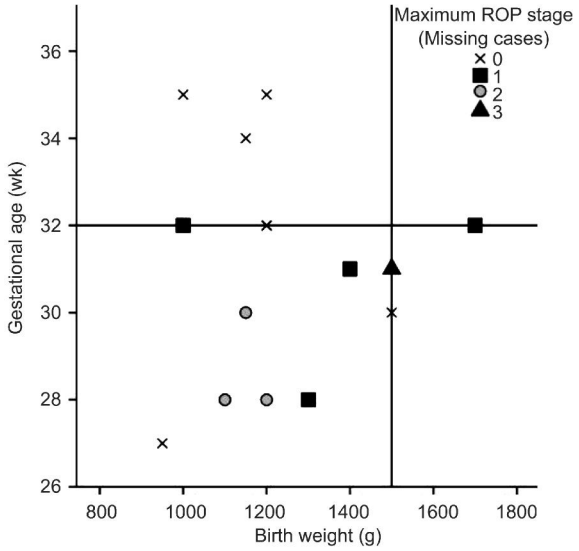

Figure 3 Missing cases scatter plot showing ROP stage, BW and GA of each missing case with cut off lines highlighting screening inclusion criteria.

Table 4 Comparison with other population based studies

Authors	Year	Location	Incidence (%)
Studies with similar incidence			
Al-Amro *et al*[11]	2003	Saudi Arabia	37.40
Karkhaneh *et al*[12]	2008	Iran	34.50
Sarikabadayi *et al*[13]	2011	Turkey	32.70
Hadi and Hamdy[14]	2013	Egypt	34.40
Ali *et al*[15]	2013	Brunei	34.80
Bedda *et al*[16]	2014	Egypt	33.74
Studies with lower incidence			
Al Hazzani *et al*[17]	2011	Saudia Arabia	28.30
El-Mekawey[18]	2011	Egypt	23.00
Amer *et al*[19]	2012	Saudia Arabia	23.31
Hakeem *et al*[2]	2012	Egypt	19.20
Chaudhry *et al*[20]	2013	Pakistan	11.50

Whereas most studies identify both GA and BW as significant risk factors of ROP severity, the current study identifies GA rather than BW as significantly associated with ROP severity and this was in agreement with results from China on discordant twins by Wang *et al*[1]. A possible explanation could be the fact that all included neonates had low/nearly similar BW as this is the main cause of admission into neonatal ICU in Minia University Hospital; therefore GA becomes the main changing variable.

In this study infants with ROP stage 2 were found to have the lowest GA and BW; unfortunately the final outcome of these infants is uncertain as more than half (3/5) were lost to follow up. Additionally there was no formal input from neonatologists on other potential risk factors (including concurrent infection and anaemia). Bearing in mind the aforementioned along with our small sample size, apparently healthier infants may seem to progress to ROP stage 3 than those who stay at stage 2.

Considering number of visits, the current study (2.24±2.1) had slightly fewer number of visits compared to those recorded by Ali *et al*[15] (3.19±1.1).

Only a hand full of studies were published from Egypt on the incidence of ROP, in 2012 Hakeem *et al*[2] published a study from the same locality that enrolled 172 infants within 2y and found ROP in 19.2%. The authors explained this very low incidence by enrolling heavier and more mature infants with additional risk factors (11 added risk factor other that BW and GA) thus having a mean GA 33.02±1.72wk and mean BW 1510±245 g. However, they neglected the fact that the vast majority of their infants (148/172) had a GA >32wk, furthermore, they failed to present the ratio and demography of these mature high risk infants compared to those meeting the ROP screening criteria only. A second study with lower incidence (23%) was by El-Mekawey [18] in 2011, however, this study was conducted in the private sector with poor resemblance to public hospitals. The remaining two studies were from Alexandria, Egypt and both had resembling incidence[14,16].

To conclude, ROP in a single site in upper Egypt appears to have comparable incidence to other areas worldwide. The main screening obstacle was the cases that were lost to follow-up. At this point in the absence of a national/regional liaison between neonatologists and ophthalmologists, we are not in a position to evaluate the suitability of the UK screening protocol to our children; furthermore, there is no intention on lowering these criteria as suggested by other studies as we have not yet included older and heavier neonates with other risk factors into ROP screening.

Limitations of this study include: small numbers, infants lost to follow up, limited pre-screening counselling with parents, absence of an administrative compliance in the neonatal ICU and screening was conducted purely from the ophthalmology point with no integration of other neonatal risk factors.

ROP is known for its sequential nature and for its probability of progression to vision threatening tractional retinal detachment hence screening protocols have been set for timely examination of high risk neonates. Whereas using a standardised protocol for ROP screening in upper Egypt is in its early stages; this study acknowledges the need for improved communication between neonatologists, ophthalmologists and parents. We are hoping for better adherence and increasing the awareness of this condition among parents to overcome the current obstacles and avoid the devastating effect of this preventable disease.

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Conflicts of Interest: Nassar MM, None.

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