Commentary: Predicting need for treatment in retinopathy of prematurity – The elusive Holy Grail

The World Health Organization has estimated that over 15 million babies are born preterm worldwide every year.[1] India leads the world in the highest number of preterm births. Among the many complications that can occur in premature babies, retinopathy of prematurity (ROP) is an important cause of preventable blindness. Screening for ROP is vital in neonatal health care. Unfortunately, there is a huge gap between the need for ROP screening and its delivery. Moreover, the incidence of ROP also varies widely from country to country and from region to region. All babies born premature do not develop ROP, and all those who develop any stage of ROP do not require treatment. This raises the important issue of bridging the gap between the need to screen and the need to treat. While screening can be done remotely via telescreening, diagnosis of ROP needs expert opinion. Ability to predict which babies born preterm are likely to develop ROP that requires treatment can be the Holy Grail that reduces the screening burden. Various methods have been used to predict development of ROP, including hemogram,[2] postnatal weight gain ratio,[3] image grading by trained readers/e-ROP,[4] and the widely used WINROP application.[5]

In the article titled "The retinal vascular growth rate in babies with retinopathy of prematurity could indicate treatment need," the authors present data on the rate of retinal vascular growth.[6] They cross-sectionally measured vascular length on fundus images in various quadrants to derive an average rate of growth. These measurements were carried out at one time point – just prior to treatment in the treatment group and at the last available image with both the disk and the end of blood vessels in the non-treatment group. The post-menstrual age (PMA) at measurement was lesser in the treatment (36.52 ± 2.37 weeks) group as compared to the non-treatment group (38.65 ± 2.92 weeks). The average rate of growth for babies requiring treatment was 0.49 ± 0.12 DD/week as against 0.612 ± 0.10 DD/week in the low-risk prethreshold group and 0.719 ± 0.09 DD/week in the no ROP group. The authors conclude that more than 80% of babies with a vascular growth rate of 0.54 DD/week or less required treatment. The inference one may draw from this data is that babies with slower vascular growth develop ROP that requires treatment. The main limitation of the study is that data from one time point are used to draw inferences about the vascular growth that occurred temporally. In babies who required treatment, was the growth slow throughout or was it affected by an external agent like oxygen exposure, sepsis, anemia of prematurity, etc.? What was the vasular growth rate in babies who did not require treatment at the same PMA as those who were treated? These are a few vital questions that still remain unanswered.

In another study, Jang *et al.* studied the vascular development and other findings on fundus imaging at a uniform predefined time point of 33–34 weeks PMA of the babies screened for ROP who were born before 31 weeks Gestational age (GA).[7] They noted that 55% of eyes requiring treatment had incomplete vascularization into Zone 1. Their data indicated that ROP development was 24.58 times more likely in those babies with a retinal hemorrhage at the leading edge of vascular development, 9.70 times more if the leading vascular edge was within Zone 2 posterior, 6.71 times more if demarcation line was seen, 7.35 times more in the presence of circumferential vessel, and 8.02 times more in cases with pre-plus. This evaluation of image at one predefined time point in the early vasoproliferative stage of ROP has great predictive value for ROP development. This study also has not analyzed the influence of any perinatal factors that are known to be associated with ROP development.

The inference from the data of these two studies is that babies with lesser vascular development, and thereby larger avascular area are more likely to develop treatment-requiring ROP. While this interpretation may appear to be quiet obvious, these studies put into perspective the need to analyze how the vasculature develops in premature babies after birth. A prospective study that measures vasular growth at diferent time points, possibly even before the conventional time points for commencemnt of ROP screening till babies need treatment or retina is vascularized completely may help us determine the true predictive value of retinal vascular growth rate. Regression analysis of the vascular growth against all factors that can influence ROP development can help determine which factors actually hamper vascular development. This information can lay the foundation to predict not only the need for treatment, but also the interventions to limit development of treatable ROP.

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