

Newborns Vitamin E Level and Its Relationship with Retinopathy of Prematurity

Rahman MM¹, Mannan MA², Khan MKA³, Jahan I⁴, Hasan MZ⁵, Dey AC⁶,
Dey SK⁷, Moly KN⁸, Shahidullah M⁹

1. Dr. Mohammad Mozibur Rahman, Assistant Professor, Department of Neonatology, Institute of Child and Mother Health, Matuail, Dhaka
2. Professor Dr M A Mannan, Professor, Department of Neonatology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka
3. Dr. Md. Kamrul Ahsan Khan, Junior Consultant, Department of Neonatology, Institute of Child and Mother Health, Matuail, Dhaka
4. Dr. Ismat Jahan, Medical officer, Department of Neonatology, Bangabandhu Sheikh Mujib Medical University
5. Dr. Md. Zahidul Hasan, Consultant, Department of Neonatology, Asgar Ali Hospital, Gendaria, Dhaka.
6. Dr Arjun Chandra Dey, Associate Professor, Department of Neonatology, Bangabandhu Sheikh Mujib Medical University
7. Dr Sanjoy Kumer Dey, Associate Professor, Department of Neonatology, Bangabandhu Sheikh Mujib Medical University
8. Dr. Kazi Nilufar Moly, Assistant Professor, Department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University
9. Professor Dr Mohammad Shahidullah, Professor, Department of Neonatology, Bangabandhu Sheikh Mujib Medical University

Correspondence: Dr Mohammad Mozibur Rahman

Abstract: Introduction: Vitamin E status in newborn is not well established. Many studies showed that vitamin-E level is low in premature babies and without supplementation complications may occur including retinopathy of prematurity (ROP). So this study was aimed to estimate serum tocopherol (vitamin-E) level in infants and to find out the relationship of low serum vitamin E level with the development of ROP.

Method: This cross sectional analytic study was performed in the department of Neonatology, BSMMU over a period of 6 months. Total 75 stable term (38-42wk) and preterm (30-35wk) newborn infants admitted in BSMMU were consecutively enrolled. Newborns of <30 weeks and 36-37 weeks of gestation, hemodynamically unstable or with major congenital anomalies were excluded. After informed written consent from parents, 3 ml free flow venous blood was collected at 3-5 days of life. Serum Vitamin E level estimation was done by high performance liquid chromatography (HPLC) and ROP screening was done by a qualified ophthalmologist by binocular indirect ophthalmoscope. Data was analyzed by SPSS software version 20. Level of significance was tested by appropriate statistical tests.

Result: Among 75 enrolled infants, parents of 5 infants refused to give blood and thus excluded. Finally 70 neonates were available for vitamin E estimation and among them 40 preterm infants were advised for ROP screening. Vitamin E level in preterm newborns was 0.3773 ± 0.2447 mg/dl and in term newborns it was 0.8038 ± 0.4257 mg/dl and the difference was statistically significant ($P < 0.001$). Among the 40 preterm infants 12(30%) were found to have ROP. Step wise logistic regression showed that vitamin E deficiency is a significant risk factor for the development of ROP (RR: 4.71; $p < 0.05$).

Conclusion: Serum vitamin E level was found significantly lower in preterm newborns in comparison to term newborns and vitamin E deficiency was significantly related with the development of ROP.

Key Words: Vitamin E, ROP, Preterm and term new born infants

Date of Submission: 16-03-2018

Date of acceptance: 31-03-2018

I. Introduction

Vitamin E is one of the four fat-soluble vitamins largely synthesized by plants. It has eight different isoforms (vitamers) divided into two classes of four vitamers each. Compounds having saturated side chains are classified as tocopherols, and having unsaturated side chains known as tocotrienols (trienols). Vitamers are identified as alpha, beta, gamma or delta. A large number of research currently focuses on the alpha tocopherol form of vitamin E, which is biologically most active^{1,2}. Vitamin E is an important micronutrient and effective lipid

membrane antioxidant, essential in maintaining integrity and functional ability of plasma membrane. They prevent cellular injury by lipid peroxidation and also plays an important role in normal immune function^{3,4,5}.

Newborns are more susceptible to oxidative stress due to increased production of free radicals at birth, and incompletely developed antioxidant mechanisms including Vitamin E deficiency. Vitamin E protects the cell membrane from lipid peroxidation and thus protects the neonates from oxidative related disease, such as Hemolytic disease, Retinopathy of prematurity (ROP), Bronchopulmonary dysplasia (BPD), and Intraventricular hemorrhage (IVH)^{6,7}. It is well documented that, placental transfer of vitamin E is limited⁸⁻¹⁰.

Although normal adult plasma vitamin E level is well established, but there has been very little written about the level in the newborn group¹¹ and in this group it is very unsatisfactory, because most of the studies done in neonates are based on cord blood estimation only¹². The average level of plasma tocopherol in term infants was first determined by Wechsler. The only report on premature infants was by Wens¹¹. Vitamin E has been credited with a variety of beneficial effects in premature infants and has been thought its deficiency is at least partly responsible for the anemia of prematurity and ROP^{13,14}.

Every year fifteen million infants are born preterm and more than one million children die from complications of prematurity and millions more face life time disability. Vitamin E is an important antioxidant for the health and wellbeing of premature neonates^{15,16}. Retinopathy of prematurity is one of most important disability¹⁷. It is a vasoproliferative retinopathy occurring primarily, but not exclusively, in premature infants, and is a major cause of pediatric blindness in developed countries. While ROP was considered untreatable 10 to 20 years ago, the condition has become controllable in recent years. Cryopexy or laser is useful for arresting progression of ROP to avoid vitreo-retinal complications¹⁸. So as no original work is available in the literature about the vitamin E status and its relationship with ROP in Bangladeshi neonates, the present study is intended to document the vitamin E level in Bangladeshi neonates and to examine relationship of Vitamin E level with ROP.

II. Materials And Methods

It was a cross-sectional analytic study, conducted in the Neonatal Intensive Care Unit (NICU), Department of Neonatology, Bangabandhu Sheikh Mujib Medical University over a period of 6 months (April 2013 to September 2013). Ophthalmoscopic examinations were performed in the Department of Ophthalmology of this University.

After taking informed written consent from parents, stable term (38-42 weeks of gestation) and preterm (30-35 weeks of gestation) infants of both sexes within first 3 days of life were included consecutively in the study. Hemodynamically unstable infants, infants with congenital anomalies were excluded. A total of 75 neonates were enrolled. Five parents denied giving blood for serum vitamin E estimation. A total of 70 neonates (30 term and 40 preterm) were retained and completed the follow up. Detailed maternal history was taken, regarding-age, gravida, parity, LMP, EDD, any significant illness during the pregnancy period, APH, HTN, and antenatal steroid administration, presence of PROM, place and mode of delivery. Birth weight has been recorded from labor room or neonatal referral sheet in case of out born infants. If the neonate was admitted within 6 hours of birth, his/her admission weight (taken by a digital weighing scale, SALTER, Model-914) was taken as birth wt.

Blood Sample for vitamin E estimation was collected between 72 hours to 120 hours of age, because <72 hours of life vitamin E level may reveal falsely low due to unknown cause. Provisional diagnosis, problems and complications were also recorded. Daily follow up was given regarding clinical course, When the baby got oxygen inhalation, its flow rate, and duration were noted, volume of whole blood transfusion if any were also recorded. Immediate outcome (death or discharge) were noted. All the information was recorded in a pretested questionnaire.

Parents or attendants of all the premature neonates were counseled for routine follow up and date of eye examination was adjusted to the date of routine follow up. Date of first ROP examination was fixed at 4 to 6 weeks of chronological age of the baby as ROP usually is not developed before this period. Ophthalmoscopic examinations in all preterm infants were performed by an ophthalmologist of the Department of Ophthalmology, BSMMU, experienced in ROP screening. Pupils were dilated with 1% phenylephrine and 0.5% tropicamide eye drop, instilled twice 5 minutes apart. The examination is performed 30 minutes later using a binocular indirect ophthalmoscope and 20D lenses. If necessary, scleral indentation was done to see the periphery of the retina.

Details ophthalmological reports were written in the questionnaire along with the advice for further examination (if required). Numbers of preterm newborns gradually decreasing from 1st to 3rd screening. If the ophthalmologist found that the retina is normal in consecutive two examinations 1-2 weeks apart, then subsequent examination is not required. Term babies were not examined for ROP as they don't develop retinopathy in stable condition. Study was approved by Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University.

Procedure of Blood Sample collection and Vitamin E estimation: Three ml of free flow venous

blood was drawn with strict asepsis, in a red top test tube supplied by the laboratory, wrapped by aluminum foil paper to protect it from sun light and transported to local office of the testing lab in Dhaka within 30 minutes in a cool box. Serum was separated by centrifuging at 4000 rpm and was then frozen. Sample was then sent to central lab in **India** in a zip lock bag placed in a thermal cool box with pre-frozen gel pack at 0°C and was transported in sealed cardboard box labeled “Frozen Sample”. Vitamin E estimation was done by high performance liquid chromatography (HPLC) system with ultra violet (UV) detector from Waters Pvt. Ltd. USA.

Data analysis: Quantitative data were expressed as mean \pm standard deviation and categorical data presented as frequency. Level of significance was tested by Independent t-test, Chi-square test, Odds ratio or Relative risk and Step wise multiple logistic regression test where applicable. Data analysis was done by the statistical software IBM SPSS Statistics version 20 (SPSS Chicago, IL) and results were considered statistically significant at p value < 0.05 .

III. Results

During the study period of six months, total 75 neonates were enrolled. Among them 33 were term (38-42 weeks) and 42 were preterm (30-35 weeks). Parents of 5 neonates (3 term and 2 preterm) did not give consent to collect blood for vitamin E estimation. So, ultimately 70 neonates (30 Term and 40 Preterm) were available. Parents of all preterm infants (40) were counseled for ROP screening and all of them (40) presented for first screening.

Demographic and perinatal characteristics of studied infants are presented in table-I. Of the 70 infants, male:female ratio was surprisingly equal and most of the newborns delivered by LUCS and 87% babies were inborn. Eighteen neonates (25.87%) were born at 30-32 weeks of gestation and 31.28% neonates were born at 33-35 weeks of gestation. Thirty (42.85%) neonates were in gestational age group 38-42 weeks. Among the preterm 25% were small for gestational age (SGA), having birth weight falling below the 10th percentile of his particular gestational age.(Table-1). No significant difference was observed among SGA and AGA groups of preterm and term infants and no sex difference was also observed in Vitamin E level.

Serum Vitamin E level in preterm newborns was 0.3773 ± 0.2447 mg/dl (ranging from 0.20-1.52mg/dl) and in term newborns it was 0.8038 ± 0.4257 mg/dl (ranging from 0.08-1.23mg/dl). Level is much lower in preterm group than term group (p value 0.001). Vitamin E deficiency was 33% in case of term newborns (10 out of 30) whereas in preterm group it was 70% (28 out of 40) (p -0.002).

The ideal time of ROP screening is 4-6 weeks of chronological age but may be done up to 8 weeks. For first screening 62.5% infants presented at 4 weeks of chronological age, 25% at 5th & 6th weeks. Rest was examined at 7th and 8th week. At first screening, 25% (10) revealed ROP. At second screening, 35 infant were examined, among them 22.85% (8) were found to have ROP. Among the 8 cases two were newly developed ROP who had normal findings at first screening.

Twenty two neonates were examined for third screening. Of which 3 (13.63%) were abnormal. So ultimately, 12 infants among 40 were diagnosed to have ROP.

Among the 40 preterm newborns, 28 were vitamin E deficient, of which 11 develop ROP and one preterm newborn developed ROP with normal vitamin E level (p value < 0.05), that indicates vitamin E deficiency is associated with the development of ROP (Table II). Mean vitamin E level in 12 newborns with ROP was 0.304 ± 0.096 and in newborns without ROP it was 0.4086 ± 0.282 . Newborns with ROP have lower vitamin E than without ROP (p value < 0.05). There was no significant relationship of ROP with gestational age, sepsis, O₂ inhalation and blood transfusion (Table III) and no significant association of ROP was documented with duration and concentration of oxygen and volume of blood transfusion among studied infants (table IV).

Table V shows, the stepwise multiple logistic regressions of risk factors. Here study risk factor vitamin E deficiency shows significant risk of developing ROP when other risk factors are intercepted. When all other independent variables are made zero statistically step by step, then vitamin E deficiency is an independent risk factor for the development of ROP.

IV. Discussion

Vitamin E was 1st discovered by Evans and Bishop in 1922 and 1st clinical use was done in 1942, since then there were much controversy about the normal level of vitamin E in newborn and role of vitamin E in ROP¹⁹. In the present study, vitamin E level in preterm newborns was 0.3773 ± 0.2270 mg/dl and in term newborns was 0.8038 ± 0.4257 mg/dl. Level is much lower in preterm than term group which is statistically significant ($p < .001$). This finding is similar to Malik et al and Giyasettin et al^{3,8} but contrary to other reported no significant difference of vitamin E levels between preterm and term babies⁵. Raksha et al¹⁰, stated that premature infants have lower levels of serum vitamin E at birth, also been supported by several others^{14,20}. These differences have been found to persist at 10 day of life⁹. The relative deficiency of vitamin E in premature infants is attributed to factors such as limited tissue storage and also, perhaps immature transport mechanisms¹¹. The low values seen in preterm infants may have consequential clinical importance⁸.

According to the WHO criteria, vitamin E deficiency is defined as tocopherol <500 µg/dl⁶. Body fat is increased during late gestation; therefore, preterm VLBW infants are born with lower storage of fat-soluble vitamins and are at high risk of fat-soluble vitamin deficiency. Moreover, fat absorption in these infants is impaired, and they usually have a higher requirement than term infants⁶. This is because absorption of fat-soluble vitamins depends on fat absorption that requires the presence of food, bile salt and pancreatic lipase activity. These components may not function properly in premature infants and SGA infants have less body fat.

Regarding vitamin E status, there are several ways to determine vitamin E sufficiency such as vitamin E/ total lipid, cellular vitamin E concentrations and plasma tocopherol level. In our study, we used plasma tocopherol because of the ease of using this test, and it has a clear cutoff for deficiency according to the WHO criteria⁶. Vitamin E deficiency was observed in 33% in term infants whereas in preterm infants it was 70%. There was no difference in the Vitamin E status between SGA or AGA infants of either term or preterm group. Winfield T. Moyer¹¹ found no significant difference in the tocopherol levels of term infants of different weight group similar to our study. Jitka et al¹² is also in agreement with this. No significant sex difference was observed in serum vitamin E levels between term and preterm group, is in agreement with the findings of Pratik et al⁹.

ROP is a multifactorial disease. With the advancement in the neonatal care, survival rate of premature VLBW neonates has increased in developing countries and the incidence of ROP has also been proportionately increased²¹. It has a well-known variation in the incidence as well as associated risk factors among centers and among countries, related to differences in case ascertainment, sampling variability, and aspects of both obstetric and neonatal clinical practice²². The same variables that have been occasionally reported is associated to an increased risk of ROP by some authors, on the contrary is found to be not associated or even protective by some others. For example, many studies have confirmed the association of Oxygen supplementation with occurrence of ROP^{23,24,25}, but this was refuted by Shohat et al²⁶ who did not demonstrate any significant association between ROP and duration of supplemental oxygen or the mean maximum oxygen concentration.

Plasma vitamin E levels are low in preterm neonates, and it has been suggested that the antioxidant properties of vitamin E may be important for the developing retina from the harmful effects of oxygen free radicals. Recently Kretzer's intriguing observations of the ultra structure of the developing retina in infants supplemented with vitamin E and others not supplemented, who died in the neonatal period has given new prominence in the relation of vitamin E and retinopathy of prematurity^{27,28}. The use of vitamin E supplementation as a means of reducing the incidence and severity of ROP remains controversial. In recent years the proposition has been subjected to a number of clinical trials, but a convincing answer has yet to be vouchsafed²⁹.

We found significantly lower serum vitamin E levels in the premature newborn infants with ROP than who didn't develop ROP, which is in agreement with WA Silverman³⁰. Five confounders were analyzed, that could contribute to the development of ROP like low gestational age, septicemia, oxygen therapy, blood transfusion and low birth weight. Younger gestational age has been found to be a significant risk factor³¹ but this study did not find any significant relationship of gestational age with occurrence of ROP. Many studies have confirmed the association of Oxygen supplementation with occurrence of ROP^{23,24,26}. Shohat et al²⁶ refute this findings and demonstrated no significant association between ROP and length of time on supplemental oxygen or the mean maximum oxygen concentration, which also similar to the current study. Transfusion may adversely influence the retina, not only by increasing oxygen delivery to the retina, but also by overloading iron, which in turn increases free oxygen radicals²⁹. Transfused adult haemoglobin increases oxygen delivery to the retina which may increase the risk of ROP³². Shaheen et al³³ and Babaei et al³⁴ observed a significant correlation between ROP and Blood transfusion, but this study did not found any significance, may be due to small sample size. Among the 40 premature neonates, 10 (25%) were small for gestational age (SGA). A significant relationship was observed between SGA and ROP. There have been reports on the impact of growth restriction on the development of ROP³⁵. Braian et al found the similar result³⁶.

Finally the stepwise multiple logistic regressions of risk factors of the study showed that Vitamin E deficiency is a significant risk of developing ROP when other risk factors are intercepted and Lois Johnson et al³⁷ stated the similar result.

V. Conclusion

Serum vitamin E level was found significantly lower in preterm newborn in comparison to term newborns. Vitamin E deficiency was significantly related with the development of ROP.

Recommendation

Multicenter study is recommended for generalization of this finding. Awareness building is essential about ROP.

VI. Limitations Of The Study

It is a single center study. Serum vitamin E estimation facility is not available in the country and the specimen was sent to a neighboring country. It is a costly investigation. Preterm < 30 weeks' newborns were excluded from the study, those who are more prone to develop ROP. Whether Vitamin E supplementation reduces risk of development of ROP not estimated in this study. Retinal camera is not yet available in BSMMU to delineate retinal vessels accurately.

Acknowledgment

We gratefully acknowledge the sincere cooperation of the parents as well as the contribution of all doctors, staffs of the department of neonatology, obstetrics & gynecology, department of ophthalmology and the department of radiology of BSMMU. We also grateful to Topbright research team.

References

- [1]. Groff JL, Gropper SS, Hunt SM. The Fat Soluble Vitamins. Available from: <http://Vitamin E-ExRx.net/> accessed on March 11, 2013.
- [2]. Vitamin E. Wikipedia, the free encyclopedia available from http://en.wikipedia.org/wiki/Vitamin_E accessed on March 10, 2013.
- [3]. Mallik GK, Singhal R, Misra PK, Ali B, Das V. Serum Vitamin E in Cord Blood and Early Neonatal Period. *Indian pediatrics* 1994; 31: 852-854.
- [4]. Dancheck B, Nussenblatt V, Kumwenda N, Lema V. Status of Carotenoids, Vitamin A, and Vitamin E in the Mother- Infant Day and Anthropometric status of Infants in Malawi. *J Health Popul Nutr* 2005; 23(4):343-350.
- [5]. Ashok K, Rajib R, Sriparna B, Khanna HD, Bhargava V. Antioxidant level in Cord blood of Low Birth Weight Newborns. *Indian Pediatrics* 2008; 45: 583-586.
- [6]. Kositamongkol SU, Suthutvoravut N, Chongviriyaphan B, Feungpean B, Nuntnarumit P. Vitamin A and E status in very low birth weight infants. *Journal of Perinatology* 5 2011; 31: 471-476.
- [7]. Brion LP, Bell EF, Raghuvver TS. Vitamin E supplementation for prevention of morbidity and mortality in preterm infants (Review). *The Cochrane Library* 2008;4:1-102
- [8]. Giyasettin B, Karatas F, Gursu MF, Bozkart HA, Ilhan N, Yasar A, et. al. Antioxidant vitamin levels in the term and preterm infants and their relation to Maternal Vitamin status. *The Archives of medical Research* 2002; 33: 276-280.
- [9]. Patrick J, Leonard P, Eric D, William H. Levels of vitamin E in the plasma of newborn infants and of the mothers. *The American Journal of Clinical Nutrition* 1972; 25:480-484.
- [10]. Raksha SS, Rajalakshmi R. Vitamin E status of the newborn in relation to gestational age, birth weight and maternal vitamin E status. *British Journal of Nutrition* 1987; 58:191-198.
- [11]. Winfield T, Moyer. Vitamin E levels in term and Premature Newborn infants. *Pediatrics* 1950; 6: 893-896.
- [12]. Jitka SV, Josef V, Roger B. Vitamin E and C level in infants during the first year of life. *The American Journal of Clinical Nutrition* 1976; 29: 766-771.
- [13]. Edward F. Bell LJ, File JR. The role of Vitamin E in the nutrition of premature infants. *The American Journal of Clinical Nutrition* 1981;34:414-422.
- [14]. Frank A, Oski M, Barness AL. Haemolytic Anaemia in Vitamin E Deficiency. *The American Journal of Clinical Nutrition* 1968; 2(1): 45-50.
- [15]. Vitatamin E supplementation for the prevention of morbidity and mortality in preterm infants; WHO, e-Library of Evidence for Nutrition Actions (eLENA) available at: http://www.who.int/elena/titles/vitamine_preterm/en/ accessed on February 20, 2013.
- [16]. Sankar MJ, Sankar J. Vitamin E supplementation for prevention of morbidity and mortality in preterm infants. RHL Commentary August 2011. WHO reproductive Health library, Geneva: World Health Organization.
- [17]. Ahmed ASMNU, Humaira M, Anwar KS, Khan NZ, Chowdhury MAKA, Saha SK, Darmstadt LG. Retinopathy of Prematurity in Bangladeshi Neonates. *Journal of Tropical Pediatrics* 2008; 54(5):333-39.
- [18]. Patrick KW, Tak-Chuen KW. Retinopathy of prematurity - past, present, and future in this battle against pediatric blindness. *HKJ Ophthalmol* 2003; 6(1):41-51
- [19]. The Discovery of Vitamin E. downloaded from: <http://historyofsciences.blogspot.com/2011/03/discovery-of-vitamin-e.html>. Accessed on March 28, 2013.
- [20]. Shah RS, Rajalakshmi R, Bhatt RV, Hazra MN, Patel BC, Swamy NB, Patel TV. Vitamin E status of the newborn in relation to gestational age, birth weight and maternal vitamin E status. *Br J Nutr* 1987; 58(2):191-8.
- [21]. Wheatley CM, Dickinson JL, Mackey DA, Craig JE, Sale MM. Retinopathy of prematurity: recent advances in our understanding. *Br J Ophthalmol* 2002; 86: 696-700.
- [22]. Manjoni P, Farina D, Maestri A, Giovvanozzi C, Leonessa ML, Arisio R et al. Mode of delivery and threshold retinopathy of prematurity in preterm ELBW neonates. *Acta Paediatrica* 2007; 96: 221-26.
- [23]. Maheshwari R, Kumar H, Paul VK, Singh M, Deorari AK, Tiwari HK. Incidence and risk factors of retinopathy of prematurity in a tertiary care newborn unit in New Delhi. *Journal-Natl Med J Ind* 1996;9:211-14.
- [24]. Bassiouny MR. Risk Factors Associated with Retinopathy of Prematurity: A Study from Oman. *J Trop Pediatr* 1996; 42 (6): 355-358.
- [25]. Dutta S, Narang S, Narang A, Dogra M, Gupta A. Risk Factors of Threshold Retinopathy of Prematurity. *Indian pediatr* 2004;41:665-71.
- [26]. Shohat M, Reisner SH, Krikler R, Nissenkorn I, Yassur Y, Bensira I. Retinopathy of prematurity: incidence and risk factors. *Pediatrics* 1983; 72(2):159-63.
- [27]. Kretzer FL, Mehta RS, Johnson AT, Hunter DG, Brown ES, Hittner HM. Vitamin E protect against retinopathy of prematurity through action on spindle cells. Cullen Eye institute, Program in Neuroscience and Departments of Cell Biology and Pediatrics, Baylor College of Medicine, Houston Texas 77030, USA.

- [28]. Kretzer FL, Hittner HM, Godio LB, Speer ME, Rudolph AJ, Taylor MM, Blifeld C. Retrolental fibroplasia: further clinical evidence and ultrastructural support for efficacy of vitamin E in the preterm infant. *Paediatrics* 1983; 71: 423-32.
- [29]. Kim TI, Sohn J, Pi SY, Yoon YH. Postnatal risk factors of retinopathy of prematurity. *Paediatric and Perinatal Epidemiology* 2004;18:130-34.
- [30]. SILVERMAN WA. Epoche in retinopathy of prematurity. *Archives of Disease in Childhood* 1986; 61: 522-525.
- [31]. Early Treatment for Retinopathy of Prematurity Cooperative Group: Revised Indications for the Treatment of Retinopathy of Prematurity: Results of the Early Treatment for Retinopathy of Prematurity Randomized Trial. *Arch Ophthalmol* 2003 121: 1684-1694.
- [32]. Raju TN, Langenberg P, Bhutani V, Quinn GE. Vitamin E prophylaxis to reduce retinopathy of prematurity: a reappraisal of published trials. *J pediatr.* 1997; 131(6):844-50.
- [33]. Shaheen Akter, Hossain MM, Mahfuza Shirin, Ibrahim K, Anwar KS. Blood Transfusion: A Risk Factor in Retinopathy of Prematurity. *Bangladesh J Child Health* 2010; 34(2): 38-43.
- [34]. Babaei H, Ansari RM, Alipour AA, Shokofe A, Faramani RS, Vakili J. Incidence and Risk Factors for Retinopathy of Prematurity in Very Low Birth Weight Infants in Kermanshah, Iran. *World Applied Sciences Journal* 2012;18(5):600-604.
- [35]. Brion LP, Bell EF, Raghuvveer TS. Vitamin E supplementation for prevention of morbidity and mortality in preterm infants. *Pediatrics, Section of Neonatology, Albert Einstein College of Medicine, Children’s Hospital at Montefiore, Weiler Hospital Room 725, 1825 Eastchester Road, Bronx, NY 10461, USA* brionlp@aol.com.
- [36]. Braian AD, Jolie LH, David JHS, Judy MS, Nicolas JE. Prenatal Risk Factors for Severe Retinopathy of Prematurity among Very Preterm Infants of the Australian and New Zealand Neonatal Network. *Pediatr* 2005; 115: 990-96.

Johnson SL, Schaffer SD, Thomas RB. The premature infant, vitamin E deficiency and retrolental fibroplasias. *The American Journal of Nutrition* 1974; 27: 1158-73.

Table I : Base line characteristics of the study neonates (N=70)		
Parameters	N	Percentage (%)
Sex		
Male	35	50.0
Female	35	50.0
Mode of delivery		
LUCS	53	75.7
NVD	17	24.3
Place of delivery		
Inborn	61	87.0
Out born	9	13.0
Preterm (n=40)		
30-32	18	25.87
33-35	22	31.28
Term(n= 30)		
38-42	30	42.85
Birth weight (gram) of preterm infants (40)		
SGA	10	25.0
AGA	30	75.0

Table II: Association between ROP and Vit-E level (N=40)

ROP	Vit-E deficient (n=28)	Vit-E normal (n=12)	RR	P value
Present	11	1	4.71 (1.07-32.5)	0.048
Absent	17	11		
Total	28	12		

Chi-squared Test

Table III: Association between ROP with gestational weeks, sepsis, O₂ therapy and blood transfusion (N=40)

Parameters	ROP		RR	P value
	Present	Absent		
30-32 wks (n=18)	5	13	0.87	0.78
33-35 wks (n=22)	7	15	(0.33-2.29)	
Sepsis present (n=22)	8	14	1.64	0.33
Sepsis absent (n=18)	4	14	(0.59-4.57)	
O ₂ therapy given (n=17)	7	10	1.89	0.18
			(0.72-4.95)	
O ₂ not given (n=23)	5	18		
Transfusion given (n=11)	3	8	0.88	0.82
Transfusion not given (n=29)	9	20	(0.29-2.66)	

Table IV: Association of ROP with duration and concentration of oxygen and volume of BT (N=40)

Parameters	ROP	N	Mean	Std. Deviation	p value
Duration of Oxygen (hour)	No	10	88.9	35.31	0.61
	Yes	7	100.0	52.60	
Concentration of Oxygen (liter/min)	No	10	2.4	.39	0.25
	Yes	7	3.0	1.53	
Volume of blood transfusion (ml)	No	8	30.0	11.02	0.68
	Yes	3	33.3	12.58	

Independent t-test

Table V: Stepwise multiple logistic regression of risk factors

ROP Intercept	P Value	95% Confidence Interval	
		Lower Bound	Upper Bound
Vitamin E	.000	4.08	4.09
Oxygen therapy	.097	.635	238.39
Blood Transfusion	.097	.006	1.52
Sepsis	.261	.015	3.13
Birth Weight	.063	.008	1.13

Dr Mohammad Mozibur Rahman. " Newborns Vitamin E Level and Its Relationship with Retinopathy of Prematurity."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 3, 2018, pp 73-79.