EFFECT OF HUMAN MILK ON DEVELOPMENT OF RETINOPATHY OF PREMATURITY

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ABSTRACT

Objective: To determine the protective effect of human milk on development of retinopathy of prematurity (ROP) in preterm babies.

Study Design: Observational study.

Place and Duration of Study: King Edward Medical University Lahore, Department of pediatrics over a period of 11 months, from Feb 2016 to Dec 2016.

Material and Methods: A total 142 preterm babies with birth weight <2.5kg and gestation age <37 weeks were included by non-probability convenient sampling. Neonates were assessed and grouped according to the type of feeding. Eye examination was performed minimally at 4 weeks of life and then serially by trained consultant in the Department of Ophthalmology. Data were analyzed through SPSS 20.0 and Chi square test was applied.

Results: Mean age at enrollment was 11.22 ± 16.48 days. Mean gestational age was 33.1 ± 13.06 weeks and mean birth weight recorded was 1.7 ± 0.43 kilograms. Among the study cases, 84 (59.2%) babies were on human milk and 58 (40.8%) were taking formula milk. Mean duration of oxygen therapy was 3.7 ± 3.77 days. Changes compatible with ROP was found in 9 (6.3%) cases. Among human milk fed babies, three babies (3.57%) developed ROP and in formula fed group, 6 (10.3%) babies developed changes of ROP. Thus, the risk of developing ROP was higher in formula milk fed babies as compared to human milk. However protective effect was not statistically significant as shown by value of Chi-square test: 2.65 (*p*-value=0.103).

Conclusion: Though human milk was protective for the development of ROP but result was not statistically significant.

Keywords: Formula milk, Human milk, Preterm babies, Retinopathy of prematurity.

INTRODUCTION

Prematurity is defined as birth of babies before completed 37 weeks of gestation[1]. The preterm birth rate varies among developing and developed countries. It ranges from 5% in European countries to 18% in Malawi. In Pakistan preterm birth rate has been estimated as 15.8%[2,3].

Premature infants may develop complications including respiratory distress syndrome, bronchopulmonary dysplasia, necrotising enterocolitis, intraventricular haemorrhage, hyperbilirubinemia, patent ductus arteriosus and retinopathy of prematurity (ROP)[4].

ROP is a preventable and treatable vascular proliferative disorder affecting immature retina in preterm babies. Prematurity, low birth weight, high flow oxygen therapy, inappropriate nutritional supplemen-tation, all contributes to the pathogenesis of ROP[5,6]. Neonates with ROP may develop visual complications including refractive errors, blind-ness, strabismus, visual field defects and abnor-mal colour vision[7].

ROP prevalence varies, according to the availability of resources, from 5-8% in developed countries to 30% in developing countries[8]. Sohaila *et al*[9] from Pakistan reported incidence of ROP in premature babies as 10.5% and in urban Punjab ROP incidence was reported as 24.6%[10].

The risk factors which are associated with ROP are not fully understood, but prematurity, low birth weight and immature retina are the major risk factors. Other risk factors are oxygen administration, congenital heart disease, acidosis, anemia, septicemia and blood transfusions.

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Human milk may protect against the development of ROP due to the antioxidant[11] and immuneprotective[12] properties of human milk. Human milk contains vitamin C, E, and b-carotene and has greater antioxidant properties as compared to formula[13,14]. In addition to antioxidant component of human milk it also contains some of immunomodulatory substances like secretory immunoglobulin A, lactoferrin, cytokines, lyzozymes and some cellular components[14,15]. These components influence immune system of babies and this may be the explanation for the lower risk of necrotizing enterocolitis (NEC) and septicaemia in breast fed babies and hence indirectly protect the development of retinopathy of prematurity[16,17].

Pakistan is a developing country and because treatment and screening programs for ROP are not well developed and no large multicentre studies have been conducted, so exact incidence of ROP in Pakistan is not estimated. Moreover factors which may have protective role are not studied. Based on this review, we planned to conduct the study to determine the protective effect of human milk for the development of retinopathy of prematurity. This study will help in streng-thening the guidelines for earliest initiation of human milk in premature babies to prevent ROP and blindness in survivors.

PATIENTS AND METHODS

This observational study was conducted in the department of paediatrics King Edward Medical University Lahore (KEMU) from February 2016 to December 2016 after approval by Institutional Review Board.

An informed consent was taken from the parents. Neonates with birth weight <2.5kg and <37 completed weeks of gestation who were admitted in the neonatal unit or presented in follow up clinic during the study period were included and feeding pattern of these babies was recorded and at 4 weeks of life first eye examination was done for ROP.

Total of 142 preterm neonates were included by non-probability convenient sampling.

Gestational age was assessed on the basis of date of last menstrual period and antenatal ultrasound findings. Ballard scoring to assess gestational age of patient was done if they presented within 72 hours of birth. Neonates who had major malformation, congenital cataract and tumours of eye were excluded. Study variables were age, sex, gestational age, socioeconomic status, birth weight, mode of delivery, type of feeding, stages of retinopathy, duration of oxygen therapy and mechanical ventilation. Neonates were assessed for type of feeding weather human milk or on formula milk. Human milk group included those with exclusive breast feeding or >60% of feed from mother, Formula fed group included those with exclusive formula feeding or >60% feed of formula milk.

Eye examination was performed minimally at 4 weeks of life and then serially according to eye examination findings by trained ophthalmologist. Before the examination, eye drops containing 1% tropicamide and 0.5% phenylephrine were instilled three times (5 minute apart) to dilate the pupils. Indirect ophthalmoscopy with indentation was performed using a binocular indirect ophthalmoscope. All examination results were recorded using a predesigned form.

Data were analysed through SPSS 20.0. Quantitative variables (age, gestational age, maternal age, birth weight, duration of mechanical ventilation and duration of oxygen therapy) were presented as mean ± S.D and qualitative variables (sex, mode of delivery, socioeconomic status, type of feeding, stages of retinopathy) were presented as frequency and percentages. The chi square test was applied to determine the effect of breast milk for the development of ROP.

RESULTS

The study population consisted of 142 preterm newborns. Mean age at the time of enrolment was 11.22 ± 16.48 days. Mean gestational age was 33.1 ± 13.06 weeks and 69% babies were

born at >32 weeks of gestation. There was male predominance with 86 (60.6%). Mean birth weight recorded was 1.7 ± 0.43 kilograms. Among total cases, 135 (95.1%) belong to poor socioeconomic status and 7(4.9%) were of middle class status. Regarding mode of delivery, 95 (66.9%) were delivered by spontaneous vaginal delivery (SVD) and 47 (33.1%) were born by C section. Changes compatible with ROP were found in 9 (6.3%) cases. Among ROP cases, one baby had stage I disease, 2 babies had stage II disease, 3 cases were of stage III, 2 cases of stage IV and one case was in stage V disease (table-I). Mean duration of oxygen therapy was 3.7 ± 3.79 days.

Table-I: Demographic characteristics of study population (n=142).

Variables	Categories	Frequency (% age)
Sex	Male	86 (60.6%)
	Female	56 (39.4%)
Socioeconomic status	Lower class	135 (95.1%)
	Middle class	7 (4.9%)
Mode of delivery	SVD	95 (66.9%)
	C-Section	47 (33.1%)
Mechanical ventilation		15 (10.6%)
Feeding pattern	Human milk	84 (59.2%)
	Formula milk	58 (40.8%)
ROP	Yes	9 (6.3%)
	No	133 (93.7%)
Stages of ROP	Stage I	1 (0.007%)
	Stage II	2 (0.01%)
	Stage III	3 (0.02 %)
	Stage IV	2 (0.01%)
	Stage V	1 (0.007%)

Table-II: Comparison of ROP in relation to feeding pattern (n=142).

		Any stage ROP		Total
		Yes	No	
Type of feed	Human milk	3	81	84
		33.3%	60.9%	59.2%
	Formula milk	6	52	58
		66.7%	39.1%	40.8%
Total		9	133	142

p-value = 0.103

Babies were assessed regarding type of feeding. Out of total 142 cases, 84 (59.2%) babies were on human milk and 58 (40.8%) babies were taking formula milk. Mean weight of babies with ROP was 1.2kg (range 0.8-1.8kg) and mean gestation age of these cases was 31.5 weeks (range 27-36 weeks). Five cases of ROP were born at <32 weeks of gestation. Among human milk fed, 3 babies (3/84 = 3.57%) developed ROP and in formula fed babies, 6/58 (10.3%) developed changes of ROP. Thus, the risk of developing ROP was higher in formula milk fed babies compared to human milk feeding babies. However this observation was not statistically significant (*p*-value=0.103).

DISCUSSION

ROP is a multifactorial disease and risk factors like oxygen therapy, prematurity and low birth weight are associated with its pathogenesis. The frequency of ROP in our study was lower as compare to Khalid *et al*[18], this observation may be due to inclusion of preterm less than 37 weeks

in our study. Our study was conducted to determine whether human milk is protective against development of ROP. Our results are comparable to the findings from meta-analysis by Zhou *et al*[19] that breast feeding potentially plays a strong role in protecting preterm babies from any stage and severe ROP. Manzoni *et al*[20] and Ginovart *et al*[21] observed that exclusive breast feeding is associated with lower rate of ROP. Maayan-Metzger *et al*[22] and Okamoto *et al*[23] detected lower incidence of ROP in preterm born between 24-28 weeks who were breast fed but authors found no differences among infants born before gestational week[23]. Porcelli *et al*[24] reported that extremely low birth weight infant who received breast milk in second week of life but not on 4th week of life, were at lower risk of ROP, suggesting that earlier intake of breast milk is associated with lower risk of ROP. However, our study did not address the difference between early and late feeding.

The results from our study favour the protective role of human milk for the development of ROP. In contrast, infants in study by Keraan *et al*[25] who were exclusively breast fed were more likely to develop ROP. This finding is unusual but is not justified by the authors in their circumstances. Our findings are not favouring this observation.

To summarize, in this study, we have attempted to fill some of the gaps in our local population. If breast feeding does lower the risk of development of ROP then it is more likely to be effective when infants are expose to high level of oxidant stress and at that time antioxidant component of human milk protect retina from injury. Our findings suggest a protective effect of human milk for the development of ROP. However, there are conflicting reports regarding effect of breast feeding with the development of ROP. Possible sources of variations include the gestational age, age of initiation of enteral feeding and amount of breast milk fed to infant.

The study was limited to one tertiary care centre with limited sample size. Furthermore, the medical benefits of breast milk and routine recommendation of breast milk as preferred feeding for the preterm infants limited this study as observational study instead of randomized trial. Long term follow up was not made for visual dysfunction. If it would have been done, the results might have been different.

CONCLUSION

The frequency of retinopathy of prematurity was 6.3%. Although human milk protect the preterm babies from development of retinopathy of prematurity, but the protective effect was statistically not significant.

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CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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