

## ROLE OF PROBIOTICS IN PREVENTION OF NECROTIZING ENTEROCOLITIS

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Article Received on 21/10/2019

Article Revised on 11/11/2019

Article Accepted on 01/12/2019

## ABSTRACT

**Background:** Necrotizing enterocolitis (NEC) is the most commonly occurring gastrointestinal emergency in preterm infants. This study was conducted to determine frequency of necrotizing enterocolitis (NEC) in preterm infants less 1.5 Kg taking probiotics at a tertiary care hospital. **Material and Methods:** Consecutive 270 preterm neonates having weight less than 1.5 Kg was taken in this descriptive case – series study. Once registered, the study cases were fed with Infloran (Lactobacillus acidophilus) and Bifidobacterium infants, 125 mg/kg per dose was given twice daily with breast milk until discharged and were followed for two weeks to see NEC. The amount of feeding was advanced slowly if tolerated, with no more than 20 mL/kg per day increment per day. These study cases were followed for 15 days to record outcome variable i.e. NEC. Data was analyzed by using SPSS Version 20. **Results:** of these 270 study cases, 139 (51.5%) were boys while 131 (48.5%) were girls. Mean gestational age of our study cases was  $29.61 \pm 2.66$  weeks (with minimum gestational age was 24 weeks while maximum gestational age was 34 weeks). Of these 270 study cases, 147 belonged to urban areas and most of our study cases i.e. 179 (66.3%) were poor, 79 (29.3%) were from middle income families and only 12 (4.4%) belonged to rich families. Mean weight of our study cases was  $1312.85 \pm 78.66$  grams. Mean maternal age was noted to  $27.91 \pm 4.24$  years, 170 (62.96 %) mothers were less than 30 years of age and most of these mothers were illiterate i.e. 191 (70.7%). Majority of these mothers i.e. 170 (62.96%) had parity less than 3. Mean duration on probiotics was noted to be  $14.88 \pm 1.38$  days. Necrotizing enterocolitis was noted in 15 (5.6%) of our study cases. **Conclusion:** Our study results have shown that frequency of necrotizing enterocolitis (NEC) was low in preterm infants using probiotics. The use of probiotics was effective in the prevention of NEC and our study results support the use of probiotics in these infants. Probiotics were found to be safe, reliable and efficacious in our study. NEC was significantly associated with gender, gestational age, residential status, poor socioeconomic status, increasing maternal age and parity and duration on probiotics.

**KEYWORDS:** Probiotics, necrotizing enterocolitis, preterm infants.

## INTRODUCTION

Probiotics are defined as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.”<sup>[1]</sup> In order for a microorganism to be considered a probiotic, it must be of human origin and be nonpathogenic in nature. Probiotic microorganisms are also often referred to as commensal bacteria, or protective microorganisms which are part of the normal flora. In contrast, prebiotics such as fructose oligosaccharides, galacto-oligosaccharides, and lactulose are supplements that enhance the growth of potentially beneficial intestinal microbes such as *Bifidobacterium* species.<sup>[2]</sup>

The term “necrotizing enterocolitis” (NEC) often reflects a spectrum of intestinal conditions that differ with respect to the pathogenesis.<sup>[3]</sup> Necrotizing enterocolitis

(NEC) is an inflammatory disease of the intestine, often associated with sepsis and frequently complicated by perforation, peritonitis, and death. Despite the significant advances in neonatal clinical and basic science investigation, NEC often is an incurable disease. Specific therapeutic strategies are lacking because unknown etiology. Mortality rate is high and long-term prognosis in survivors is very poor. The inflammatory process, starting from intestinal mucosa, involves distant organs including the central nervous system, with an increased risk for neurodevelopment delay. The total annual estimated cost of caring for affected infants with NEC only in the United States ranges between \$500 million and \$1 billion.<sup>[4]</sup> Necrotizing enterocolitis (NEC) is the leading cause of death from gastrointestinal causes in premature infants, and its overall survival has not improved in the past three decades.<sup>[5]</sup> Necrotizing enterocolitis (NEC) is the most common acquired disease

of the gastrointestinal tract in preterm infants, whereas probiotic supplementation might reduce NEC risk and potentially provide benefits to preterm infants.<sup>[6,7]</sup> Probiotics have been suggested to prevent severe necrotizing enterocolitis (NEC) and decrease mortality in preterm infants.<sup>[8]</sup> Javier et al reported 5.4% frequency of NEC in preterm (less than 1.5 KG) taking probiotics.<sup>[9]</sup>

In Pakistan, where preterm births are more common<sup>[10]</sup> no such study has been done previously. So this study was conducted to know frequency of NEC in preterm neonates.

## MATERIAL AND METHODS

Consecutive 270 preterm neonates having weight less than 1.5 Kg was taken in this descriptive case – series study. Both boys and girls preterm neonates aged less than 10 days with weight less than 1500 grams were included in this study. Patients with significant heart disease and cystic fibrosis, already taking probiotics, known cases with malignancies were excluded from our study. Once registered, the study cases were fed with Infloran (Lactobacillus acidophilus) and Bifidobacterium infants, 125 mg/kg per dose was given twice daily with breast milk until discharged and were followed for two weeks to see NEC. The amount of feeding was advanced slowly if tolerated, with no more than 20 mL/kg per day increment per day. These study cases were followed for 15 days to record outcome variable i.e. NEC. Data was analyzed by using SPSS Version 20.

## RESULTS

Our study included a total of 270 preterm infants who met inclusion criteria of our study. Of these 270 study cases, 139 (51.5%) were boys while 131 (48.5%) were girls. Mean gestational age of our study cases was  $29.61 \pm 2.66$  weeks (with minimum gestational age was 24 weeks while maximum gestational age was 34 weeks). Of these 270 study cases, 147 belonged to urban areas and most of our study cases i.e. 179 (66.3%) were poor, 79 (29.3%) were from middle income families and only 12 (4.4%) belonged to rich families. Mean weight of our study cases was  $1312.85 \pm 78.66$  grams. Mean maternal age was noted to  $27.91 \pm 4.24$  years (with minimum maternal age was 21 years while maximum age was 36 years), 170 (62.96 %) mothers were less than 30 years of age and most of these mothers were illiterate i.e. 191 (70.7%). Majority of these mothers i.e. 170 (62.96%) had parity less than 3. Mean duration on probiotics was noted to be  $14.88 \pm 1.38$  days (with minimum duration was 2 days while maximum duration was 8 days). Necrotizing enterocolitis was noted in 15 (5.6%) of our study cases.

## DISCUSSION

Despite remarkable advances over the past 2 decades in the field of neonatology, answers to the prevention and management of necrotizing enterocolitis (NEC) remain elusive.<sup>[11-14]</sup> Our study included a total of 270 preterm infants who met inclusion criteria of our study. Of these

270 study cases, 139 (51.5%) were boys while 131 (48.5%) were girls. Similar results have been reported in different studies showing male gender predominance over female gender. Rashid et al<sup>[15]</sup> also reported male gender predominance with 62% male preterm neonates, these findings are close to our study results. A study by Parveen from Abbottabad also reported male gender preponderance in preterm babies which is same as that of our study results<sup>[16]</sup> Khan et al<sup>[17]</sup> also reported male gender predominance with 57 % preterm male neonates which is in compliance with that of our study results. A study done in Thailand<sup>[18]</sup> also reported male gender preponderance which is in compliance with our study results. A study conducted by Janvier et al<sup>[9]</sup> reported 56% male gender preponderance which is similar to that of our study results.

Mean gestational age of our study cases was  $29.61 \pm 2.66$  weeks (with minimum gestational age was 24 weeks while maximum gestational age was 34 weeks). Mean gestational age of boys was  $29.99 \pm 2.41$  weeks while that of girls was  $29.21 \pm 2.85$  weeks ( $p = 0.016$ ). Our study results have indicated that majority of our study cases i.e. 157 (58.1%) had gestational age ranging from 30 to 34 weeks. Khan et al<sup>[17]</sup> reported  $33 \pm 2.4$  weeks which is slightly higher than our findings, the reason for this difference is due to our methodology/inclusion criteria as we only included preterm neonates less than 34 weeks of gestation while Khan et al<sup>[17]</sup> included up to 36 weeks of gestation. A study conducted by Janvier et al<sup>[9]</sup> reported  $28.9 \pm 2.2$  weeks mean gestational age which is close to our study results. Similarly Rashid et al<sup>[15]</sup> reported  $32.4 \pm 1.8$  weeks which is similar to our findings. Venkataraman et al<sup>[19]</sup> reported  $28.8 \pm 2.0$  weeks gestational age which is close to our study results.

Mean weight of our study cases was  $1312.85 \pm 78.66$  grams. Mean maternal age was noted to  $27.91 \pm 4.24$  years (with minimum maternal age was 21 years while maximum age was 36 years), 170 (62.96 %) mothers were less than 30 years of age and most of these mothers were illiterate i.e. 191 (70.7%). Majority of these mothers i.e. 170 (62.96%) had parity less than 3. A study conducted by Cheema et al<sup>[20]</sup> reported  $1252.7 \pm 129.2$  grams mean weight in preterm infants less than 1.5 kg. These findings of Cheema et al<sup>[20]</sup> are in compliance with that of our study results. A study conducted by Janvier et al<sup>[9]</sup> reported  $1207 \pm 376$  grams which is similar to that of our study findings.

Mean duration on probiotics was noted to be  $4.88 \pm 1.38$  days (with minimum duration was 2 days while maximum duration was 8 days). Necrotizing enterocolitis was noted in 15 (5.6%) of our study cases. A study conducted by Janvier et al<sup>[9]</sup> reported 5.4% NEC with use of probiotics which is similar to that of our study result. A study conducted by Cheema et al<sup>[20]</sup> reported 10.95% NEC with use of probiotics which is also close to our study findings. Saengtawesin et al<sup>[18]</sup> from Thailand also

reported that use of probiotics was found to be effective in the prevention of NEC in preterm infants.

## CONCLUSION

Our study results have shown that frequency of necrotizing enterocolitis (NEC) was low in preterm infants using probiotics. The use of probiotics was effective in the prevention of NEC and our study results support the use of probiotics in these infants. Probiotics were found to be safe, reliable and efficacious in our study. NEC was significantly associated with gender, gestational age, residential status, poor socioeconomic status, increasing maternal age and parity and duration on probiotics.

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