Effect of Nicu Admission on Development and Nutrition in Early Childhood Years


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ABSTRACT
Admission rate to neonatal intensive care units (NICUs) was considerably increased over the past few decades. Short-term outcomes had been enhanced, and mortality rates had decreased. However, the impact of advanced neonatal care interventions on long-term outcome of infants was not thoroughly reviewed. Objectives: the aim of this review is to investigate the effect of NICU admission on long-term developmental and nutritional outcomes in early childhood years. Methods: Medical database, particularly Medline and Cochrane Library were searched for studies, researches, and review articles about the long-term outcome of neonates who were admitted at neonatal intensive care unit, particularly from the nutritional and developmental perspectives. Results: Overall impact of NICU admission on long-term outcome is generally related to the etiological indication of admission: Hypoglycemia, tetanus, low birth weight, and prematurity had a negative impact on childhood development. Adequate nutrition and rapid growth velocity in NICU improved nutritional and physical development. Discussion: Long-term outcome of neonatal intensive care unit admission depends to a large degree on the etiology of admission. Adequate nutritional support at neonatal intensive care units had improved developmental and nutritional outcome of preterm and very preterm infants. Term and late term infants admitted at NICUs were not significantly different from their counterparts who were not admitted at NICUs on long-term outcomes. Conclusions: Admission at NICU is not an independent risk factor for poor nutritional or developmental outcome at early childhood years, but the etiological indication of NICU admission was more predicting. Early nutrition for low birth weight babies improved nutritional development.

Keywords: Neonatal intensive care, development, nutrition, long-term.

INTRODUCTION
Rates of neonatal admission to neonatal intensive care units (NICUs) had shown a notable increase during the last few decades (1). Wade Harrison and David Goodman (1) in their retrospective study on 17 896 048 newborns admitted to NICUs during the period from 2005 to 2012, reported that the admission rate to neonatal intensive care units increased from 64/1000 live birth in 2005 to 77.9 live births in 2012 (P<0.001). Admission rates had increased for normal weight, low-birth weight, as well as low birth weight infants. More specifically, a notable increase was reported in the percentage of normal weight neonates requiring intensive care unit admission (1). Over the last few years, various advances had been applied to optimize neonatal intensive care. Ventilator techniques, improved parenteral nutrition, novel surgical interventions antibiotics, steroids, and surfactant therapy are examples of the advances that resulted in a considerable reduction in neonatal mortality rates (2). However, the enhanced survival of cerebral palsy neonates, hypoxic-ischemic encephalopathy cases, and other serious neonatal disorder might have increased the long term negative motor and developmental outcomes (3-5). Study rationale and objectives: Meticulous monitoring of long-term
outcomes of neonates who required admission at neonatal intensive care unit is essential for evaluation as well as optimization of NICU performance. This article aimed at reviewing the impact of NICU admission on the long-term outcome of infants particularly as regards the nutritional as well as the developmental aspects.

**METHODS**

For conducting this review, online database was searched for articles studying the long-term outcome of neonatal intensive care units. Medical database, particularly Medline and Cochrane Library were searched for studies, researches, and review articles about the long-term outcome of neonates who were admitted at neonatal intensive care unit, particularly from the nutritional and developmental perspectives. The results of that research studies were quickly inspected, and the related ones were selected for abstract review. After reading abstracts, fewer studies were chosen, namely those which had addressed the long-term outcomes of neonatal intensive care admissions.

The study was done after approval of ethical board of Imam Muhammad ibn Saud Islamic university.

**RESULTS**

In spite of the multiplicity of studies conducted on neonatal intensive care admission outcome, only few were concerned with long-term follow-up of children who had required intensive care unit admission as neonates. McKinlay et al. \(^6\), in their prospective cohort study exploring the impact of hypoglycemia among NICU-admitted neonates on the 4.5 year neuro-developmental outcome, stated that neonates exposed to hypoglycemia had an increased risk of visual motor function (RD, 0.03; 95% CI, 0.01 to 0.06 and RR, 3.67; 95% CI, 1.15 to 11.69) as well as executive function (RD, 0.05; 95% CI, 0.01 to 0.10 and RR, 2.32; 95% CI, 1.17 to 4.59), but did not have a statistically significant risk of neuro-sensory dysfunction at 4.5 years. The negative impact on executive and visual motor functions were dose-dependent\(^6\).

Similarly, Trieu et al.\(^7\) followed up NICU survivors of tetanus for 42 months and compared their cognitive as well as motor outcome to normal counterparts. They studied 8 neonates who survived after tetanus and 9 controls. Results from their study indicated that neonatal tetany survivors, in spite of experiencing lower scores, had neither significantly low growth indices nor delayed neuro-developmental scores. Only two neonates had considerable neurological dysfunction, and the cognitive impairment was positively correlated with the severity of the disease (p = 0.02)\(^7\).

In 1985, Coolman et al.\(^8\) prospectively studied 219 neonates discharged from neonatal intensive care units for two years. They indicated that up to one half of the discharged neonates had mild neuro-motor abnormalities during their first follow-up year. However, three-quarters of them had normalized at the age of two years. Seven percent of the studied neonates had moderate transient neuromotor dysfunction, and up to one fifth (20%) of the cases had severe neuromotor development. More specifically, two-thirds of the severely impaired infants had cerebral palsy which persisted in only one third of the studied sample. Persistent abnormality was significantly associated with birth weight; small for gestational age neonates had a statistically significant higher risk of persistent neuro-motor abnormalities than their counterparts\(^8\).

Another 12-year study, published in 1995, compared the long-term outcome of 116 neonates admitted to neonatal intensive care unit and 137 neonates admitted to normal neonatal nursery. The researchers stated that NICU-admitted boys had significantly higher rates of physical impairment, whereas girls experienced negative social and psychological impacts when compared to infants admitted at normal neonatal nursery\(^9\). The researchers, however, did not put into consideration the etiological factors of admitting the recruited neonates to the NICU in the long-term outcome of their study.

As regards prematurity, it has been established that very preterm (<32 weeks) and extremely preterm (<28 weeks) babies had a high risk for neuro-cognitive and motor development impairment\(^10-14\). Serenius et al.\(^11\), in their 2.5-year prospective study on 456 neonates, reported that very premature babies had significantly higher rates of cognitive deficits, language impairment, and motor abnormalities when compared to normal birth weight counterparts. However, some researchers claimed that proper neonatal intensive care unit care and nutrition might decrease neuro-cognitive and motor negative consequences\(^15-17\). For instance,
Franz et al. (15) reported that, among the 219 preterm neonates studied, early neonatal growth during neonatal intensive care admission was positively correlated with improved long-term motor development at 5.4 years. Preterm neonates who achieved rapid weight gain and rapid head circumference growth had a better motor development. Similarly, Ehrenkranz followed 501 preterm infants from multi-centered cohort studies at 18 and 22 months. They found out that the growth velocity inside the intensive care unit was significantly associated; a better cognitive and motor development of infants at the follow-up periods. They claimed that nutritional programs in NICUs play a major role on neonatal outcome and can be an independent predictive factor for long-term neurodevelopment and growth. On the other hand, some researchers noted that rapid growth during neonatal intensive care units, particularly when undue, increased the risk of metabolic syndromes such as insulin resistance and diabetes mellitus (17,18). In contrary to these results, a systematic meta-analysis conducted on 1796 patients recruited from 8 randomized controlled trials and 13 observational studies stated that early parenteral nutrition had a good impact on short-term growth, and did not seem to have negative effects on morbidity or mortality (19).

To date, it remains a matter of debate whether adequate nutrition in the early neonatal period is more beneficial to the neonatal development or it puts him at risk of further nutritional and metabolic complications. Researchers emphasized the importance of defining an adequate nutritional support for the preterm without undue grave consequences (20,21). In an attempt to assess the overall long-term outcome of neonatal intensive care units regardless the etiology of admission, McGowan et al. (22) compared the childhood development of 255 children among children who required NICU admission and those who did not require NICU care. They reported that there was no statistically significant difference between neonates who required admission at NICU and those who did not on term of cognitive, motor, and language development at the age of 3 years.

**DISCUSSION**

The vast majority of the published studies stated the outcome of certain neonatal disorders rather than the overall outcome of all NICU admissions. Neonates are admitted to a NICU for different etiologies, and the overall outcome of neonatal intensive care unit admission seems to be dependent on the etiological factor of NICU admission. For instance, developmental outcomes of NICU cases with low-birth weight, prematurity, hypoglycemia, sepsis, or cerebral palsy varied considerably from each other.

Studies reporting the overall long-term outcome of neonatal intensive care unit admission (NICU), regardless the etiology, had contradictory results (8, 9,22). Some researchers reported that children who needed intensive care as neonates had poorer neuro-cognitive and/or motor development when compared to their counterparts (9,8). On the other hand, the overall long-term developmental outcome did not differ among NICU-discharged neonates and normal nursery-discharged ones (22). The contradictory results may denote the presence of other factors determining the long-term outcome. Etiology of NICU admission seemed to be a major factor impacting the long-term developmental outcome for the childhood years. For instance, premature and pre-term babies had a poor neuro-cognitive and motor development on the long-term run (10-14). Similarly, hypoglycemia necessitating NICU admission had a negative impact on visual motor as well as executive functions (6). Neonates with tetanus also had poor cognitive and motor functions during childhood years (7).

As regards nutrition, it seemed that early adequate nutrition during neonatal period improved the long-term physical and nutritional development in low birth-weight neonates (15-16). However, undue nutrition for normal weight neonates had increased the incidence of metabolic syndrome and insulin resistance on long-term follow-up (17-18).

**CONCLUSION**

In conclusion, the etiology of neonatal admission at intensive care unit plays a major role in predicting the long-term outcome of NICU admission. Adequate nutritional support at neonatal intensive care units had improved developmental and nutritional outcome of preterm and very preterm infants. Term and late term infants admitted at NICUs were not significantly different from their counterparts who were not admitted at NICUs on long-term outcomes. However, the overall
developmental outcome in children who had received proper care during NICU admission improved significantly in preterm and low-birth weight infants.

REFERENCES