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Randomized Control Trial: Age of Presentation of Denver-II Test Items for Developmental Outcomes from Birth Till Infancy

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Abstract

Objectives: To compare growth and development outcomes in the interventional and control groups through infancy.

Methodology: This prospective, time series, randomized, partially blind, interventional controlled study was conducted from 1st June 2014 to 31st July 2016 at MGM Medical College hospital for Mother and Child Kalamboli, Navi Mumbai, India. Prior approval of the MGMIHS Institutional Ethics Committee was obtained. Inclusion Criteria: Full term newborns with normal vaginal delivery. Pregnant women with single full-term fetus and without any known high-risk pregnancy subjected to their written informed consent. 268 babies each in the intervention group and control group. Babies were randomized to either group, following computer generated random numbers.

Data Analysis: Demographic data was analysed by frequency and percentage. Unpaired t tests at respective individual percentiles of P_{25}, P_{50}, P_{75} and P_{90} of test items as per DDST-II.

Results: Growth and development at 4-6, 8-10, 12-14 weeks; at 6, 9 and 12 months of follow-up. Developmental milestones (DDST-II): Gross motor: Out of total 15 items found relevant under one year of age, the intervention group achieved individual milestones earlier than the control in 6 items and advanced in 3 more items. Language: Advantage of intervention group over control was maintained by I-SUC (Intervention) group in language domain too particularly at 4-6 weeks age (p=0.001) and at one year of age (p=0.005).

Fine Motor: Out of 12 items under the broad domains of fine motor development under one year of age, the intervention group achieved several milestones earlier than the control in 4 items.

Personal Social: The difference was highly significant at 9 months of age (p=0.005).

Conclusion: The I-SUC can safely replace DCC. The great advantage of consistently higher red-cell mass and hemoglobin level through-out in infancy in intervention group all through, on long term follow up till infancy was considered very encouraging.

Keywords: *DDST-II: Denver's Developmental Screening Tool, PCV: Hematocrit.*

Introduction

According to National Family Health Survey (NFHS-3) India, 79.2% children aged between 6 months and 35 months are anemic.[1] In the recent survey (NFHS-4), 36.6%under five children were found anemic still. Most of them are born to anemic mother was so common among 55% to 60% of expectant mothers in India (NFHS-4)[2]. Persistence of poor functioning of cognitive, motor[3], affective and sensory systems in children, who were anemic as infants, highlighted the need to study

innovative ways[4] to prevent iron deficiency in infancy. To explore the benefits and real risks involved if any following intact stripping of umbilical cord (I-SUC) at birth, the present study was planned comprising of term newborn babies and following them up for hemodynamic, neurodevelopmental outcome[5,6] and morbidity pattern throughout their infancy.

Objectives:

1. To assess the immediate neonatal outcome of stripping umbilical cord blood towards baby at birth.
2. To compare nutrition, growth and development outcomes in the interventional and control groups through infancy.

Methodology: This prospective, time series, randomized, partially blind, interventional controlled study[7] at MGM Medical College hospital for Mother and Child Kalamboli, Navi Mumbai, India., Navi Mumbai. It is the sole provider of maternal-infant care in the area and served as a referral hospital for the catchment area in Raigad district, Maharashtra. The selected site had birth rate of approximately 1,291 child births during the fiscal year 2013-2014. Out of 592 total deliveries,517 (87.3%) mothers had normal vaginal delivery with full term babies. Given a conservative 5- 8% loss to follow-up, it was expected that approximately 250 participants would be recruited in each arm in 12-month period. In the attached pediatric OPD, at least 100 children attend OPD daily. Immunization clinic is functional on three days a week (Monday, Wednesday and Friday) at MGM hospital Kamothe and three days a week (Tuesday, Thursday and Saturday) at MGM hospital Kalamboli. Mothers received the standard in-hospital antenatal and postpartum care. They all avail healthcare facilities which included patient care, immunization, breastfeeding support and health education provided by doctors and nurses at pediatric and postpartum unit. Home visits or telephone calls are made for those who fail to turn up for follow up on appointment days.. Moreover, there is a regular and daily pediatric OPD with facilities for immunization, growth monitoring and developmental screening[8] and nutrition advise under expert supervision in the hospital itself.

Inclusion criteria 1. Full term Neonates born by vaginal delivery to the mothers having undergone antenatal care at least three months in the same hospital as a booked case.

Exclusion Criteria:

1. Neonates born to mothers with very high-risk pregnancy such as PIH, Severe Heart Disease, Gestational Diabetes, DM2 Multiple Pregnancy, Rh-iso Immunization, Severe anemia[9], short stature, tuberculosis, cancer etc.
2. Birth asphyxia having APGAR score less than 7/10.
3. Meconium aspiration syndrome
4. Cord prolapse.
5. Very low birth weight[10] (less than 2000 gms) and IUGR.

Consent: Eligible, mothers were randomly allocated to the stripping of the umbilical cord towards the baby (Intervention group) or the standard routine care group (Control group) after obtaining informed consent of the expectant mothers in the obstetric ward before they were shifted to labour room for delivery[11-13]. The informed consent sheet was developed. English as well as Marathi and Hindi consent sheets were provided after translation and retranslation from English version prepared .

Randomization: To ensure confidentiality of the participants, the code number were recorded on a master information sheet that included the participant's name, telephone number, group assignment, and enrollment date; secured under lock and key with the labour room nurse in-charge on duty, to be decoded after tabulation of the result on completion of the study. Recruitment of cases conducted daily from 8 am to 8 pm to avoid operator bias. Randomization[19] was achieved by computer generated random number table using the seed number 2004201601 for randomization schedule and use of statistical software SAS 9.1. Assignment of the participants to either of the groups was done by using computer generated randomized number sequence list into either intervention or control group in advance in consultation with statistician.

Procedure of the Main Study: This prospective time series randomized partially blind controlled study was conducted from 1st June 2014 to July 2016 (26 months) at the MGM Hospital for Mother and Child Kalamboli, Navi Mumbai. Pregnant women admitted to this for delivery with single full-term fetus were allowed to participate in the study subjected to their written informed consent. The Exclusion criteria was strictly applied to finalize the subjects. The screening

proforma was completed for every pregnant woman screened for enrollment of the baby after delivery to the study. A structured survey questionnaire was used to gather obstetric and medical history of expectant mothers. Baseline maternal data about age, drug history, parity, iron/folic acid supplementation, socio economic status, detailed medical history was noted for all women. Detailed obstetric history was taken from all participants to recognize any high-risk factor. A general physical examination and systematic examination including obstetric examination was done for all women. The diagnosis was noted as recorded by the in-charge obstetrician. There was no mention made in the neonate's chart about the randomization to prevent any bias. Demographic and outcome data were obtained from the medical records of the mother and their neonates. Baseline data of the neonate such as birth weight, sex, gestational age was recorded in all cases. The coded subject ID was assigned to the enrolled mother and baby pair by the labour room sister in charge for follow-up. **Follow-up for growth and development through infancy at 4-6 weeks, 8-10 weeks,12-14 weeks, 6 months, 9 months and 12 months of age were assessed Development milestones**: DDST-II (1) Gross motor, (2) language, (3) fine motor, (4) personal social developmental milestones till one year. The babies in the intervention and control groups were followed up for a period of one-year monitoring their further growth and development and Morbi ties if any, as they attended immunization clinics for polio, HBV, HIB, DPT, MMR doses. These intervals were selected as they facilitated mothers to get the babies for immunization to achieve maximum compliance on follow-ups. Their mothers were given timely reminder to the visit as per appointment date for subsequent follow-up personally and by telephones one week before and one day prior to the appointment date as reminder. Home visits were accomplished for those mothers who failed to get the baby for follow-up within four days of appointment dates. At each visit babies were assessed for growth by anthropometry developmental milestones by DDST-II, general physical examination and history of any inter-current infections.

Assessment of DDST-II: The mother was assured that this developmental assessment process would purely non-invasive and harmless, just to obtain an estimate of the child's level of development in four different domains. This test relied on observation of what child could do in front of the evaluator and also based on report of certain activities by a parent. One test item at each time is administered to avoid distractions.

Content Validity: The tool was prepared and given to 20 experts for scrutinizing for its adequacy and relevance. Individual evaluation reports obtained were from all pediatric nursing, obstetrical nursing, pediatrician, statistician, clinical psychologist.

Reliability of the Tool: Procedure in the DDST-II technical manual[14] was followed in letter and spirit to interpret the findings (whether pass or delayed (fail) or refusal /advanced) in presence of pediatrician and one more pediatric nurse standardized for intra and inter observer reliability coefficient is 0.872.

Results

Table 1: Comparison of intervention out-comes in gross motor milestones from birth to one year of age between control and intervention groups by z-score.

Gross Motor Development (9 months)	Pass (P)	Advance (A)	P+A=O	Fail (F)	Total (P+A+F)
Control	640	9	649	80	729
Percentage	87.79	1.23	89	10.97	50.13
Intervention	640	21	704	64	725
Percentage	88.2	2.89	97	8.82	49.86
P Value	0.779	*0.025	0.17	0.170	
Gross Motor Development (12 months)					
Control	621	7	628	84	712
Percentage	87.2%	0.009%	88	11.7%	49.79%
Intervention	635	15	650	68	718
Percentage	88%	2.08%	90	9.4%	50.20%
P value	0.4777	0.089	0.152	0.152	

Note: It is clearly appreciated that a higher proportion of babies passed and advanced for their age in gross motor mile stones than those in control group at all ages, serially and prospectively screened monthly from 1 to 3 months and thereafter every 3 monthly until one year of age. On the other hand, more babies failed in test items in the control group, as compared to intervention group. Such a difference was found to be highly significant at 8-10 weeks (p=0.006) and at 9 months (advanced for age p=0.02) of age.

Table 2: Comparison of interventional out-comes in language milestones from birth to one year of age between control and intervention groups by z-scores

Language (9 Months)	Pass (P)	Advance (A)	P+A=O	Fail (F)	Total (P+A+F)
Control	840	18	858	100	958
Percentage	87	1.87	89	10.43	49
Intervention	860	28	888	90	978
Percentage	87	2.86	90	9.20	50
P Value	0.865	0.155	0.362	0.362	
Language (12 Months)					
Control	380	6	386	64	450
Percentage	84.4%	1.33%	85	14.22%	49%
Intervention	410	6	416	37	453
Percentage	90.5%	1.32%	91	8.16%	50.1%
P Value	*0.005	0.992	*0.003	*0.003	

Note: Significantly higher proportion of babies in the intervention group passed in the language domain as compared to that of control group at all ages; particularly at 4-6 weeks (p=0.001) and at 12 months (p=0.005) of age. More number of babies in the control group incidentally were found delayed (Failed) in language domain as compared to the intervention group. The difference was statically significant right from 4-6 weeks (p=0.003) and at 12 months (p=0.003) of age**.**

Discussion

Developmental Milestones: Like growth monitoring, development assessment is very important component of monitoring neurodevelopmental skills in a child for early detection and early intervention if required. The second version of Denver Developmental Screening Tool (DDST-II) happens to be very popular. **DDST-II:** Since no Indian adaptation, suitable for Maharashtrian population was available, the original DDST-II items in all 4 domains were used in the present study. The Trivandrum developmental screening tool (**TDST**)[15] was adapted from DDST-II happened to be merely its abridged version, reducing the number of items to be tested in each domain at a given age for convenience of office practice. The pediatrician and one more pediatric nurse were made to observe to ensure intra and inter observer reliability **Gross motor domain:** Out of 15 items under the broad domains of gross motor under one year of age the intervention group achieved individual milestones (Items) earlier than the control in 6 items (Lifts head up 45-degree, head holding, chest up. Roll over, pull to sit–no head lag and sit without support). These were considered as major motor milestones under broad gross motor domain **Language:** Out of 14 items under the broad domains of language under one year of age the intervention group achieved individual milestones (Items) earlier in 8 items (Vocalizes, Ohhahh, laughs, turns to rattling sound, combine syllable, jabbers turn to voice, dada mamma specific) than those in control group. These were considered as major language milestones under broad language domain. **Fine motor development:** Out of 12 items under the broad domains of fine motor development under one year of age the intervention group achieved 4 individual milestones (Items) earlier than the control (Follow midline, hands together, regards raisin and look for yarn) .The intervention group was found at par with the control in achieving individual 7 items such as grasp rattle, rake raisin,pass cube, thumb finger grasp,bangs 2 cubes held in hand, put block in cup and reaches. **Personal social development:** Out of 11 items under the broad domains of personal social development under one year of age the intervention group achieved individual milestones (Items) earlier than the control in 4 items (Social smile, smile responsively, feeding self, play pat a cake).No study is available in literature to report such

an advantage on achieving developmental milestones conducted prospectively in term babies, followed up from birth through one year of age in a controlled study as ours.

Conclusions

Poor iron stores in the first year of life are known to harm the developing brain as myelination at hippocampus and cortical brain development are at peak. Persistence of poor functioning of cognitive, motor, affective and sensory systems in children, who were anaemic as infants, highlighted the need to study innovative ways to prevent iron deficiency in infancy.

What the present study adds?: I-SUC helps achieving various developmental milestones earlier than excepted as compared to the matched controls through infancy.

Role of Funding Source: There was no source of funding for this study.

Ethical Committee Clearance: Prior approval of the MGMIHS Institutional.

Ethics Committee: Administrative authorities of hospital had been obtained,vide Approval letter no. MGM /HIS/RS/2013/41 dated 28th March 2013.

Declaration of Interests: We declare no competing interests.

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