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A study of perinatal asphyxia in a tertiary care hospital with reference to perinatal risk factors and short term outcome

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Abstract:
Background: *Perinatal asphyxia a leading cause of mortality and morbidity in under 5 years age group children is a manifestation of both maternal and child health status of a country. Identifying both maternal and fetal health risk factors contributing to perinatal asphyxia, proper intervention and appropriate newborn care and follow up of NICU graduates can plummet the health burden of asphyxia. Our study aims at identifying both maternal and fetal risk factors precipitating perinatal asphyxia, monitoring the outcome of asphyxia on standard treatment protocol, and follow up of surviving asphyxiated babies and their neurological impairment.*
Materials and Methods*: It's a combination of cross sectional descriptive and observational prospective single center based study with a cohort of 98 newborns who satisfied the inclusion criteria and got enrolled consecutively. The study was conducted at Pediatric Medicine department at a tertiary care hospital over a time period of 1 year from May 2018 till April 2019. We followed the definition of perinatal asphyxia enunciated by WHO and NNF, and excluded babies with birth weight < 1500gm or with major congenital anomalies.*
Results: *Out of 98 enrolled newborn who suffered perinatal asphyxia, 6 babies died during hospital stay and rest 92 got discharged and they were followed up till next 6 months. The mean maternal age is 23.98 ± 3.38 years and mean birth weight of the babies were 2.34 ± 0.38 kg , with Anemia being the commonest maternal risk factor (34.69%) and preterm delivery (42.85%) was the commonest fetal risk factor. Vaginal delivery (73.47%) being the commonest mode of delivery and most of the labour cases were booked (75.5%) and multigravida (52.04%). 68.3% babies suffered mild to moderate asphyxia and rest 31.6% had severe asphyxia but total 55% total had hypoxic-ischemic encephalopathy(HIE) consequences. There was variable level of organ damage with perinatal asphyxia and most of them had statistically significant correlation with extent of asphyxia except necrotizing enterocolitis (NEC). On post discharge 6 months follow up we recorded and found, 26.08% having feeding problem, 19.55% having microcephaly, 22.83% neurological problem as per Hammersmith infant neurological examination chart (HINE) , 7.6% having hearing loss, 17.39% having vision problem.*
Conclusion: *Anemia correction among mothers, adequate antenatal care, essential newborn care and socio-economic elevation can bring down incidence of perinatal asphyxia. Also early neurological assessment of newborn can detect post asphyxia neuronal damage anomaly and an early intervention will minimize neurological handicap due to neuronal plasticity.*
Key words*: Asphyxia, anemia, Hypoxic-ischemic encephalopathy, Microcephaly, Neonate, Perinatal*
Abbreviations: *AKI (acute kidney injury), GDM (gestational diabetes mellitus), PROM (premature rupture of membrane), IUGR (intra-uterine growth restriction), Hypoxic-ischemic encephalopathy (HIE),*

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I. Introduction:

Perinatal Asphyxia is one of the leading causes of neonatal mortality and morbidity in developing countries. Perinatal period commences from 22 completed weeks of gestation and ends 7 completed days after birth, thus the causality assessment of perinatal asphyxia reflects both maternal and child health status of the society. Along with prematurity and sepsis, perinatal asphyxia is one of the three commonest causes of neonatal deaths in India and perinatal asphyxia alone contributes to 28.8% of total neonatal death [1, 2, 3.] Perinatal asphyxia is a multiorgan system disorder affecting brain, heart, lung, kidneys, and intestine to the frequency of 50%, 45%, 28%, 25%, and 25% respectively [4]. Thus survivors of perinatal asphyxia are at increased risk for neurodevelopmental squeal including motor and cognitive disabilities. Ellis et al reported that 18% survivors of mild to moderate birth asphyxia had neonatal encephalopathy and permanent severe neurological impairment like mental retardation, cerebral palsy, epilepsy, vision loss and hearing impairment [5]. But because of neuronal plasticity in newborns an early intervention can minimize the impairment and improve the long-term neurological and cognitive outcome. This study aims at finding out the risk factors of perinatal asphyxia and

outcome of asphyxiated neonates' up to 6 months of age in a tertiary care hospital which will help in early detection and intervention to reduce both mortality and disability.

II. Materials and Methods

We conducted a combination of cross sectional descriptive study and observational prospective single center based study during the time frame of May 2018 to April 2019, at the department of pediatric medicine Medical College, Kolkata. A total 98 newborns both male and female were included in the study.

Study Design: a combination of cross sectional descriptive and observational prospective study

Study Location: At Department of Pediatric Medicine / Medical College, Kolkata. It's a tertiary care superspeciality hospital cum medical college at the capital city Kolkata, West Bengal, India.

Study Duration: May 2018 to April 2018

Sample Size: 98 neonates inborn.

Sample size Calculation: The number of subjects for this study will be 97 – 100.4 with power 86.4%. (From the different studies done, expected proportion of the patients, amongst the cases had been assumed to be 60%).

The formula used for sample size

$n= 4pq/L^2$

Where n is the required sample size, p is the approximate prevalence rate for which the study is to be conducted. The knowledge of this is to be obtained from previous study.

q= 1 -p and L is the permissible error in the estimate

- at present by using the above formula $n = 4pq/L^2$

Where, n= required sample size, p= 0.10, q=1-p=0.90

L = Loss % (Loss of information),

n= (4 X 0. 1 X 0.9)/ (0.0037) (L^2) = 98

Total study population = 98 patients

Sample design: All consecutive subjects will be taken till required sample size reached. In this study different control group not required.

Inclusion criteria: Neonates suffering from perinatal asphyxia fulfilling one or more of the following criteria

- ✓ Required resuscitation > 1 minute
- ✓ 5 minute APGAR score < 7
- ✓ Profound metabolic or mixed academia (pH < 7.00) in umbilical cord blood.
- ✓ Post asphyxia seizure or multi organ failure in the 1st 72 hrs. of life.

Exclusion criteria:

- ✓ Birth weight < 1500 gram
- ✓ Neonates with major congenital anomaly of CNS ,CVS and respiratory system
- ✓ Other causes of CNS encephalopathy
- ✓ Opium or anesthesia related perinatal depression
- ✓ All out born babies
- ✓ Parents not consenting for the study

Procedure methodology:

All inborn newborns satisfying the definition of perinatal asphyxia by National Neonatal Forum of India (NNF) and WHO were included in the study consecutively till required sample size was reached. However newborns with birth weight < 1500 gm., neonates with major congenital anomaly and other causes of CNS encephalopathy, maternal anesthesia related sedation were excluded from study. Ethical clearance from Institutional Ethics committee was obtained and proper consent taken from parents. A well designed questionnaire was used to collect data of the recruited patients consecutively. We evaluated detailed maternal history sheet to record the perinatal risk factors related to perinatal asphyxia in our study population. Any newborn who failed to initiate or sustain breathing after birth (WHO) or APGAR score less than 7 at five minute of age (NNF) were diagnosed as birth asphyxia and enrolled in the study. We did umbilical artery pH estimation where possible but not in every case. Subsequently they were followed up both during hospital stay as well as post discharge in newborn follow-up clinic till 6 months of their age. Detailed recording of clinical complications, like respiratory distress, convulsion, shock, renal failure, necrotizing enterocolitis, DIC and death done for all newborns during their hospital stay. After discharge follow up data collected regarding feeding problem, head circumference, neurological exam at 1 month, 3 month, and 6 months of age during their neurodevelopmental clinic visit. . Routine Oto-acoustic emission (OAE), at 4weeks, if failed BAER at 3 months and Visual evoked potential (VEP) at 3 months done for all newborns. For neurological assessment of newborn we used Hammersmith infant neurological examination chart. Outcome of neurostimulations therapy done at neurodevelopmental clinic was not included in our study.

Statistical Analysis:

Standardized case record form were used to record relevant demographic, clinical, laboratory data. MS excel and SPSS 26 used for analysis of variables. For perinatal risk factors of birth asphyxia descriptive statistics used to calculate mean and standard deviations, frequencies and percentages of the variables. Regarding outcome and correlation of variables Chi square test, Z test (with / without Yates Corrections) used.

III. Results.

Out of 98 babies enrolled for the study, 6 (6.12%) babies died during hospital stay and we followed up rest 92 babies till 6 months age. The cohort had almost equal sex distribution (M: F: 54: 44) with a mean birth weight of 2.34 ± 0.386 kg. The mean age of the mothers was 23.98 years and most of them were multiparous (52.04%) & booked (75.5%) cases. Normal vaginal delivery was the commonest mode of delivery (73.47%) followed by LUCS (21.43%). Among the maternal risk factors, Anemia (43.69%) was the commonest followed by prolonged labour (26.53%), pregnancy induced hypertension (20.41%), malpresentation (8.16%), oligohydraminos (11.2%), gestational diabetes (6.12%), ***Table 1***. Among fetal risk factors, preterm (42.85%) was the commonest followed by fetal distress (30.16%), small for gestational age (14.29%), and cord collapse (7.14%), ***Figure 1***. HIE (Hypoxic ischemic encephalopathy) was evident subsequently to perinatal asphyxia in 53 (54%) babies and the frequency of its subtypes were HIE-1 (25.51%), HIE-2 (19.39%), HIE-3 (9.18%) as per Saranat staging, ***Figure 3***. During hospital stay 58.16 % newborns had respiratory distress, followed by Shock (27.55%), AKI (12.24%), and NEC (18.37%) ***Figure 4***. We found no significant association of perinatal asphyxia with maternal age, birth parity, birth weight of newborn, and mode of delivery ***Table 2***, however a significant association exists between severity of perinatal asphyxia and organ damage, except NEC where we found no significant association. On post discharge follow up we recorded feeding problem in 20.65% neonates at 1 month of age which increased over next 6 months to (26.08%) ***Figure 6***. 19.55% infants had microcephalyat 6 months of age and 22.83% infants had abnormal neurological score (HINE scoring) at the same age. Out of surviving 92 newborns, 7 infants had hearing loss and 16 infants had vision problem.

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Table 1: Distribution of neonates according to maternal risk factor

RISK FACTORS	NO OF MOTHER	PERCENTAGE
Pallor	**34**	**34.69%**
APH	**4**	**4.08%**
PROM	**5**	**5.10%**
Prolonged labour	**26**	**26.53%**
Malpresentation	**8**	**8.16%**
Poly hydramnios	**8**	**8.16%**
Oligo hydramnios	**11**	**11.22%**
Multiple gestation	**3**	**3.06%**
GDM	**6**	**6.12%**
Meconium stained liquor	**15**	**15.31%**
PIH	**20**	**20.41%**

Table 2: Association of severity of Perinatal Asphyxia with clinical complications.

Clinical status	Severity of Perinatal asphyxia		Total number of patients =98	Chi square value	Degree of freedom	P value
	Mild to Moderate (n=67)	Severe (n=31)				
HIE	24 (35.8%)	29 (93.5%)	53 (54%)	26.16	1	< 0.05
AKI	3 (4.5%)	9 (29%)	12 (12.2%)	9.72	1	< 0.05
NEC	12 (17.9%)	6 (19.4%)	18 (18.3%)	0.0295	1	< 0.05
Respiratory distress	35 (53.3%)	14 (58.3%)	49 (50%)	0.1996	1	>0.05
Hepatic dysfunction	23 (34.3%)	28 (90%)	51 (52%)	24.43	1	< 0.05
Shock	10 (14.9%)	17 (54.8%)	27 (27.5%)	16.92	1	< 0.05

Table 3 : Association of neurological outcome with severity of Perinatal asphyxia at 6 months of age on follow up at Neurodevelopmental clinic.

Clinical parameters at 6 months of age	Severity of Perinatal Asphyxia		Total Number =92	Chi Square value with Yates correction	Degree of Freedom	P value
	Mild to Moderate n=67	Severe n=25	Number of cases			
Visual Impairment	4 (6%)	12 (48%)	16 (17.3%)	19.57	1	< 0.05
Hearing Impairment	3 (4.5%)	4 (16%)	7 (7.6%)	1.99	1	> 0.05
Neurological Impairment	3 (4.5%)	18 (72%)	21 (22.8%)	43.37	1	< 0.05
Feeding problem	5 (7.5%)	19 (76%)	24 (26%)	48.41	1	< 0.05

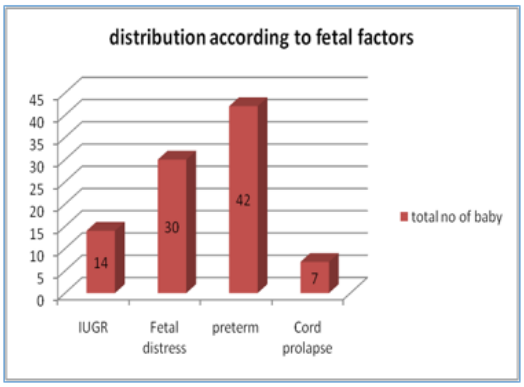

Figure 1: Distribution of neonates according to fetal risk factors

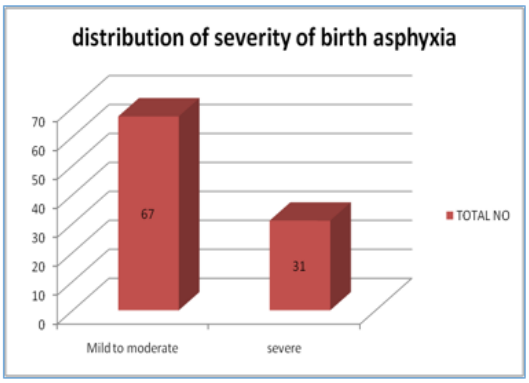

Figure 2: Distribution of neonates according to severity of perinatal asphyxia

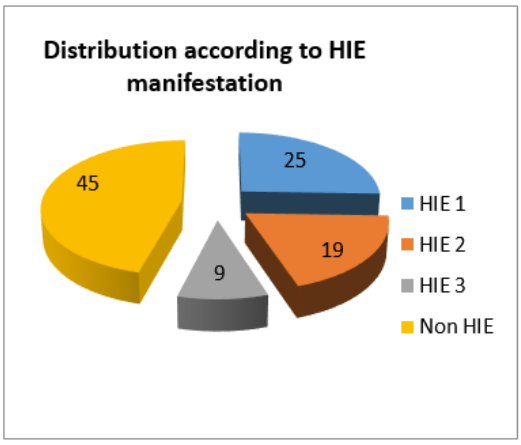

Figure 3: Distribution of types of HIE among total neonates with perinatal asphyxia

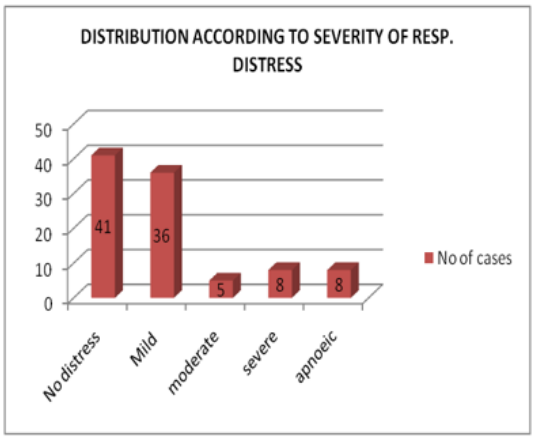

Figure 4. Distribution of respiratory distress among study population

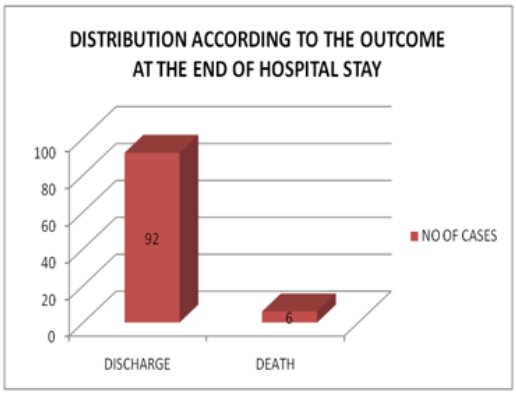

Figure 5: Distribution according to outcome at the end of study population

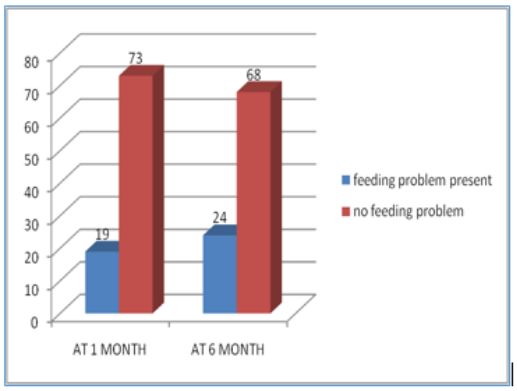

Figure 6: Distribution of feeding problem at the end of 6 month of discharged babies.

IV. Discussion

A similar study at Maharashtra by Nishant Yadav et al found that the commonest risk factor for perinatal asphyxia was anemia (91.4%) which was very high compared to our findings of anemia prevalence (34.69%) probably due to improved maternal care in recent years and routine iron-folic acid supplementation at all antenatal units [6] . In their study mean maternal age was 24.28 years and most of the mothers were primiparous (51.25%) and birth weight of newborns was 2.24 kg which was identical to our study. In another study in north India by Bhavna Tiwari et al, the commonest maternal risk factor for perinatal asphyxia was prolonged labour (20%) followed by antepartum hemorrhage (13.3%) , anemia 10% and pregnancy induced hypertension (8.3%) and (PET) [7]. Similar study at Karachi, Pakistan reported anemia (48%), premature rupture of membrane (33.3%), PET 15.4%.were the commonest maternal risk factors for perinatal asphyxia. In their study mean age of mother was 24.22 years and most of them were unbooked cases (74.7%) [8]. From the point of booked maternal cases we had bettered but still anemia an important problem in our society.

During hospital stay, total 53 (54.1%) neonates developed HIE. Among them 25 (25.51%) cases were HIE-1, 19 (19.39%) cases developed HIE-2 and 9 (9.18%) cases developed HIE-3. 45 (45.92%) asphyxiated babies showed no signs of HIE. Most of the neonates with severe birth asphyxia (93.5%) later developed HIE, in comparison to 35.8% mild to moderate birth asphyxiated neonates developed HIE subsequently. There is a definite association between severity of birth asphyxia and occurrence of HIE.

A study in Tanzania by Simiyu IN et al showed , 49% cases of total birth asphyxia ended up with HIE , among which 39% were HIE-2 and 10.2% were HIE-3 [9] . In one study by Bhavna Tiwari et al total 66% of asphyxiated baby developed HIE , of which 20% HIE 1 , 30% is HIE 2 and 16.6% babies developed HIE 3 . In our study most of the babies with HIE are in stage 1 category may be due to better neonatal care in present days. There was statistically significant association between severity of perinatal asphyxia and severity of encephalopathy which we found in our study Table 2.

In our study total 12 (12.24%) developed AKI during hospital stay , of which 9 (29%) cases were from severely asphyxiated baby and 3 (4.5%) cases from mild to moderate asphyxiated baby .There is clear association between severity of birth asphyxia and occurrence of AKI Table 2.

Study by Alaro d et al showed out of the 60 infants 36.6% had HIE I, 51.6% HIE II and 11.8% HIE III [10]. The prevalence of AKI was 11.7 %. There was a 15 fold increase risk of developing AKI in HIE III versus HIE I. Another Study by J Soni et al showed out of the 70 asphyxiated babies 33 (47.1 %) had renal failure. Severity of renal function abnormality correlates well with degree of asphyxia [11].

In our study, total 8.16% patients went apneic and required ventilator support at birth. 58.16% cases developed respiratory distress of which 36.73% cases have mild respiratory distress, 5.11% and 8.16% cases have moderate and severe respiratory distress respectively Figure 4. Out of 8 apneic baby, 7 baby has severe birth asphyxia. But we didn't found any significant association between severity of birth asphyxia and development of respiratory distress. Among 98 neonates 18.37% cases developed NEC during hospital stay.

Brahmiah et al in a study showed decrease in APGAR score was associated with increase in respiratory distress [12]. Study by Rohit v et al found out of 152 asphyxiated neonates admitted to NICU, respiratory system involvement was in 68 (45%) neonates.112 neonates (73.6%) had no/ mild respiratory distress (Downe's score 0-3) while 24% and 35% of children who had asphyxia had moderate and severe respiratory distress respectively [13]. A total of 24 (15.79%) neonates had features suggestive of NEC out of which 17 had grade I, Grade II NEC was seen 6 neonates while only one had grade III NEC. In our study, there is no case of grade 3 NEC and this finding is quite similar to our study.

In our study, 27.55% of patient required inotrope support, of which 54.8% were among severely asphyxiated group and 14.9% among mild to moderately asphyxiated group. There was distinct relation between severity of birth asphyxia and presence of cardiovascular dysfunction.

Vohra R et al, in their study showed Cardiovascular involvement in 48 (32%) of the infants who had birth asphyxia. Cardiovascular dysfunction most commonly manifested by the requirement of inotropes (32%) followed by abnormal echocardiography (27%), electrocardiography (ECG) changes (13%), and elevated creatinine kinase-MB (14.5%) [14]. Wenberger et al showed in their study that low APGAR score at birth require more cardiorespiratory support in immediate postnatal period [15].

In our study, among the total 98 cases, 6 (6.12%) deaths occurred during hospital stay and all were from severe birth asphyxia group. Remaining 92 cases are followed up to 6 month of age. No death occurred during follow up period.

Similar result found in the study by Selvakumar et al where, all 4 deaths were from severe birth asphyxia group and there was no death in mild and moderate birth asphyxia group [16].

In our follow up study total 19 (20.65%) cases presented with feeding problem at 1 months of age and the number reached 24 (26.08%) at 6 months of age which was due to more problem with introduction of semi-solid foods during weaning phase at 5-6 month of age. There was a clear association between severity of birth asphyxia and feeding problem at 6 months of age .In later stage it was found that many babies who have feeding problem at 1 month of age, also having abnormal neurological out come at 6 months of age.

A study by Slattery j et al showed that prolonged dysphagia or swallowing difficulties in very preterm infants may represent an early marker of undiagnosed brain injury and there is a relation exists between early sucking and swallowing difficulties and later neurodevelopmental outcome [17].

In our study, total 21 (22.83%) infants had abnormal neurological examination finding at 6 month of age and they were mostly from severe birth asphyxia group (72%). Thus there was a distinct relationship between severity of birth asphyxia and neurological outcome at 6 month of age.

A study in Canada by Razaz N et al showed that Low 5 min Apgar scores are associated with adverse short-term and long-term cognitive outcomes and developmental impairment. The risk of developmental vulnerability at 5 years of age is inversely associated with the 5 min Apgar score across its entire range, and the score can serve as a population level indicator of developmental risk [18].

In this study, we found total 7 (7.6%) cases of hearing impairment at 3 months of age and we found no significant association between severity of birth asphyxia and presence of hearing impairment.

Similar study by Jiang Z et all found that , occurrence of hearing loss does not appear to be closely related to the degree of perinatal asphyxia , although hearing loss mostly occurred in the children who survived severe perinatal asphyxia and exhibit neurodevelopmental deficit [19].

In our study we found that , total 16 (17.4%) cases have visual impairment (by VEP study at 3 months of age) and among them 12 cases from severely asphyxiated group and 4 cases from mild to moderately asphyxiated group and there was a significant association between severity of birth asphyxia and abnormal VEP finding at 3 months of age .

In a study by Mcculloch DL et al stated that perinatal indicators of asphyxia, including neurologic status, APGAR scores, and arterial pH values, were poor predictors of visual outcome [20]. The risk of visual impairment was limited to those survivors with neurodevelopmental deficits. Another study by Whyte HE et al showed good correlation of VEP with neurodevelopmental outcome in infants with asphyxia and VEP may be useful prognostic indicator [21].

The strength of the study is a larger cohort with mixed population from all strata of society as it was conducted at a tertiary care center. Being a Superspeciality center it was possible for long term follow up and assessment of neurodevelopment status and appropriate timely intervention. However the study is having limitations, where we didn't worked out in establishing correlation between MRI imaging and outcome predictors of perinatal asphyxia.

V. Conclusion

In a developing country like India, perinatal asphyxia still a challenge even at institutional deliveries. A proper maternal antenatal & peripartum care will minimize the maternal and fetal risk factors of perinatal asphyxia and thus it will reduce the overall burden of birth asphyxia. Also neuronal assessment during early infancy will ease the detection of future neuro-handicapped and cognitive impairment by introduction of early neuro-stimulation, taking the advantage of neuro-plasticity in newborns.

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