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Original Research Article

An Evaluation of Neonatal Hypoglycaemia in Developing Children

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Abstract

Background: Many new born babies experience low blood glucose concentrations, a condition referred to as neonatal hypoglycaemia (NH). Neonatal hypoglycemia is a frequently encountered metabolic derangement confronted in neonates leading to developmental delay in later life. Early identification of delay can help the treating paediatrician to start early stimulation and improve the outcome of these children. Various developmental screening tests are available but these require expertise administration and interpretation.
Aims and objectives: To evaluate a wide spectrum of neonatal hypoglycaemia in developing children. Compare DDST II with TDSC for screening for developmental delay and LEST for screening of language delay in children with neonatal hypoglycemia.
Material and Methods: We conducted a hospital based analytical cross-sectional study at Muzaffarnagar Medical College in Muzaffarnagar, Uttar Pradesh, India from Aug 2019 toJuly 2020. We conducted a Descriptive Hospital based cross-sectional study after Institutional ethics committee approval and written informed consent. Children with history of neonatal hypoglycemia were identified and their details were collected in a structured proforma. All these children were assessed for developmental delay by DDST II, TDSC and LEST scale by different individuals.
Results and Observations: Total of 82 children was enrolled in the age group of 6 months to 6 years. On comparing TDSC to DDST II, sensitivity of the TDSC is 93.18% and specificity is 100%. Kappa value is 0.92 (0.70-1.14). While LEST has sensitivity is 88.64% specificity is 97.3% and Kappa value is 0.852 (1.071-0.6367) as compared to the Language domain of DDST II.
Conclusion: TDSC and LEST are simple scales with good sensitivity and specificity. Nurse, receptionist or peripheral health workers can be taught to use these scales with minimum training to augment early identification and early referral of developmental delay.

Keywords: Neonatal hypoglycaemia, developing children, developmental delay, language delay, Specificity, sensitivity, growth, overall growth, DDST II, TDSC

Introduction

It remains difficult to define neonatal hypoglycemia using a single glucose value [1]. In the first 48 to 72 hours post-birth, infants may develop signs of hypoglycemia, with blood glucose at levels that are substantially lower than normal adult levels. In adults or older children, Whipple's triad (signs and symptoms of hypoglycemia, low serum glucose level, and the resolution of signs and symptoms with the provision of glucose) can be used, but this is often impractical in the neonate yet the principles should be adhered to if possible. Studies of exclusively breastfed, appropriate-for-gestational-age (AGA), term infants have shown that blood glucose levels fall immediately after birth, from two-thirds of maternal levels to as low as 1.8 mmol/L at 1 hour of age (Level 2b) [3, 4] They subsequently rise to levels >2.0 mmol/L, which are generally maintained for 72 hours. Some 12% to 14% of well, AGA, breastfed newborns have a blood glucose level of <2.6 mmol/L in the first 72 hours after birth [5].Past this point, they generally maintain a glucose level >3.3 mmol/L[2] Preterm infants may take longer to reach this threshold. Neonatal hypoglycemia is the most common metabolic issue in the newborn, the definition of neonatal hypoglycemia remains controversial, however hypoglycemia was defined as blood sugar levels less than 45 mg/dl, Hypoglycemia in neonates can be symptomatic or asymptomatic. The most common symptoms include jitteriness, convulsions, apathy, hypotonia, coma, refusal to feed, cyanosis, high pitched cry and hypothermia. These symptoms are very non-specific and may be easily missed especially in small sick infants. Therefore, hypoglycemia must always be confirmed biochemically and by response to treatment. Many newborn babies experience low blood glucose concentrations, a condition referred to as neonatal hypoglycaemia

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(NH). Neonatal hypoglycemia is one of the frequently encountered metabolic derangements confronted in neonates. Hypoglycemia occurs in 1.3-4.4 per 1000 fullterm newborns and 15-55 per 1000 preterm newborns [6]. Hypoglycemia had a deleterious effect on the brain. Neonatal hypoglycemia leads to various neurodevelopmental disabilities in children like microcephaly, cerebral palsy, behavioural disorders, seizures, and visual disturbances and developmental delays. Early identification of these delays can help the treating paediatrician to start early stimulation and improve the outcome of these children. The various screening tests used for developmental assessment are available like Denver developmental screening test (DDST II) and Bayley developmental screening test. The DDST II is a valid scale with a strong relationship between classification on the DDST and scores on the StanfordBinet intelligence scales and the Bayley infant scales [7]. DDST-II classifies the assessment of child's development into 4 areas personal-social (25 items), fine motoradaptive (29 items), language (39 items), and gross motor (32 items) [8, 9]. These tools require more expertise in administering the test. Screening tools like Trivandrum Developmental Screening Chart (TDSC) for children of 0- 6 years and Language evaluation Scale Trivandrum (LEST) 0-6 years are simple tools which can be administered by the nursing staff [10,11,12]. This study was undertaken to compare DDST II with TDSC for screening for developmental delay and LEST for screening of language delay.

Material and Methods

Compare DDST II with TDSC for screening for developmental delay and LEST for screening of language delay in children with neonatal hypoglycemia.

Objectives

1. To identify children with neonatal hypoglycemia and classify them into symptomatic and asymptomatic neonatal hypoglycemia.
2. To assess the various domains of DDST II and compare them among the two groups.
3. To study the sensitivity and specificity of TDSC for screening for developmental delay in comparison with DDST II in children with neonatal hypoglycemia.
4. To study the sensitivity and specificity of LEST for screening for language delay in comparison with DDST II in children with neonatal hypoglycemia.

Type of study: Analytical hospital-based cross-sectional study.

Inclusion criteria

1. Children with history of neonatal hypoglycemia.
2. Age group 6 months to 6 years.

Exclusion criteria: Children with severe congenital anomalies and syndromic children were excluded from the study.

Place of study: Muzaffarnagar Medical College Muzaffarnagar,UP, India.

All children coming to the OPD or IPD of Muzaffarnagar Medical College Muzaffarnagar, from August 2019 to July 2020 were our study population. They were screened for history of neonatal hypoglycemia. All subjects with documented evidence of neonatal hypoglycemia were enrolled in the study after parents voluntarily signed the written informed consent. Details of their sociodemographic profile and perinatal history were documented in a structured proforma. Subjects were classified into Symptomatic and Asymptomatic hypoglycemia depending on the presence or absence of symptoms of hypoglycemia during neonatal period. Details of the presenting complains were noted. Structured neurological examination was done in all patients. All patients underwent detail developmental screening by using DDST II, TDSC and LEST charts at the same setting. A line is drawn at the chronological age of the child on the chart and developmental millstones assessed. If the child fails any item on the left side of the line it is labelled as Delay on DDST II and TDSC. For LEST 1 item is taken as suspect and 2 items as delay. Assessment by DDST II, TDSC and LEST was done by independent individuals who were trained on how to administer the scale to avoid bias. All these findings were recorded in the case sheet and later entered into excel. Detail statistical analysis was done using SPSS 22 software.

Results and Observations

We included 82 children in the study who had definite history of neonatal hypoglycemia. We had 62(75.60%) males out of 82. The maximum number i.e.: 32 (39.02%) belong to the 6 to 12 months age group, followed by 25 (30.5%), 8(9.75%) and 7 (8.53%) and 6(7.31%), 4(4.87%) in age group of 13 – 24 months, 25-36, 37-48, 49-60 and 61-72 months respectively. Out of the total 82 patients 48 (58.53%) patients had symptomatic hypoglycemia and 34 (41.46%) had asymptomatic hypoglycemia. In our study total 44 (53.65%) children had

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developmental delay by using DDST II as screening tool. Statistically significant delay was seen in the number of children with symptomatic hypoglycemia {32 (72.7%)} as compared to asymptomatic hypoglycemia children. Table 2 shows distribution of various domains of DDST II in detail among children with symptomatic and asymptomatic hypoglycemia. On using TDSC, developmental delay was found in 41 children. Thus 3 children were picked up in addition when we applied DDST II. Details are shown in table 3. Language domain was again assessed by LEST which picked up 37 (45.12%) children with language delay and 3 children were suspect for language delay. DDST II language domain had picked up 40 children with speech delay which matches well
with LEST (Table 4). In table 5, out of the 50.6% cases who had delay on TDSC also had delay on DENVER II. There were only 3 children who were normal on TDSC and were found to have delay on DDST II. Sensitivity of the TDSC is 93.18% and specificity is 100%. Kappa value is 0.92 (0.70- 1.14). This indicates a strong agreement between TDSC and DENVER II. Table 6 shows 39 (97.5%) children had language delay on LEST. Sensitivity is 88.64% specificity is 97.3% and Kappa value is 0.852 (1.071- 0.6367). This indicates a strong agreement between LEST and DENVER II for classification of patients into language delay and normal.

Table 1: Distribution of symptomatic and asymptomatic neonatal hypoglycemia cases according to Denver developmental screening test II (DDST II)

Denver II	Symptomatic	Asymptomatic	Total	P Value
Delay	32(72.7%)	12(27.3%)	45(54.3%)	
No Delay	16(43.2%)	22(56.8%)	37(45.7%)	0.0075
Total	48(59.3%)	34(40.7%)	82(100%)	

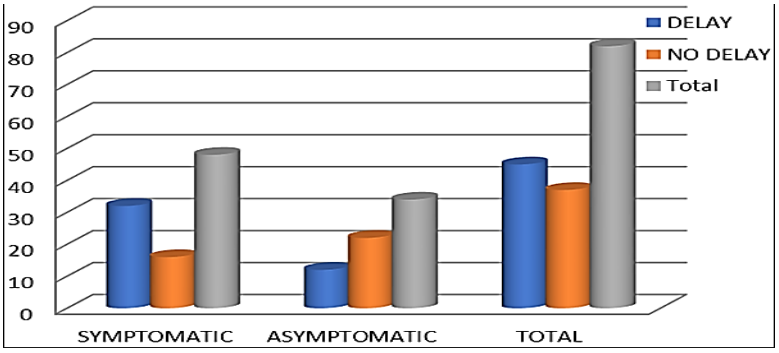

Fig 1: Symptomatic and asymptomatic neonatal hypoglycemia cases vs.Denver developmental screening test II (DDST II)

Table 1 and Figure 1, are showing that total 44 children had delay according to DDST II of which 32 (72.7%) children had symptomatic hypoglycemia. There was statistically significant difference between the two groups.

Table 2: Distribution of symptomatic and asymptomatic neonatal hypoglycemia cases according to various domains of DDST II

Denver II	Symptomatic		Asymptomatic		Total		P Value
	Number	%	Number	%	Number	%	
Gross motor Delay	31	73.8	11	26.2	42	51.9	0.0060
Fine Motor Delay	30	75.0	10	25.0	40	49.4	0.0047
Language Delay	29	72.5	11	27.5	40	49.4	0.0173
Personal Social Delay	30	75.0	10	25.0	40	49.4	0.0047

Table 2 shows distribution of various domains assessed by DDST II among symptomatic and asymptomatic hypoglycemia. Symptomatic hypoglycemia children had statistically significant delay in all the domain's when compared to asymptomatic hypoglycemia children.

Table 3: Distribution of symptomatic and asymptomatic neonatal hypoglycemia cases according to Trivandrum developmental assessment scale (TDSC)

Denver II	Symptomatic	Asymptomatic	Total	P Value
Delay	30(73.2%)	11(26.8%)	41(50.0%)	
No Delay	18(45%)	23(55%)	41(50.0%)	0.0104
Total	48(59.3%)	34(40.7%)	82(100%)	

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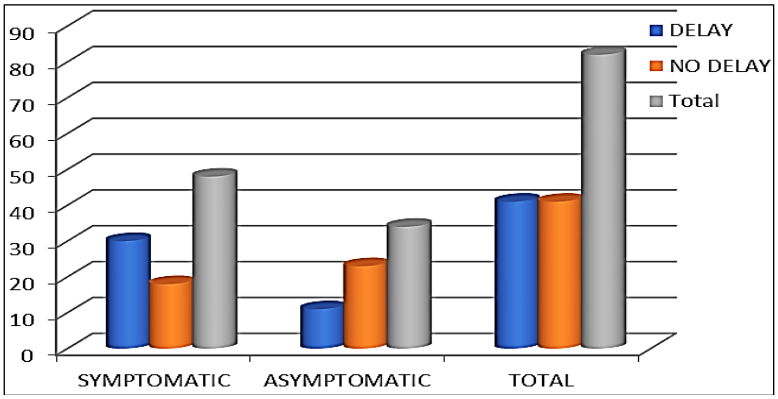

Fig 2: Symptomatic and asymptomatic neonatal hypoglycemia cases vs. Trivandrum developmental assessment scale (TDSC)

The table no 3 and Figure 2 are showing that total 41 children had delay on TDSC of which 30 (73.2%) children belonged to the symptomatic hypoglycemia. This difference was statistically significant.

Table 4: Distribution of symptomatic and asymptomatic neonatal hypoglycemia cases according to Language assessment scale Trivandrum (LEST)

Lest	Symptomatic	Asymptomatic	Total	P Value
Delay	26(70.3%)	11(29.7%)	37(45.7%)	
No Delay	21(51.2%)	21(48.8%)	42(50.6%)	
Suspect	1(33%)	2(67.7%)	3(3.7%)	0.1502
Total	48(59.3%)	34(40.7%)	82(100%)	

In table 4 we see that 37 (45.7%) of total had language delay. 26 (70.3 %) children among symptomatic group had delay on LEST while 3 children were suspect for delay. The difference between the two groups was not statistically significant.

Table 5: Comparison of neonatal hypoglycemia cases according to DDST II and TDSC

TDSC Outcome	Denver II outcome			P Value
	Delay	Normal	Total	
Delay	41(100%)	0(0%)	41(50.0%)	
Normal	3(7.5%)	38(92.5%)	41(50.0%)	0.0001
Total	44(59.3%)	38(40.7%)	82(100%)	

As indicated in table 5, out of the 50.6% cases that had delay on TDSC also had delay on DENVER II. There were only 3 children who were normal on TDSC and were found to have delay on DDST II. Sensitivity of the TDSC is 93.18% and specificity is 100%. Kappa value is
0.92 (0.70-1.14). This indicates a strong agreement between TDSC and DENVER II.

Table 6: Distribution of neonatal hypoglycemia cases according to DDST II and LEST

LEST Outcome	Denver II outcome			P Value
	Delay	Normal	Total	
Delay	39(97.5%)	1(2.5%)	40(48.8%)	
Normal	5(12.2%)	37(87.8%)	42(51.2%)	0.0001
Total	44(59.3%)	38(45.7%)	82(100%)	

Table 6 shows 39 (97.5 %) children had language delay on LEST. On applying DDST II an additional 5 children were picked up which increased the count to 44 (53.65%). Sensitivity is 88.64% specificity is 97.3% and Kappa value is 0.852 (1.071-0.6367). This indicates a strong agreement between LEST and DENVER II for classification of patients into language delay and normal.

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Discussion

In our study, 10.5% of newborns who admitted in NICU had admission glucose concentrations < 40 mg/dl or even lower according to hours of age). In our sample of 82 children we had dominance of male sex {62(75.60%)}, which was similar to study done by Singh *et al.* [13]. S Thirumalaikumarasamy*et al.* found a female preponderance seen in their study [14]. In our study forty four (53.65%) children had delay on DDST-II, of which 32 (72.7%) were symptomatic (P = 0.0075). Singh *et al.* found that 8 (1.9%) developed symptomatic hypoglycemia out of 107 babies. Mejri*et al.* found that hypoglycemia was symptomatic in four infants, all of whom were below the fifth percentile for BW[15]. On comparing individual domains of DDST II which includes the Gross Motor, Fine Motor, Language, and Personal social domain, all domains are statistically significantly affected in children with symptomatic hypoglycemia. Melana*et al.* in their prospective study of 39 neonates found that the prevalence of abnormal neurodevelopmental outcome in children with neonatal hypoglycemia by DDST 2 method was 71.79% [n=28] and 66.6% [n=26] at 3 and 6 months respectively [16]. TDSC and LEST were the other scales used to assess development which showed a similar correlation. On comparing the assessment by DDST II with TDSC we found that TDSC has a sensitivity of 93.18% and specificity of 100% over DDST-II. %. Kappa value is 0.92 (0.70-1.14). This indicates a strong agreement between TDSC and Denver II. Also, on comparing DDST II with LEST, we found a sensitivity of 88.64% and specificity of 97.3% and Kappa of 0.852 (1.071-0.6367). This indicates a strong agreement between LEST and Denver II for the classification of patients into Language delay and normal. Nair *et al.* conducted a study on "Development and Validation of Trivandrum Development Screening Chart for Children Aged 0-6 years" using DDST as the refence standard. On delay in one item on TDSC (0-6 y) being considered as 'TDSC delay' (test positive), the sensitivity of TDSC (0-6 y) was found to be 84.62% (95% CI: 71.92-93.12) and specificity was 90.8% (95% CI: 88.97-92.43). The Negative Predictive Value of 99.23% (95% CI: 98.48-99.67) and LR (negative) of 0.17(95% CI: 0.09-0.32). Nair *et al.* also validated LEST against Receptive Expressive Emergent Language Scale (REELS) for 0-3 years[17]and Extended REELS for 3-6 years age group6. The LEST 0-3 screening tool showed a sensitivity of 84.4%, specificity of 80.3%, Positive Predictive Value (PPV) of 91.5%, Negative Predictive Value (NPV) of 67.1% and accuracy (83.2%) against the reference standard REELS. For LEST 3-6 years scale showed a sensitivity of (81%, 47%); specificity (68%,94%), PPV (12%, 31%); NPV (98%, 97%) and accuracy (68.5%, 92%), respectively. Kishore *et al.* in their study "To identify clinical utility of TDSC in screening of developmental delay in children (0-3 yrs.) as compared to DDST" concluded a sensitivity of 57.4% and specificity of 100% for TDSC as against DDST for screening developmental delay. We did not find any study comparing DDST II and LEST for language evaluation in the literature that we reviewed till date [18]. "Development of High-Risk Newborns-A Follow-up Study from Birth to One Year" by Elenjickal*et al.* found the sensitivity of 57.4% and specificity of 100% for TDSC as against DDST for screening developmental delay [19]. Ryu and Sim conducted a study on "The validity and reliability of DDST II and Bayley III in children with language development delay". They proposed that DDST II is a useful screening test to identify infants with delayed language development [20]. Shahshahani*et al.* have validated a Persian version of the DDST II for use in Iranian children [21].

Conclusion

Early neonatal hypoglycemia is a dangerous phase. The strongest risk factors were early GA, LGA, SGA, infant of maternal diabetes. Developmental screening is very important specially among the high-risk group children. It gives an idea to the care giver about the domain's affected and a rough idea of the severity of delay. This helps them work with focus and can reinforce therapies to promote further development. DDST II even though simpler is time consuming and requires adequate training and experience to administer. TDSC and LEST are quick and simpler tests. Thus, we conclude that TDSC and LEST are simple scales with good sensitivity and specificity. These are simpler to use specially in busy OPDs and can be administered by the receptionist or nurse for primary screening of developmental delay in children.

Our limitations: We have not used this scale in the community level population. Targeting to a high-risk group may have some fallacies in the results.

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Conflict of interest: None**.**

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