Correlating Novel 3D/4D ultrasound-CSF score in foetal CNS anomalies with neurological outcome

Dr. Mamatha Gowda[1], Dr. Shruthy Mohan[1], Dr. Nivedita Mondal[2]

Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry

Introduction

- Prenatal prognostication of fetal CNS anomalies is challenging as direct assessment of nervous system is not possible as in the neonate.[1]

Objective

- To apply Combined Structural and Functional (**CSF**) score by 2D/3D/4D USG incorporating both structural aspects and foetal neuro-behaviour.
- Assess the correlation with postnatal survival and neurodevelopment.

Materials and Methods

- Singleton fetuses with CNS anomalies on scan at ≥ 20 weeks included.
- Neurosonogram with 3D/4D evaluation done to assign a score, considering both structural components of anomaly and foetal behavioural aspects after ≥ 30 minutes of assessment.
- Score correlated to postnatal outcome by neurodevelopmental assessment performed at birth with APGAR and Hammersmith Infant Neurological Examination (HINE) score on survivors at 3months.

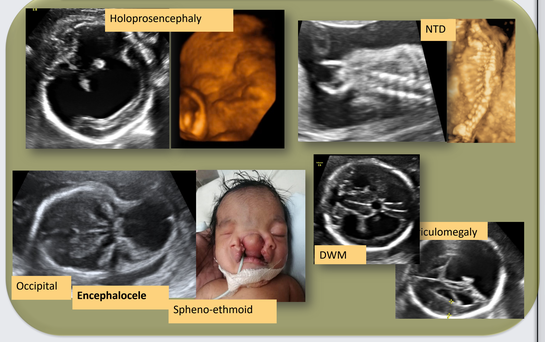
Structural Components			Functional Components			
Parameter	Scores		Sign	Score		
Skull: Size/HC Sutures Defect	± 3SD	± 2 SD		0	1	2
	Grossly overlapping/ wide open	Obliterated	Head movements	Abrupt	Small range	Full range
	Encephalocele	Without herniation of brain	Facial movements (eye, grimace, tongue, mouth opening, yawn)	None present	At least 2 facial movement	> 2 facial movements
Spine	Open NTD	Closed defect	Sucking, swallowing reflexes	None		Present
Cerebrum: Parietal mantle Sulci/gyri	Extremely thin (<1cm)	Thin (1-1.5 cm)	Gross body movements	<1	1-3	>3
	Lissencephaly/ Schizencephaly	Focal defects	Respiratory efforts	None	Dysrhythmic	>1 rhythmic
Prosencephalon division	Alobar/Semilobar holoprosencephaly	Lobar holoprosencephaly	Leg movement	Cramped or nil	Small in range or full <3	Full range (>3)
Ventricles	Severe (>20mm)	Moderate (15-20mm)	Hand movement	Cramped or nil	Small in range or full <3	Full range (>3)
Corpus callosum Posterior fossa	Complete agenesis	Partial agenesis	Opening and closing of fist	Clenched fist		Opening and closing Normal
	Cerebellar Hypoplasia	DWM/Arnold-Chiari	Hand and foot posturing	Fixed abnormal posture		
TOTAL	-2	-1	TOTAL SCORE	18		
Others	For milder lesions like mild Ventriculomegaly: 0					

CNS Anomalies	N=43
Open Neural Tube Defect	
Lumbosacral Meningomyelocele	10
Posterior Fossa Anomalies	
Arnold Chiari Malformation II	6
Blake Pouch Cyst	1
Cerebellar Hypoplasia	7
Dandy Walker Malformation	2
Mega Cisterna Magna	3
Posterior Fossa Arachnoid Cyst	2
Cortical	
Alobar Holoprosencephaly	2
Midline Defects	
Colpocephaly	3
Complete Corpus Callosal Agenesis	6
Partial Corpus Callosal Agenesis	8
Septooptic Dysplasia	1
Ventricular	
Mild Ventriculomegaly	4
Moderate Ventriculomegaly	7
Severe Ventriculomegaly	12
Cephaloceles	
Occipital Encephalocele	1
Spheno-ethmoid encephalocele	1

Results

- Results analysed by plotting ROC curves
- **Total CSF scores** correlated strongly with postnatal outcomes: Apgar at 1 & 5 minutes(r=0.76), Survival at 6 months(r=0.86), Days of survival (0.75), Strong statistically significant association with postnatal HINE scores predictive of cerebral palsy(p=0.000) and severe non-ambulatory CP(p=0.000). A cut-off score of 13 demarcated statistically significant differences.
- **Structural Score** also correlated strongly with postnatal outcomes: Apgar scores(r=0.735), survival(r=0.817) at 6 and HINE scores(r=0.730) at 3 months. A cut-off score of -3 was predictive of optimal/suboptimal HINE score (Sen-90.5%, Spe-86%, +ve LR-6.33).
- The **functional score** did not correlate strongly with HINE score(r=0.285) at 3, survival at 6 months(r=0.464) or Apgar scores (r=0.48). Significant difference in outcomes was found only at a high cut-off score of 17 out of 18.

Images of Structural anomalies

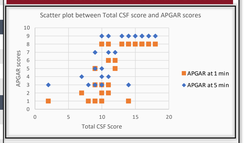


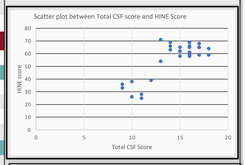
Images of Functional Components

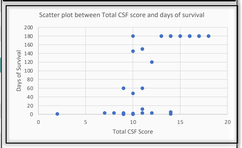
Association between CSF Score with Postnatal Parameters								
Apgar at 1 min	TOTAL CSF SCORE			STRUCTURAL SCORE			FUNCTIONAL	
	<13 (%)	≥13 (%)	TOTAL	< -3 (%)	≥ -3 (%)	TOTAL	< 17 (%)	≥ 17 (%)	TOTAL
<7	17(89.47)	2(10.53)	19(100)	18(94.74)	1(5.26)	19(100)	14(73.68)	5(26.32)	19(100)
7-10	3(12.5)	21(87.5)	24(100)	5(20.83)	19(79.17)	24(100)	6(25)	18(75)	24(100)
TOTAL	20(46.5)	23(53.49)	43(100)	23(53.49)	20(46.51)	43(100)	20(46.51)	23(53.49)	43(100)
p-value		0.000	SIGNIFICANT		0.000	SIGNIFICANT		0.001	SIGNIFICANT
	Apgar at 5 min								
<7	11(84.62)	2(15.38)	13(100)	13(100)	0(0)	13(100)	11(84.62)	2(15.38)	13(100)
7-10	9(30)	21(70)	30(100)	10(33.33)	20(66.67)	30(100)	9(30)	21(70)	30(100)
TOTAL	20(46.51)	23(53.49)	43(100)	23(53.49)	20(46.51)	43(100)	20(46.51)	23(53.49)	43(100)
p-value		0.001	SIGNIFICANT		0.000	SIGNIFICANT		0.002	SIGNIFICANT
	Survival at 6 months								
Not Survived	19(90.48)	2(9.52)	21(100)	20(95.24)	1(4.76)	21(100)	15(71.43)	6(28.57)	21(100)
Survived	1(4.55)	21(95.45)	22(100)	3(13.64)	19(86.36)	22(100)	5(22.73)	17(77.27)	22(100)
TOTAL	20(46.5)	23(53.49)	43(100)	23(53.49)	20(46.51)	43(100)	20(46.51)	23(53.49)	43(100)
p-value		0.000	SIGNIFICANT		0.000	SIGNIFICANT		0.001	SIGNIFICANT
Association between CSF Score and HINE Score									
HINE Score	<13 (%)	≥13 (%)	TOTAL	< -3 (%)	≥ -3 (%)	TOTAL	< 17 (%)	≥ 17 (%)	TOTAL
In terms of predicting non-ambulatory CP									
<40	7 (100)	0(0)	7(100)	6(85.71)	1(14.29)	7(100)	5(71.43)	2(28.57)	7(100)
≥40 (low risk)	0(0)	21(100)	21(100)	2(9.52)	19(90.48)	21(100)	4(19.05)	17(80.95)	21(100)
TOTAL	7(25)	21(75)	28(100)	8(28.57)	20(71.43)	28(100)	9(32.14)	19(67.86)	28(100)
p-value		0.000	SIGNIFICANT		0.000	SIGNIFICANT		0.020	SIGNIFICANT
Association between Total CSF Score and HINE Score in terms of predicting CP									
<57	7 (87.50)	1(12.50)	8(100.00)	7(87.50)	1(12.50)	8(100.00)	5(62.50)	3(37.50)	8(100.00)
≥57 (low risk)	0(0.00)	20(100.00)	20(100.00)	1(5.00)	19(95.00)	20(100.00)	4(20.00)	16(80.00)	20(100.00)
TOTAL	7(25.00)	21(75.00)	28(100.00)	8(28.57)	20(71.43)	28(100.00)	9(32.14)	19(67.86)	28(100.00)
p-value		0.000	SIGNIFICANT		0.000	SIGNIFICANT		0.385	SIGNIFICANT
Association between Total CSF Score and HINE Score in terms of predicting optimal neurological development									
<67 (suboptimal)	7(29.17)	17(70.83)	24(100.00)	8(33.33)	16(66.67)	24(100.00)	7(29.17)	17(70.83)	24(100.00)
≥67 (optimal)	0(0.00)	4(100.00)	4(100.00)	0(0.00)	4(100.00)	4(100.00)	2(50.00)	2(50.00)	4(100.00)
TOTAL	7(25.00)	21(75.00)	28(100.00)	8(28.57)	20(71.43)	28(100.00)	9(32.14)	19(67.86)	28(100.00)
p-value		0.292	(Fisher's ex)		0.237	(Fisher's ex)			

Kindly watch the video adjoining the poster

Scatter plots showing the relation between Prenatal Total CSF Scores and Postnatal Outcomes







Other studies evaluating similar Fetal Neuro-behaviour or Brain Structure in Fetal CNS Anomalies				
	Kurjak et al.[2]	Glatter et al.[69]	Hayat et al.[70]	Our study
Study period	2008, Retrospective	2011-19, Prospective	2007-10, Prospective	2019-21, Prospective
Sample size	100 normal, 120 high risk pregnancies	137 singleton foetuses	21 normal, 22 with abnormal foetal brain MRI	43 CNS anomalies
Sample population	Diabetes, preeclampsia, prematurity, IUGR	Corpus callosal agenesis	Ventriculomegaly, other CNS anomalies	NTDs, ventriculomegaly and other major CNS malformations
Imaging	Ultrasound based	MRI based	Cine MRI based	3D/4D USG based
Scoring system and Score range	8 Foetal movement parameters: 0 to 20	7 Structural features: 0 to 11	Quality of general movements (GMs): Categorized as normal and abnormal	Structural score from 0 to -9, Functional score from 0 to 18, Combined score as a sum of these.
PN test	ATNAT	Bayley Scale	Bayley Scales	Hammersmith Examinations(HINE)
Results	Normal neonates score:14-20 Mild/mod abnormal: 5-13 Abnormal:0-5	MRI scores predicted outcome in 90.7% of isolated corpus callosum agenesis at cutoff of ≤3 for good outcome	Significant relationship of outcome, general movement quality, and structural MRI of brain (p=0 .020).	Total CSF score correlated with survival at 6 & HINE at 3 months but functional score did not correlate strongly with HINE or survival

Discussion

- Fetal Neuro-behaviour has been assessed previously using KANET score in high-risk pregnancies such as Diabetes.
- Two studies in the past on fetuses with CNS anomalies have assessed mainly the structural aspects, with limited evaluation of functional components using Fetal MRI.
- Fetal Neuro-behaviour in fetal CNS anomalies, especially taking structural aspects also into consideration has not been studied before exclusively with ultrasound, which was evaluated in this study.

Conclusion

CSF score correlated strongly with postnatal neurological outcomes and could guide the clinicians in prognostication and counselling of pregnant women with fetal CNS anomalies.

References

1. Hepper PG. Foetal behaviour: why so sceptical?: Editorial. *Ultrasound Obstet Gynecol* 1996; 8(3):145–8.
2. Kurjak AMiskovic B, Stanojevic M, et al. New scoring system for foetal neurobehavior assessed by three- and four-dimensional sonography. J Perinat Med 2008; 36(1).
3. Maitre NL, Chorna O, Romeo DM, et al. Implementation of the Hammersmith Infant Neurological Examination in a High-Risk Infant Follow-Up Program. Pediatr Neurol 2016; 65:31–38
4. Hayat TTA, Martinez-Biarge M, Kyriakopoulou V, et al. Neurodevelopmental Correlates of Foetal Motor Behavior Assessed Using Cine MR Imaging. Am J Neuroradiol 2018; :ajnr:A5694v1.
5. Glatter et al. Beyond Isolated and Associated: A Novel Foetal MRI–Based scoring system helps in the Prenatal prognostication of Callosal Agenesis. Am J Neuroradiol 2021; 42(4):782–6.