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Factors affecting the performance of routine gestational screening ultrasound for detection of neural tube defects

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Abstract
Context: Myelomeningocele (MMC) is one of the most devastating, nonlethal congenital anomalies worldwide. Ultrasonography is the modality of choice for imaging of an in-utero fetus. In spite of technological advances, differential professional experiences amongst imaging experts from various back grounds has however led to a heterogeneity in results generated from screening gestational sonography in different clinical set-up.
Aim: To evaluate the discrepancy between results obtained from sonography done in semi-urban or urban centres for antenatal diagnosis of fetal neural tube defects (NTD) in terms of performance of various diagnostic surrogates for the same. **Study Setting & Design:** Retrospective observational study conducted over a cross-section of referrals, at a university based teaching institute over a period of two years.
Patients and Methods: 38 cases with antenatal of NTD were included. Correlation of factors like presence of cystic swelling, spinal anomaly and ventriculomegaly to each other were done to bring out the differential pattern of observations between sonograms performed at various centers. ROC curves were plotted to evaluate the accuracy, sensitivity and specificity of various parameters.
Statistical Analysis: Pearson's Chi-squared test was applied to assess dependence of antenatal detection of NTD on qualitative variables. Independent sample t-test was employed to compare mean size of the MMC and number of ultrasounds in cases with and without antenatal MMC detection. ROC curve was drawn to assess size of MMC.
Results: Difference in size of MMC was not significant for antenatal diagnosis of NTD. Hydrocephalus as a surrogate for NTD performed significantly better than the above direct sign. Cases which had more number of scans had more chances of a correct antenatal diagnosis while a lesion higher up in the vertebral column was less likely to be missed.
Conclusion: Sonography in rural centres may miss out significant number of NTD, however ventriculomegaly performs better than detection of MMC in such centers.

Keywords: neural tube defects, gestational ultrasound, myelomeningocele

Introduction

Neural tube defects consist of the most common congenital anomalies of the CNS which occur due to failure of spontaneous closure of neural tube between 3 rd and 4 th week of intrauterine life [1].

Delivery of a child with neural tube defect (NTDs) causes distress and lots of apprehension to the affected families. Variable degree of handicaps may persist even after surgical correction of neural tube defects [2, 3]. Antenatal sonographic detection of these lesions helps the affected parents to consider termination or to prepare for surgical correction soon after birth. With advancement in surgical techniques these lesions are being repaired in - utero and this might bring revolution in management of surgically correctable anomalies. Although these intrauterine surgical techniques are associated with high feto-maternal risks, however a randomized control trial revealed reduced need for ventricular peritoneal shunts along with improvement in motor function and mental development comparing prenatal versus postnatal repair of myelomeningocele [4, 5]. In future, validation and popularisation of these techniques may further mandate assistance from a reliable sonographic evaluation, facilitating early prenatal diagnosis.

With this background the present study was preconceived to evaluate NTDs (myelomeningoceles and cephaloceles) post natally as well as assessment of the performance of sonography in detection of NTDs in antenatal period in northern India and to analyse the factors responsible for non-detection of these lesions on antenatal sonography.

Materials and Methods

This was a retrospective study and the ethical clearance was obtained from the Institute review board (IRB) before the commencement of this study. Cases in the study were recruited from amongst those who were either detected at birth or posted for surgical correction of confirmed neural tube defect over 1 year period. The clinical records of these neonates along with the maternal data on pregnancy and antenatal sonographic reports were analysed. Cases with USG reports of routine screening sonographic scans were included whereas the cases in which the USG reports of "level II scan", "anomaly scan" and "TIFA (targated imaging for fetal anomalies)" were not included in the study.

Detailed maternal history and focused neonatal examination to look for other associated anomalies was done. Data regarding the type of the lesions (open or close), site of the lesions (occipital, cervical, thoracic, thoracolumbar, lumbar,

lumbosacral or sacral), size of the cystic lesions (assessed clinically at birth), number of antenatal ultrasounds, presence or absence of coexistent hydrocephalus were cumulated and analysed.

Statistics was performed using SPSS software (IBM Corp 2013. Version 22.0. Armonk, NY). Z- test was applied to assess dependence of antenatal detection of MMCs on qualitative variables such as type of the myelomeningoceles and presence or absence of hydrocephalus on antenatal USG. Independent sample t-test was employed to compare mean size of the MMC and number of ultrasounds in cases with and without antenatal MMC detection. P≤ 0.05 was considered as significant. ROC curve was drawn to assess size of MMC in various cases to predict USG detection and Area under curve (AUC) was calculated. At all steps patient anonymity and issues pertaining to human ethics were ensured.

Results

Average maternal age was 25 years and out of 38 subjects 32 were multiparous and only 6 were primiparous. With variable initiation of time and duration 57% mothers received folic acid antenatally but none of them preconceptionally. Nearly 39% parents studied till middle class; none of the mothers were graduate or professional whereas 7% fathers were postgraduate and 13% were professionals. Monthly income of family was INR 5658 Rs. 25 (66%) neonates were male whereas 13(34%) were female with mean birth weight of 2540 gm. Other associated anomaly in form of chiary malformation, absent kidney and undescended testes was observed in 1 subject each whereas lower limb involvement was observed in 20 subjects (52%) and this included CTEV, genu recurvatum, CDH, rocker bottom foot, club foot and flexion at hip. Among these CTEV was the commonest found in 8(21%) out of 38. More than half of the cases (52%) had bladder involvement.

Out of 38 cases included in the analysis, 34 were myelomeningoceles and 4 occipital encephaloceles. Antenatal USG could detect the lesions in only 17(45%) cases whereas the underlying defects were missed in 21(55%) cases. Bye the time cases were detected most of them had already crossed 2 nd trimester with average gestational age of 30 weeks for detection. 9 cases got their first USG done in first or 2 nd trimester whereas 8 cases reported to sonologist in 3 rd trimester for their first scan. USG were mostly done by the centers outside the institutes, predominantly at private centres form Delhi and neighbouring states. Average size of MMC was 50 mm. The mean size (measured at birth) of the lesions in cases which were detected by antenatal USG was 52.6± 13.82 mm whereas the size of the lesions that were missed by antenatal ultrasound was 47.6 ± 15.7 mm. Independent t-test to compare the two means yielded an insignificant difference with p-value of 0.33. ROC (receiver operated characteristic) curve drawn for size of the lesions to predict sonographic detection produced an AUC (area under curve) of 0.636, signifying the poor predictive value of the size of the lesion for being identified on ultrasound (Fig 1). Based on the ROC curve, we obtained a cut-off value of 47.5 mm which had a sensitivity of 66.7% and a poor specificity of only 55%.

Table 1 shows the cross tabulation comparing type of the myelomeningocele to the antenatal sonographic detection. Z - test comparing the two variable showed a p-value of <0.001, signifying open MMCs were more likely detected by antenatal sonography as compared to close. Similarly Z - test to assess the impact of hydrocephalus on detection of MMCs (Table 2) yielded a p-value of <0.001 concluding a strong statistically significant relation between the two. This means MMCs associated with hydrocephalus have fair chance of detection by antenatal sonography on comparing with those without hydrocephalus. Antenatal USG was found to have a high specificity (80%) and fairly good sensitivity (64%) for detection of MMC when Hydrocephalus was taken in to consideration.

Average number of USG in cases where the scans failed to detect MMCs was 1.9 where as the average scans in cases with USG detection was 3.17. This difference of mean was statistically significant with p-value of 0.005 (independent sample t-test). Lesser no of USG are likely to miss MMCs in antenatal scan.

Table 3 charts the cases with and without USG detection of MMCs at individual locations. All the cases with occipital encephaloceles were correctly diagnosed by USG whereas 7 out of 10 cases i.e. 70% of MMC in sacral and lumbosacral regions were missed on USG.

Table 1: Cross tabulation comparing type of the myelomeningocele to the antenatal sono graphic detection

		Type		Total
		Open	Close	
Antenatal USG	Not detected	13	8	21
	Detected	10	7	17
Total	Count	23	15	38

Z- test comparing the two group (open vs close) show p value <0.001 for cases missed on antenatal USG

Table 2: Cross tabulation comparing presence of hydrocephalus on antenatal sonography to the antenatal sonographic detection of myelomeningoceles

		Hydrocephalus on USG		Total
		Present	Not present	
Antenatal USG	Not detected	4	17	21
	Detected	11	6	17
Total	Count	15	23	38

Z –test for detection of MMCs on antenatal USG associated with hydrocephalus show p value <0.001

Table 3: Location of the meningomyeloceles in the cases with and without antenatal USG detection

Site	Detected on antenatal USG	Not detected on USG
Occipital	4	0
Cervical	0	1
Thoracic and Thoracolumbar	2	6
Lumbar	8	7
Lumbosacral and Sacral	3	7
Total	17	21

Discussion

Neural tube defects (NTD) are one of the most frequently encountered congenital anomalies affecting 0.5- 1 in every 1000 pregnancies [6]. Neural tube defects (NTD) are devastating for the child as well as for parents due to medical, socio -cultural and economical burdens. Though diagnosed antenataly by simple and effective tool of ultra

sonography yet a significant number are missed specially in unskilled hands.

The present study analysed the cases of myelomeningoceles and cephaloceles which are a type of spina bifida aperta in which the protruded cystic mass consists of thin arachnoid membrane with cerebrospinal fluid (CSF) and neural elements with or without skin covering.

Looking in to maternal factor mean age at conception was 25 years, similar to Hall *et al* but different from Al Ani *et al* where two third of cases belonged to 25-34 years [7, 8]. 57% mothers received folic acid antenatally with varying time and duration and none of them received it periconceptionaly similar to other study from developing world [8].

In a systemic review Atta C *et al* found highest prevalence of NTDs in Asia that too more in low and middle income group likewise most of our parents belonged to low to middle income group [9]. Low socioeconomic status and literacy may have impact on the health of mother during pregnancy particularly lack of folic acid supplementation may lead to increased cases of NTDs. Most of our parents studied till middle class almost similar observation made by Al Ani *et al* whose mothers cohort belonged to lower education class to illiteracy predominantly [8].

Significant female dominance have been observed in our study with a ratio of 2 similar to Al ani of 2 and Houcher B *et al* 1.4 [8, 10] however few have reported a male predominance with ratio of 93 [11, 12]. The most common associated anomaly of lower limb involvement seen in 52% neonates out of which the most common club foot have been seen in 21 % of cases; in contrast others found a higher prevalence of lower limb involvement in 82% and clubfoot in 46.6%[13] to 66.6% [8].

Ultrasound is an excellent screening modality for detection of neural tube defects and has been shown to be superior to MS-AFP by Norem *et al*. [14]. In India, at least three scans are recommended for a pregnant woman. The first trimester scan is usually done to detect, confirm, number and date the gestation, however those done at later part of first trimester can detect defects such as anencephaly and cephalocele. The objective of the third scan is usually to identify intrauterine growth retardation, assess biophysical profile. It is the second trimester scan that is ideally suited to detect fetal anomalies including the neural tube defects. Multiple numbers of scans, which implied more number of second trimester routine scans, are more likely to detect NTDs. This fact is fairly evident in our study by the fact that average number of sonographic exams was significantly higher (p value- 0.003) in those in which NTDs were detected antenatally (mean- 3.17), compared to those where the lesions were missed (mean 1.18). Average gestational age for antenatal detection was 30 weeks.

Various neural tube anomalies can be recognised by their distinctive appearance on Sonography. Anencephaly can be diagnosed as early as 10.5 week by absence of cranial structures with amorphous mass of tissue above orbits, with a 'Mickey Mouse ear' appearance [15]. Myelomeningoceles and encephaloceles manifests as cystic mass at the posterior aspect of the spine and skull respectively, with variable sized neural elements. In the absence of myelomeningoceles or meningoceles, Spina bifida are most difficult to detect by ultrasound with posterior transaxial plane showing merely splaying of the posterior elements [16,17]. The detection rate of NTDs approaches upto 98% (marrow) in targeted USG in which anomaly scan is requested because of high MS-AFP (maternal serum alfa feto protein) [18]. However, in cases of routine screening USG even at the gestational age of 18 to 22 weeks is less than 80% [19]. Since our study included only the cases with cephaloceles and myelomeningoceles with advance gestational age of 30 weeks at antenatal detection, we expected a higher detection rate by USG. Surprisingly routine screening USG could detect only 44.7% (17/38) cases similar to Lu *et al* in 43.4% [20], highlighting the fact that despite being quoted as a sensitive modality to depict NTDs, in less experienced hands USG can produce high false negative rates. A study by Goswami *et al*. in rural population of Sind, Pakistan, highlighted the poor performance of USG in detection of various NTDs [21]. Importance of well maintained, up to date equipment as well as experience in the field by expert sonologist has been documented in studies from different regions [20, 22]. Having obtained similar figures, we intended to evaluate various factors leading to non detection of NTDs on antenatal USG.

The mean size (longest diameter) of the lesions measured after birth was marginally higher (52.5 mm) in cases which were detected by antenatal USG compared to that in cases with non detection (47.5 cm), the difference was not statistically significant (p-value 0.33). A small value of 0.636 of area under receiver operated characteristic curve (AUROC) also emphasized the fact that size of the lesions did not influence their chance of getting detected on antenatal routine sonography. Comparing type of NTDs (open or closed) by Z- test show open defects are more likely detected sonographically in the present study (p value<0.001) similar to Chan *et al* with prenatal detection of 75% for open lesion while comparing with closed one [23].

There are various cranial abnormalities that raise suspicion of NTD such as ventriculomegaly, reduced biparietal diameter (BPD), unperceivable cistern magna (indicating chiari II malformation), banana sign (deformed cerebellar shape), lemon sign (concave frontal bones) [24, 25]. Spina bifida is the single most common cause of ventriculomegaly, seen in 44-86 % foetuses with spina bifida [26, 27] similar to 65% of our cases. Approximately one third to half of foetuses with enlarged ventricles have neural tube defects [18, 28] In our study, we found that there was a statistically significant impact of antenatally detected ventriculomegaly on detection of NTDs (p value< 0.001) which implies that dilated lateral ventricles prompted the sonologists towards presence of NTDs. This message needs to be reemphasized among sonologists esp the newcomer since prenatal ultrasound detection may help in validation of confirming the defect and allows the parents to choose for either in-utero surgery or termination.

On charting the finding with respect of different sites of the lesions, we found that USG had 100 % (4/4) sensitivity in detecting occipital encephalocele whereas 70% (3 /10) of the cases involving the distal spine (sacral and lumbosacral MMCs) were missed on USG (Table 3). Cases with thoracic, thoracolumbar and lumbar lesions were distributed almost equally in both groups. One case of cervical MMC was included in this study which was missed on sonography. We could not find any other study in the literature correlating the sonographic detection and anatomical site of the lesion.

We admit that this study was not without limitations. Firstly, this was a retrospective study with its inherent patient selection biases. The poor sensitivity of USG in detecting the lesions might be an overestimation, because many of the

women with early detected NTDs opt for termination of pregnancy and thus influencing the structure of the analysed cohort. Moreover, the cases in our study were retrospectively selected from those diagnosed after birth or posted for early surgery after birth, leading to inclusion of only myelomeningoceles and encephaloceles and non-inclusion of other conditions such as anencephaly, and other occult spina bifida. Secondly, we did not compare the performance of targeted imaging for fetal anomaly with the routine screening ultrasound done in second trimester, which would more accurately validate the need for the former. Moreover, the number of patient in our study was relatively small and a large multicentric study is further needed to obtain a more statistically significant result.

To conclude, this study revealed poor performance of routine USG in detection of NTDs in rural areas of India. We further showed that higher number of scans, open type of NTDs, presence of ventriculomegaly on USG and occipital location facilitates detection of NTDs while lesions in sacral location are difficult to be detected and that the detection of the lesions was independent of the size measured at birth. This study emphasises the essential check and training private USG centres especially run by unskilled persons as well as mandatory requirement of a targeted second trimester scan for fetal anomalies or level II scan in all the pregnancies.

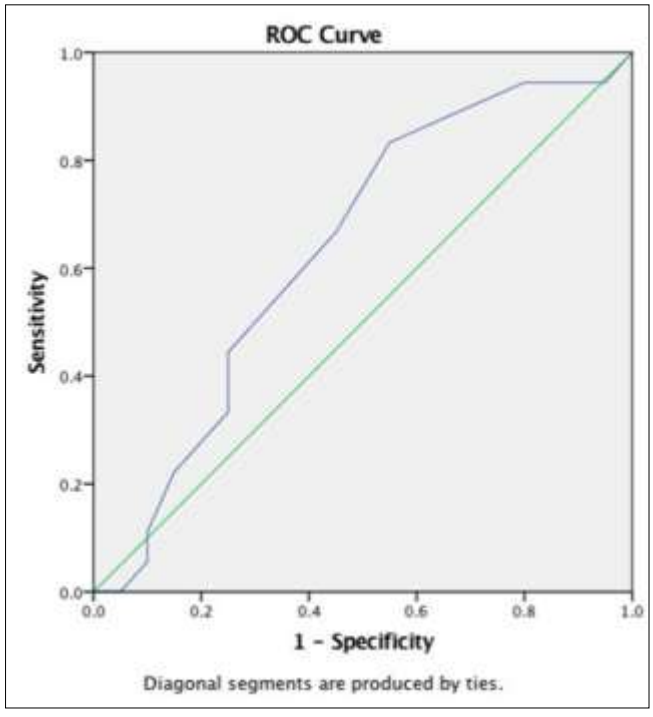

Fig 1: ROC (receiver operated characteristic) curve drawn for size of the lesions to predict sonographic detection

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References

1. Kinsman SL, Johnston MV. Neural tube defects. In Kleigman RM, Stanton BF, St Geme JW. Schor NF eds :Nelson textbook of paediatrics 20 th edn, New Delhi: Elseveir, 2015, 2802-2806.
2. Boyd PA, Wellesley DG, De Walle HEK, Tenconi R, Garcia-Minaur S, Zandwijken GRJ, *et al*. Evaluation of the prenatal diagnosis of neural tube defects by fetal ultrasonographic examination in different centres across Europe. J Med Screen. 2000; 7:169–174.
3. Hunt GM, Poulton A. Open spina bifida. A complete cohort reviewed 25 years after closure. Dev Med Child Neurol. 1995: 37:19-29.
4. Douglas Wilson R, Calgary AB. Prenatal Screening, Diagnosis, and Pregnancy Management of Fetal Neural Tube Defects. J Obstet Gynecol Can. 2014; 36(10):927-39.
5. Adzick NS, Thom EA, Spong CY, Brock JW, Burrows PK, Johnson MP, *et al*. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med. 2011; 364:993–1004.
6. Shaer CM, Chescheir N, Schulkin J. Myelomeningocele: a review of the epidemiology, genetics, risk factors for conception, prenatal diagnosis, and prognosis for affected individuals. Obstet Gynecol Surv. 2007; 62:471-479.
7. Hall JG, Friedman JM, Kena BA, Jawanda JPM, Arnoldt W. Clinical, genetic and epidemiologic factors in neural tube defects. Am J Hum Genet. 1988; 43(6):827-37.
8. Al-Ani ZR, Al-Hiali SJ, Al-Mehindi SM. Neural tube defect among neonates delivered in Al-Ramadi maternity and children's hospital, westeran Iraq. Saudi Med J. 2010; 31(2):163-169.
9. NA Atta, *et al*. Global birth prevalence of spina bifida by folic acid fortification status: A systemic review and metaanalysis. AJPH. 2016; 106(1):24-34.
10. Houcher B, Bourouba R, Djabi F, Houcher Z. The prevalence of neural tube defects in Setif university maternity hospital, Algeria-3 yrears review (2004-2006) pteridines. 2008; 19:12-18.
11. Wasant P, Sathienkijkanchai A. Neural tube defects at Siriraj hospital Bangkok Thailand- 10 years review (1990-1999). J Med Assoc Thai. 2005; 88:S92-S99.
12. Safadar OY, Al Dabbagah AA, Abuelieneen WA, Kari JA. Decline in the incidence of neural tube defects after the national fortification of flour (1997-2005). Saudi Med J. 2007; 28(8):1227-9.
13. Asindi A, Al-Shehri A. Neural tube defects in ASIR region of Saudi Arabia Ann Saudi Med. 2001; 21:26-29.
14. Norem CT, Schoen EJ, Walton DL. *et al*. Routine Ultrasonography Compared With Maternal Serum Alpha-fetoprotein for Neural Tube Defect Screening. Obstet Gynecol. 2005; 106:747-52.
15. Toi A, Levine D. The Fetal Brain. In Rumack CM, Wilson SR, Charboneau JW, Levine D, eds: Diagnostic ultrasound, 4th ed, Philadelphia: Mosby, 2011, 1197-1244.
16. Filly RA, Golbus MS. Utrasonography of the normal pathologic fetalskeleton. Radiol CLin North Am. 1982; 20:311-323.
17. Fiske CE, Filly RA. Ultrasound evaluation of the normal and abnormal f et al neural axis. Radiol Clin North Am. 1982; 20:285-296.
18. Sauerbrei EE. The F et al Spine. In Rumack CM, Wilson SR, Charboneau JW, Levine D, eds: Diagnostic ultrasound, 4th ed, Philadelphia: Mosby, 2011, 1245-1272.
19. Thiagarajah S, Henke J, Hogge WA, *et al*. Early diagnosis of spina bifida: The value of cranial ultrasound markers. Obstet Gynecol. 1990; 76:54-57.

20. Lu QB, Wang ZP, Gong R, *et al*. investigation of ultrasound screening efficiency for neural tube defects during pregnancy in rural areas of china. Public health. 2011; 125(9):639-44.
21. Goswami P, Memon S, Khimani V. Failure of Ultrasound in Prenatal Diagnosis of Neural Tube Defects in Rural Sindh, Pakistan. Int J Med Res Prof. 2016; 2(3):42-45.
22. Roberts N, Bhide A. Ultrasound prenatal diagnosis of structural abnormalities Obstet Gynaecol Reprod Med. 2007; 17:1-8.
23. Chan A, Robertson EA, Han EA, Ranjeri E, Keane RJ. The sensitivity of ultrasound and seum alpha fetoprotein in population based antenatal screening for neural tube defects, South Australia 1986-91.Br J Obest Gynaecol. 1995; 102(5):370-6.
24. Roberts AB, Campbell H, Boreham J, *et al*. Fetal head measurements in spina bifida. Br J Obstet Gynaecol. 1980; 87:927-928.
25. Wald N, Cuckle H, Boreham J, Stirrat G. Small biparietal diameter of fetuses with spina bifida: implications for antenatal screening. Br J Obstet Gynaecol. 1980; 87:219-221.
26. Nyberg DA, Mack LA, Hirsch J, *et al*. Fetal hydrocephalus: sonographic detection and clinical significance of associated anomalies. Radiology. 1987; 163:187-191.
27. Nicolaides KH, Campbell S, Gabbe SG, Guidetti R. Ultrasound screening for spina bifida: cranial and cerebellar signs. Lancet. 1986; 2:72-74.
28. Madazli R, Şal V, Erenel H, Gezer A, Ocak VJ. Characteristics and outcome of 102 fetuses withfetal cerebral ventriculomegaly: Experience of auniversity hospital in Turkey Obstet Gynaecol. 2011; 31(2):142-145.