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ORIGINAL ARTICLE

Diagnostic Accuracy of Ultrasound in Detection of Spina Bifida in the First and Second Trimester Using Post-Natal MRI as Gold Standard

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ABSTRACT

Introduction: Antenatal ultrasound has been reported to be an effective tool for detecting neural tube defects including spina bifida. Moreover, major structural abnormalities can be detected by ultrasound examination, depending on the time of ultrasound scan.

Objectives: To determine the diagnostic accuracy of ultrasound in detection of spina bifida in the first and second trimester using post-natal MRI as gold standard.

Study Design: Descriptive, Cross-sectional study

Study duration: 11th February 2019 to 10th August 2019

Settings: Department of Radiology, Jinnah Hospital, Lahore.

Materials & Methods: A total of 125 pregnant patients/Gravida presenting in first trimester (11 to 13 weeks) & second trimester (14 to 22 weeks) assessed on dating scan, at risk for spina bifida were included. Women with pre-eclempsia and eclempsia determined on systolic BP > 140 and protein urea and history of congenital heart defects were excluded. A standard ultrasound scan was performed by the same Radiologist on the same ultrasound machine and any findings associated with the spina bifida would be noted & recorded on a predesigned Performa (Attached). Patients were followed till delivery and post-natal MRI was done to evaluate spina bifida. Presence of absence of spina bifida on USG & MRI was noted.

Results: All the patients were subjected to first ultrasonography and then MRI. USG supported the diagnosis of spina bifida in 62 patients. MRI confirmed spina bifida in 63 cases. In USG positive cases, 58 were true positive and 04 were false positive. While in USG negative patients, 58 were true negative and 05 were false negative. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasound in detection of spina bifida in the first and second trimester using post-natal MRI as gold standard is 92.06%, 93.55%, 93.55%, 92.06% and 92.80% respectively.

Conclusion: This study concludes that ultrasonography is a highly sensitive and accurate modality for diagnosing spina bifida, and has not only dramatically improved our ability of diagnosing spina bifida but also be a simple, economical and readily available alternative to MRI.

Keywords: Spina Bifida, Ultrasonography, Sensitivity

INTRODUCTION

Genetic predispositions, environmental variables, and the teratogenic effects of medicines all have a role in the development of neural tube defects, the most frequent of which are anencephaly and spina bifida, both of which have a prevalence of 1-5%. Preventative measures include preconception genetic counselling and daily folic acid intake [1-2]. Spina bifida can be either (SB) occulta, in which the neural tissue is shielded from amniotic fluid, or (SB) aperta, in which the neural tissue is exposed to the amniotic environment.

Sonographic diagnosis of open spina bifida (OSB) used to rely on a thorough examination of the foetal vertebrae for anomalies, however this method often failed to detect flaws. However, after the middle of the 1980s, when the intracranial abnormalities in the second trimester were described (the "lemon sign" and the "banana sign"), prenatal diagnosis of spina bifida was improved [3]. Spina bifida and other neural tube anomalies may be spotted during an antenatal ultrasound. In addition, ultrasound examination, depending on the time of ultrasound scan, can detect serious structural abnormalities [4].

The majority (136/140, or 97.1%) of patients in an Iranian study had a prenatal ultrasound, and of them, 58 sonographic examinations were conclusive for hydrocephalus and/or meningomyelocele (MMC). Meningomyelocele was detected by prenatal ultrasonography in 16 (11.8%) cases, hydrocephalus in 25 (18.4%) cases, and in 17 (12.5%) cases MMC and hydrocephalus were detected together. Although some studies have reported varying meningomyelocele (MMC) detection rates, the general consensus is that 3.4% of MMCs are detected in the first trimester, 31% in the second, and 65.5% in the third [8]. Results from a large-scale European survey showed a range of 33% to 100% among nations, with a mean of 68% [9]. According to Lennon & Gray, ultrasound can detect open neural tube abnormalities with a sensitivity of 97% and a specificity of 100%. 10 Ultrasonographic markers for Spina bifida were analysed in a case study conducted between 11 and 14 weeks of gestation. These markers included brain stem diameter (BS), fourth ventricle/intracranial translucency (IT), cisterna magna (CM), brain stem/occipital bone distance (BSOB), and the ratio between BS and BSOB (BSOB). However, few studies evaluate all of these factors simultaneously [6], with some focusing just on intracranial translucency (IT) efficacy.

Romero et colleagues found that sonography had a sensitivity of 94.7 percent and a specificity of 97.3 percent for detecting neural tube abnormalities. A foetus with venticulomegaly, omphalocele, severe kyphosis, and scoliosis was incorrectly diagnosed with spina bifida [11]. Goswami et al. conducted another investigation in rural Sindh, Pakistan, and found Due to the lack of ulrasonography, only 9 out of 45 cases of NTDs (20%) were detected prenatally, while the remaining 38 cases (80%) were diagnosed postnatally [12].

Sayed Ali alamdara et al. demonstrated that magnetic resonance imaging (MRI) is currently the gold standard for evaluating and diagnosing spinal cord disorders; however, MRI is an expensive imaging modality and is not available at all healthcare facilities [13].

Since no comparable data exists on a national scale, yet NTDs account for the majority of all infant deaths and birth malformations worldwide, we felt it was important to conduct this study. While fetoprotein screening and amniocentesis can help find certain cases of spina bifida, there are others where the condition may go unnoticed. When performed by trained professionals, antenatal ultrasonography provides high-quality images without causing any harm to the mother or foetus. Since high-resolution ultrasound facilities are now available in secondary and tertiary-care hospitals with experienced sonographers, it is expected that the results of our study will provide a positive evaluation of this

modality, which could help reduce the number of disabled children and the mortality rate associated with NTDs. The purpose of this research is to determine the efficacy of an inexpensive and non-invasive method for detecting neural tube abnormalities (NTDs) in pregnant women, as well as to provide instructions for radiologist and gynaecologists in the process of early diagnosis of NTDs.

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Radiology, Jinnah Hospital Lahore, during from 11th February 2019 to 10th August 2019. Total 125 pregnant patients/Gravida presenting in first trimester (11 to 13 weeks) & second trimester (14 to 22 weeks) assessed on dating scan were included. Pregnant women with pre-eclampsia and eclampsia determined on systolic BP > 140 and protein urea, and pregnant women with history of congenital heart defects determined on echocardiography.

After taking written consent standard ultrasound scan was performed by the same Radiologist on the same ultrasound machine and any findings associated with the spina bifida would be noted & recorded on a predesigned Performa (Attached). Patients were followed till delivery and post-natal MRI was done to evaluate spina bifida. Presence of absence of spina bifida on USG & MRI was noted as per-operational definition.

All the data was entered in SPSS version 20 and data was analyzed and presented in the form of frequency and percentages. Qualitative variables i.e. gender and spina bifida was presented as percentages and frequencies. Whereas quantitative data i.e. age, etc was presented as mean and standard deviation. 2x2 contingency table was used to calculate sensitivity, specificity, positive predictive value and negative predictive value. Chi-square test was used to assess statistical significance with P-value <0.05 was taken as significant.

RESULTS

Age range in this study was from 16-45 years with mean age of 30.19 ± 6.53 years. Majority of the patients 63 (50.40%) were between 16 to 30 years of age as shown in Table I. Distribution of patients according to trimester is shown in Figure I. Mean BMI is 29.45 ± 3.39 kg/m2 (Table II).

All the patients were subjected to first ultrasonography and then MRI. USG supported the diagnosis of spina bifida in 62 patients. MRI confirmed spina bifida in 63 cases. In USG positive cases, 58 were true positive and 04 were false positive. While in USG negative patients, 58 were true negative and 05 were false negative (Table III). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasound in detection of spina bifida in the first and second trimester using post-natal MRI as gold standard is 92.06%, 93.55%, 93.55%, 92.06% and 92.80% respectively.

Table-1: Distribution of patients according to Age (n=125).

Age (years)	No. of Patients	%age
16-30	63	50.40
31-45	62	49.60
Total	125	100.0

Mean ± SD = 30.19 ± 6.53 years

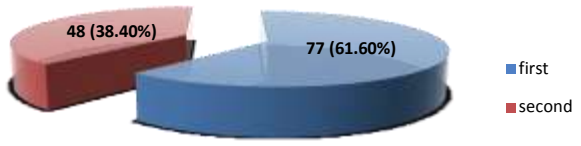

Figure-1: Distribution of patients according to trimester (n=125).

Table-2: Distribution of patients according to BMI (n=125).

BMI (kg/m2)	No. of Patients	%age
≤30	57	45.60
>30	68	54.40

Mean ± SD = 29.45 ± 3.39 kg/m2

Table-3: Diagnostic accuracy of ultrasound in detection of spina bifida in the first and second trimester using post-natal MRI as gold standard.

	Positive result on MRI	Negative result on MRI	P-value
Positive on USG	58 (TP)	04 (FP)	0.0001
Negative USG	05 (FN)	58 (TN)	

TP=True positive FP=False positive FN=False negative TN=True negative

Sensitivity: 92.06%
Specificity: 93.55%
Positive Predictive Value (PPV): 93.55%
Negative Predictive Value (NPV): 92.06%
Diagnostic Accuracy: 92.80%

DISCUSSION

Spina bifida, also known as an open or closed spinal defect, is characterised by abnormal closure of the spine during development, and can manifest in both open and concealed forms, with or without neurological involvement. Myelomeningocele and meningocele, two open forms of spina bifida that can have serious neurological consequences, account about 0.5 to 0.8 per thousand live births [14]. Environmental and genetic factors can contribute to this disorder. Folate insufficiency, maternal diabetes, zinc deficiency, alcohol consumption in the first three months of pregnancy, and exposure to medicines like carbamazepine and valproic acid during pregnancy are all possible causes [15]. Folic acid supplementation in the periconceptional period, beginning 3 months before to conception and continuing until the third month of pregnancy, can prevent spina bifida [16-17].

This abnormality has a window of opportunity for treatment, both in utero and after birth [18–20]. Prenatal foetal surgery for myelomeningocele improved cognitive and motor development at 30 months of age, according to the MOMS study (Management of Myelomeningocele Study). Fetuses with open spina bifida between trimester 1 and trimester 2 were prioritised for inclusion in this study. As a result, it is crucial to make an accurate evaluation of the lesion level prior to determining whether or not to proceed with surgery [21-24]. Ultrasonography is the gold standard for diagnosing spina bifida in the womb, detecting between eighty percent and one hundred percent of cases [25].

Evaluation of intracranial translucency between the 11th and 14th weeks of pregnancy shows promise as a first-quarter screening tool. There is no fourth ventricle in a foetus with spina bifida because the hindbrain develops too far to the back of the skull [26, 27]. Second and third quarters are optimal for evaluating the spinal lesion directly with either two- or three-dimensional ultrasonography. Counseling of the pregnant lady, her family, and the specialists involved is required because the level of the lesion is regarded to be the defining factor of foetal prognosis and the prediction of possible secondary issues. Two-dimensional ultrasonography defines exactly the post-delivery levels of the vertebral lesion in only 38% of the cases; this setting increases to 96% within two levels and reaches 100% within three levels when performed in reference centres by trained professionals. However, Bruner et al [28] stated that the method presents some limitations as to the correct diagnosis of the lesion level. The fact that mistakes of up to three levels are possible casts doubt on its utility as a deciding factor in the treatment of this malformation, as they lead to widely varying injury prognoses in terms of ambulation, motor strength, especially in the lower limbs, and control of vesical and anal sphincters.

Although 3D ultrasonography has been hailed as an invaluable adjunctive tool for assessing a wide range of prenatal abnormalities, whether or not it is more accurate than 2D ultrasonography for determining the extent of harm in a foetus with

spina bifida remains debatable [29–33]. In this study, I used post-natal MRI as the gold standard to evaluate the diagnostic accuracy of ultrasound for detecting spina bifida in the first and second trimesters of pregnancy.

Each patient was scanned using an ultrasound machine and subsequently an MRI machine. In 62 of those patients, USG confirmed the diagnosis of spina bifida. Sixty-three of the instances of spina bifida were confirmed by magnetic resonance imaging. We found that 58% of USG-positive cases were accurate readings and 4% were false positives. Among USG-negative patients, 58 were genuine negatives, while 5 were misreads. When compared to postnatal MRI as the gold standard, ultrasound's overall sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy for detecting spina bifida in the first and second trimesters are 92.80%, 92.06%, 93.55%, and 92.80%. For the diagnosis of neural tube abnormalities, Romero et al. found that sonography had an overall sensitivity of 94.7% and a specificity of 98.3%. There was a misdiagnosis of spina bifida in a foetus with venticulomegaly, omphalocele, severe kyphosis, and scoliosis [11]. Goswami et al. found that, in interior Sindh Pakistan, only 09 of 45 instances of NTDs (20%) were discovered prenatally, while the remaining 80% were diagnosed postnatally due to a lack of ulrasonography [12].

The "banana sign" of the cerebellum and the "lemon sign" of the front of the skull are ultrasound detectable indicators of open SB [34-36]. Because closed SB does less damage to the skull, it cannot be detected by ultrasonography as easily as open SB [37]. The ultrasonography has been demonstrated to have a high sensitivity and specificity for open SB, with previous investigations showing values close to 100% [38]. We identified a sensitivity of 92.8% in the Danish study population; however, because our data includes contains certain closed SB types, the true sensitivity is likely to be less than 100%.

In Denmark, 88.5% of the overall population with SB was diagnosed before gestational week 22 and 93.9% at any gestational age. Prenatal detection rates are reported to be between 81% and 90% by the EUROCAT society and other studies [39,40]. Our overall prenatal detection rate was much higher than the proportion (89.3%) reported by the EUROCA, demonstrating that the Danish prenatal screening programme exceeds that of other European nations that pursue various methodologies for prenatal screening for anomalies. The success of the Danish programme is likely attributable to its widespread adoption and popularity. This is supported by data from the Netherlands [40], where 88% of SB diagnoses occur in the second trimester and where the same percentage of pregnant women accept a second-trimester scan.

There was a high rate of termination after ultrasound diagnosis (81.6% among all Danish SB cases): 90.3% among those detected before week 22 of pregnancy. Prenatal diagnostic ToP rates were greater than those reported by the EUROCAT (66%; [41]), but comparable to those in Alsace, France (97%; [34]) and the region of Emilia-Romagna, Italy (92%; [35]) (only open SB). Third-trimester diagnosis rates of 34% were reported in Atlanta, Georgia, USA [35] and of 78.6% were reported in northern regions of the Netherlands [36]. With the advent of prenatal ultrasound, parents expecting a child with a deformity like SB with no known hereditary route can now receive genetic counselling, a service that was previously only available for children with known hereditary disorders. One tenth of the isolated SB had a chromosomal aberration, which is consistent with previous reports [34]. It is recommended that all women experiencing a pregnancy complicated by SB be offered chromosomal tests and counselling from a multispecialist team [42], as this indicates a higher chance of chromosomal defects in these pregnancies compared with normal-appearing foetuses.

CONCLUSION

The results of this research show that ultrasonography is an effective and reliable alternative to MRI for the diagnosis of spina bifida, and that it has greatly increased our capacity to detect this condition. Therefore, we advocate for universal screening for spina bifida using ultrasonography to lessen the number of disabled infants and deaths caused by neural tube defects (NTDs).

REFERENCES

1. Becker R, Wegner RD, Detailed screening for fetal anomalies and cardiac defects at the 11–13-week scan, Ultrasound Obstet Gynecol, 2006; 27(6):613–618.
2. Ali S, Azeemi AA, Shoukat S. The prevalence of spina bifida occulta in Pakistani population: A study of dry human sacra. Anaesth, Pain & Intensive Care 2014; 18(2): 157-61.
3. Meller, C., Aiello, H. & Otaño, L. Sonographic detection of open spina bifida in the first trimester: review of the literature Childs Nerv Syst 2017; 33: 1101. https://doi.org/10.1007/s00381-017-3443-9.
4. Boyd PA, Wellesley DG, De Walle HEK, Tenconi R, Garcia-Minaur S, Zandwijken GR, Stoll C, Clementi M.Evaluation of the prenatal diagnosis of neural tube defects by fetal ultrasonographic examination in different centers across Europe. J of Medical Screening 2000; 7:169-74.
5. Aubry MC, Aubry JP, Dommergues M: Sonographic prenatal diagnosis of central nervous system abnormalities. Child Nerv Syst 2003; 19:391-402.
6. Orlandi E, Rossi C, Perino A, Cucinella G& Orlandi F. Prospective sonographic detection of spina bifida at 11–14 weeks and systematic literature review. The Journal of Maternal-Fetal & Neonatal Medicine 2016; 29(14): 2363-67.
7. Beverly G. Coleman Jill E. Langer Steven C. Horii. Diagnostic Features of Spina Bifida: Role of Ultrasound. Fetal Diagn Ther 2015; 37:179–196. DOI: 10.1159/000364806
8. Kazmi SS, Nejat F, Tajik P, Roozbeh H. The prenatal ultrasonographic detection of myelomeningocele in patients referred to Children's Hospital Medical Center: a cross sectional study. Reproductive Health 2006; 3:6
9. Boyd PA, Wellesley DG, De Walle HEK, Tenconi R, Garcia-Minaur S, Zandwijken GR, Stoll C, Clementi M: Evaluation of the prenatal diagnosis of neural tube defects by fetal ultrasonographic examination in different centers across Europe. J of Medical Screening 2000; 7:169-74.
10. Chen CP. Prenatal diagnosis, fetal surgery, recurrence risk & differential diagnosis of neural tube defects. Taiwan J Obstet Gynecol 2008; 47:03, 283-89.
11. Romer R, Mathisen JM, Ghidni A, Sirtori M, Hobbins JC. Accuracy of Ultrasound in the prenatal diagnosis of spinal anomalies. Am J Perinatol. 1989;6 (3):320-23.
12. 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.
13. Alamdaran SA, Mohammadpanah N, Zabihian S, Esmaeel M, Ghane F. Diagnostic value of ultrasonography in spinal abnormalities among childrenwith neurogenic bladder. Ellectronic Physian 2017; 9(6): 4571-76.
14. American College of Obstetricians and Gynecologists. ACOG technical bulletin no. 99: prenatal detection of neural tube defects. Washington (DC): ACOG; 1986.
15. Wegner C, Nau H. Alteration of embryonic folate metabolism by valproic acid during organogenesis: implications for mechanism of teratogenesis. Neurology 1992;42(4, Suppl 5): 17-24.
16. McDonnell R, Johnson Z, Doyle A, Sayers G. Determinants of folic acid knowledge and use among antenatal women. J Public Health Med 1999;21(2):145-149.
17. Wald NJ, Law MR, Morris JK, Wald DS. Quantifying the effect of folic acid. Lancet 2001;358(9298):2069-2073.
18. Bruner JP, Tulipan N, Paschall RL, et al. Fetal surgery for myelomeningocele and the incidence of shunt-dependent hydrocephalus. JAMA 1999;282(19):1819-1825.
19. Hirose S, Farmer DL, Albanese CT. Fetal surgery for myelomeningocele. Curr Opin Obstet Gynecol 2001;13(2):215-222.
20. Bruner JP, Tulipan NE, Richards WO. Endoscopic coverage of fetal open myelomeningocele in utero. Am J Obstet Gynecol 1997;176 (1 Pt 1):256-257.
21. Adzick NS, Thom EA, Spong CY, et al; MOMS Investigators. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med 2011;364(11):993-1004.
22. Meuli M, Moehrlen U. Fetal surgery for myelomeningocele is effective: a critical look at the whys. Pediatr Surg Int 2014; 30(7):689-697.

23. Flake A. Percutaneous minimal-access fetoscopic surgery for myelomeningocele - not so minimal!. Ultrasound Obstet Gynecol 2014;44(5):499-500.
24. Adzick NS. Fetal surgery for spina bifida: past, present, future. Semin Pediatr Surg 2013;22(1):10-17.
25. Okumura M, Zugaib M. Ultra-Sonografia emobstetrícia. São Paulo: Sarvier; 2002.
26. Orlandi E, Rossi C, Perino A, Cucinella G, Orlandi F. Prospective sonographic detection of spina bifida at 11-14 weeks and systematic literature review. J Matern Fetal Neonatal Med 2015:1-5.
27. Chaoui R, Benoit B, Mitkowska-Wozniak H, Heling KS, Nicolaides KH. Assessment of intracranial translucency (IT) in the detection of spina bifida at the 11-13-week scan. Ultrasound ObstetGynecol 2009;34(3):249-252.
28. Bruner JP, Tulipan N, Dabrowiak ME, et al. Upper level of the spina bifida defect: howgood arewe? Ultrasound Obstet Gynecol 2004; 24(6):612-617.
29. Buyukkurt S, Binokay F, Seydaoglu G, et al. Prenatal determination of the upper lesion level of spina bifida with three-dimensional ultrasound. Fetal Diagn Ther 2013;33(1):36-40.
30. Cameron M, Moran P. Prenatal screening and diagnosis of neural tube defects. Prenat Diagn 2009;29(4):402-411.
31. Lee W, Chaiworapongsa T, Romero R, et al. A diagnostic approach for the evaluation of spina bifida by three-dimensional ultrasonography. J Ultrasound Med 2002;21(6):619-626.
32. Carletti A, Ghi T, Ceccarini M, et al. OC160: three-dimensional ultrasonography is of limited value in diagnosing fetal spina bifida. Ultrasound Obstet Gynecol 2007;30(4):416.
33. Wei Q, Cai A, Wang X, Xie L, Wang B, Wang X. Value of 3-dimensional sonography for prenatal diagnosis of vertebral formation failure. J Ultrasound Med 2013;32(4):595-607.
34. Nicolaides KH. Ultrasound screening for spina bifida: cranial and cerebellar signs. The Lancet, 1986;328:2–74.
35. Timbolschi D, Schaefer E, Monga B. Neural tube defects: The experience of the registry of congenital malformations of Alsace, France, 1995-2009. Fetal Diagnosis and Therapy. 2015;37:6–17.
36. Besser LM, Williams LJ, Cragan JD. Interpreting changes in the epidemiology of anencephaly and spina bifida following folic acid fortification of the U.S. grain supply in the setting of long-term trends, Atlanta, Georgia, 1968-2003. Birth Defects Research Part A - Clin Molecular Teratol. 2007;79:730–736.
37. Ghi T, Pilu G, Falco P. Prenatal diagnosis of open and closed spina bifida," Ultrasound Obstet Gynecol. 2006;28:899–903.
38. Lennon CA, Gray DL. Sensitivity and specificity of ultrasound for the detection of neural tube and ventral wall defects in a high-risk population. Obstet Gynecol. 1999; 94: 562–66.
39. Fleurke-Rozema JH, Vogel TA, Voskamp BJ. Impact of introduction of mid-trimester scan on pregnancy outcome of open spina bifida in the Netherlands. Ultrasound Obstet Gynecol. 2014; 43:553–556.
40. EUROCAT. Prenatal Detection Rates 2017 [cited 2019 2 December], http://www.eurocat-network.eu/prenatalscreeninganddiagnosis/prenataldetection(pd)rates.
41. EUROCAT. Prevalence Tables 2015 [cited 2019 2 December], http://www.eurocat-network.eu/accessprevalencedata/prevalencetables.
42. Ferreira JCP, Grati FR, Bajaj K. Frequency of fetal karyotype abnormalities in women undergoing invasive testing in the absence of ultrasound and other high-risk indications. Prenatal Diagnosis. 2016;36:1146–1155.