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Intracranial translucency as a sonographic marker for detecting open spina bifida in the first trimester

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Abstract

Background and objective: Neural tube defect is a serious congenital anomaly associated with lifelong disability, mortality and morbidity; it consists of heterogeneous group of disorders affecting brain and spinal cord. This study aimed to test the efficacy and accuracy of the intracranial translucency (fourth ventricle) in diagnosing open spina bifida.

Methods: A diagnostic prospective convenient study of intracranial translucency and open spina bifida was conducted in the Maternity Teaching Hospital / Erbil city, Kurdistan region /Iraq from the Feb 2021 till June 2022. The study included 200 pregnant women attended maternity teaching hospital for routine first trimester scan (11 wk -13 wk+6d) using a convenience method. Ultrasound examinations were performed using general electric (GE) ultrasound machine. The fetuses were classified into two groups; those fetuses which have clear visible intracranial translucency on ultrasound examination by the radiologist, and in the other group, the intracranial translucency was not clearly seen.

Results: The two studied groups were comparable in crown-rump length, number of pregnancies, number of children, maternal age, and maternal weight. Intracranial translucency was seen in 196 out of 200 (98%) and was not visible in 4 cases out of 200 (2%).

Conclusion: The intracranial translucency was considered a good sonographic marker with high accuracy and sensitivity in diagnosing cases of OSB among 11-13^{+6} weeks pregnant women.

Keywords: Intracranial translucency (IT); Open spina bifida (OSB); Neural tube defect (NTD).

Introduction

Spina bifida (SB) is a neural tube defect affecting the nervous system; it affects 3% of births in the worldwide. The prevalence of spina bifida is 33.86 per 100 000 live births[1] and constitutes 90% of birth defects. Spina bifida is one of the neural tube defects, and it consists of a group of malformation resulting from failure of neural tube closure between third and fourth week of embryonic development and failure of the closure of its caudal end lead to spina bifida [2]; meningocele, meningomyelocele, and myelocele all together could be diagnosed as spina bifida. In spina bifida, part of neural tube does not develop leading to defect in the spinal cord and bones of the spine leading to herniation of the cord and meninges.[3] Antenatal diagnosis of spina bifida is very important and ability to diagnose it in the early gestation since some cases of open spina bifida may benefit from fetal surgery in developed countries , though counseling of pregnant ladies with open spina bifida in an going pregnancy is crucial , in determining the cause, recurrence risk in future pregnancies, and preparation of the parent for either loss of their child after delivery or survive child with major disability which

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depends on the location and extended of the lesion and associated anomalies and since there is interruption in the neural function leads to major morbidities which include neurodevelopmental delay, ambulation and maintain continence. The routine sonographic screening done during the first trimester enhanced the diagnosis of open spina bifida. The risk of SB is determined by multiple factors; social, environmental, cultural, and genetic factors. Maternal folic acid deficiency is considered one of the nutritional factors predisposing to SB affected pregnancies.[4,5,6] Studies revealed other risk factors for SB which includes; diabetes before pregnancy,[7] smoking,[8] taking medication (antiepileptic),[9] and exposure to viral infections in early pregnancy.[10] The birth defects increased in Iraq during the post-war conflict due to environmental pollution as studies revealed.[11]

The incidence of neural tube defects reported in Ramadi Maternity and Children's Hospital, western Iraq was 3.3/1000 live births.[12,13] The OSB was diagnosed previously antenatally during the second trimester by maternal serum alpha-fetoprotein (AFP), amniocentesis was performed and ultrasound (US) which considered the best approach for evaluating women with high serum AFP. The ultrasound examination revealed the U-shaped neural arch, myelocele, and meningomyelocele with a sensitivity ranging from 88% to 96%.[14,15]

There are direct signs in scanning the spine that can help in the diagnosis of OSB and indirect signs in the cranium were lemon sign (deformed frontal bones) and banana sign (changed cerebellar shape) both signs occur due to caudal regression of the cerebellum with obliteration of cisterna magna.[16]

In 2009, Chaoul et al. concluded that during routine first trimester screening for chromosomal defects between 11 and 13.6 weeks in the same mid sagittal view of fetal face may be also used for early detection of open spina bifida through identification of intracranial translucency which is recognized by ultrasound and referred to forth ventricle and in the absence of this intracranial translucency the possibility of OSB raise.[17,18]

This study aimed to look for the efficacy and accuracy of the IT in the diagnosis of open spina bifida. The rationale for conducting this study was that early diagnosis before twenty weeks of gestation will improve the clinical outcome. Fetal surgery for spina bifida is not a cure, but studies show that prenatal repair can offer significantly better results than traditional postnatal repair. Fetal surgery for spina bifida greatly reduces the need to divert fluid from the brain, improves mobility and improves the chances that a child will be able to walk independently.

The objectives were; to evaluate the diagnostic performance of IT for detecting of OSB cases during 11-13^{+6} weeks gestation; to measure the sensitivity and specificity of IT.

Methods

Study design and setting

This was a prospective diagnostic accuracy study done in the Maternity Teaching Hospital / Erbil city, Kurdistan region /Iraq from the Feb 2021 till June 2022. The study included 200 pregnant women attended maternity teaching hospital for first trimester scan using convenience method The questionnaire designed and it included; maternal age, maternal weight, number of abortions, number of caesarian sections, medical conditions (hypertension, diabetes), use of medications during pregnancy (anticonvulsants), folic acid supplementation, history of OSB in the family, exposure to radiation and high fever during pregnancy.

Inclusion and exclusion criteria

Inclusion criteria are pregnant women in their first trimester 11-13^{+6} week of gestation (45-84 mm CRL), and exclusion criteria are twin pregnancy, unwilling pregnant women.

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Ethical consideration

The study approved from ethical committee and verbal consent was obtained from each participant (verbal consent was adequate because it take place at a site with agreement of the study). The pregnant women were examined during the first trimester and then asked to return for the following ultrasound scan in the second trimester between 18-22 week. Ultrasound examinations were performed using general electric (GE), Voluson E6 with curvilinear probe 4C (2-5.5 MHz).

The transabdominal approach was used, and the fetus was scanned in the mid-sagittal section, the same plane used to measure the NT according to the Fetal Medicine Foundation guidelines. The CRL must be 45 to 84 mm and the image of the fetus should be magnified to occupy at least 75% of the entire image display, a mid sagittal view of the face obtain (presence of the echogenic tip of the nose and rectangular shape palate anteriorly, the translucent diencephalon in the center and the nuchal membrane posteriorly), the fetus examine in a neutral position, supine (although forth ventricle may be visible when the fetus is in the prone position, but there is no adequate examination of the fetal cerebellum because of shadowing from fetal occipital bone. IT (or the fourth ventricle) identifies in the mid-sagittal image of the face as a clear space bounded anteriorly by the posterior border of the brainstem and posteriorly by the choroid plexus of the fourth ventricle.

The ultrasound findings included gestational age in weeks, the crown-rump length (CRL), nuchal translucency (NT) and the intracranial translucency (IT), whether clear, obliterated, or not seen during the first trimesters. Abnormalities in the spine were evaluated (for large neural tube defects and large soft tissue masses). Then all pregnant women who participated in the study asked for reassessment in second trimester between 18-22 week for detail second trimester anomaly scan including direct examination of whole spine from cervical to sacral region in axial, sagittal and coronal planes

The patients were classified into two groups; those fetuses which has clear visible IT, and in the other group, the IT was not clearly seen .

Statistical analysis

The analysis was done by the statistical package of social science (SPSS program version 25). The mean, median, and standard deviation were calculated. The rate of patients with IT seen and not seen was found. The associations between the two groups with other maternal and fetal characteristics were determined by the Chi-square or Fisher's Exact tests for categorical variables and the t-test for numerical variables. A *P*-value ≤0.05 was considered significant. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated.

Results

Out of 200 pregnant women attended maternity teaching hospital for first trimester scan, IT was visible in 196 during the first and second trimesters. In 4 cases the IT was non-visible in the first trimester. In the second-trimester two out of the four cases were diagnosed as open spina bifida cases, and gave birth to abnormal fetuses. While the other two suspected cases gave birth to normal fetuses (Figure 1).

In Table 1, the two studied groups were comparable in crown-rump length, number of pregnancies, number of children, maternal age, and maternal weight. However, the mean gestational age among the cases was higher and statistically significant (13.5 ± 0.70, *P* ≤0.005).

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Table 1 Characteristics of pregnant women and cases of OSB in the studied samples

Variables	Normal (198)	Open spina bifida cases (2)	Statistical t-test	*P*-value
CRL mm mean Median (range)	61.1 ±12.7 59.0 (38-84)	73.5 ± 9.1 73.5 (67-80)	1.236	0.173
Mean maternal age (years) Median (range)	30.6 ± 6.1 31 (18-48)	32 ± 2.8 32 (30-34)	-0.312	0.756
Mean gestational age in weeks Median (range)	12 ± 0.9 12 (10-14)	13.5 ± 0.70 13.5 (13-14)	1.939	0.005*
Mean weight of pregnant women Median (range)	70.6 ± 7.2 71 (50-95)	73.5 ± 9.1 73 (67-80)	-0.554	0.580
Mean gravida	2.7 ± 1.9	2.0± 0.1	0.258	0.612
Mean para	1.1 ± 1.3	0.5 ± 0.7	0.404	0.526

*Significant *P*-value.

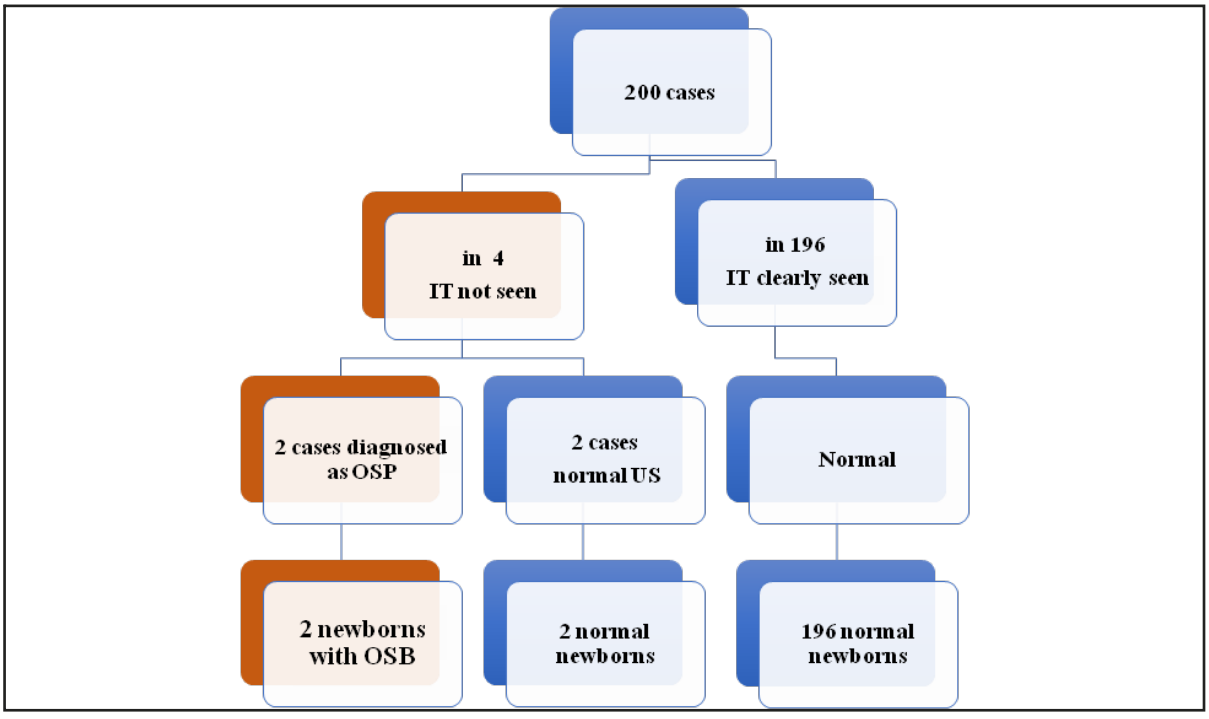

Figure 1 The distribution of the studied sample in the flowchart

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In (Table 2) IT was seen in 196 out of 200 (98%) and was not visible in 4 cases out of 200(2%). The two groups showed no statistically significant differences in comparing maternal age, maternal body mass index, and crown-rump length. The mean gestational age was different between the two groups (*P* = 0.005).

Table 2 Distribution of the studied sample by IT visibility with maternal and fetal characteristics

Variables	IT seen 196	IT not seen 4	Total 200	*P*-value
Crown-rump length mm				
< 53 mm	73 (37.24)	1 (25)	74 (37)	0.616*
≥ 53 mm	123 (62.75)	3 (75)	126 (63)	
Gestational age (weeks)				
Mean ± SD	12 ± 0.98	13 ± 1.41	12 ± 0.99	0.005†
Median	12 (10-14)	13 (11-14)	12 (10-14)	
Fetal position				
Supine	195 (99.5)	4 (100)	199 (99.5)	0.886*
Prone	1(0.51)	0	1 (0.5)	
Maternal BMI				
< 25 kg/m2	62 (31.63)	2 (50)	64 (32)	0.677*
25-29 kg/m2	120 (61.22)	2 (50)	122 (61)	
≥ 30 kg/m2	14 (7.14)	0	14 (7)	
Mean gravida	2.68 ± 1.92	4 ± 3.46	2.74 ± 2.14	0.249†
Mean para	1.1 ± 1.3	1.0 ± 1.0	1.02 ± 1.29	0.890†

*Fisher's exact test, † t-test.

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Table 3 shows the incidence of risk factors among the two groups. History of abortion was reported in 36% of the IT visible group. Folic acid supplementation was reported in 75% of the second group (*P* = 0.018).

The IT was visible in 196 out of 200 pregnant women, and 2 cases were diagnosed as OSP clinically and by ultrasound (Table 4). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of non-visualization the fourth ventricle (intracranial translucency) by ultrasound were 100%, 99%, 50%, 100% and 99%, respectively (Table 5).

Table 3 Distribution of the studied sample by risk factors for OSB

Variables	IT seen N= 196 (%)	IT not seen N= 4 (%)	Total N=200 (%)	*P* value†
History of abortion	72 (36.73)	0.0	72 (36.00)	0.130
History of medical conditions				
Diabetes	3 (1.53)	0.0	3 (1.5)	0.803
Hypertension	5 (2.55)	0.0	5 (2.5)	0.746
Folic acid supplementation	190 (96.93)	3 (75.0)	193 (96.5)	0.018*
Use of medicine (anticonvulsant)	2 (1.02)	0.0	2 (0.1)	0.839
History of anomalies	2 (1.02)	0.0	2 (0.1)	0.839
A high fever during pregnancy	2 (1.02)	0.0	2 (0.1)	0.839

**P* significant, †Fisher's Exact test.

Table 4 Distribution of the studied sample by frequency of positive and negative cases by ultrasound screening and clinical examination

Ultrasound	Open spina bifida		Total	*P*-value*
	Positive	Negative		
Positive	2	2	4	< 0.479
Negative	0	196	196	
Total	2	198	200	

*MacNemar test.

Table 5 Distribution of the studied sample by sensitivity, specificity, positive predictive value, negative predictive value, and accuracy

Ultrasound	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Total agreement
Intracranial translucency	100%	99%	50%	100%	99%

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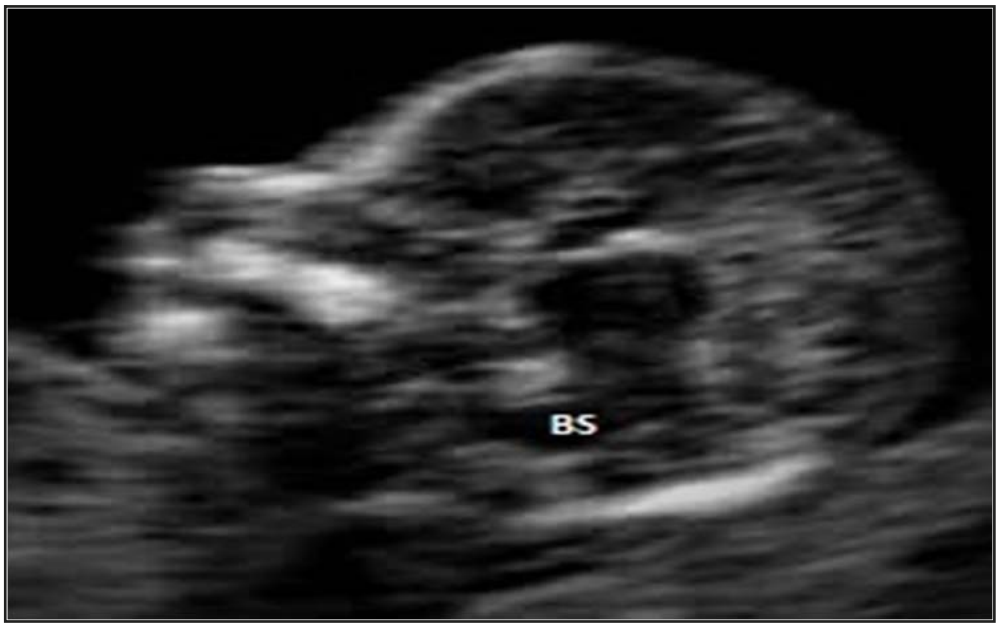

Figure 2 first trimester fetal posterior brain in case of spina bifida with absence of intracranial translucency and displacement of brain stem (BS)

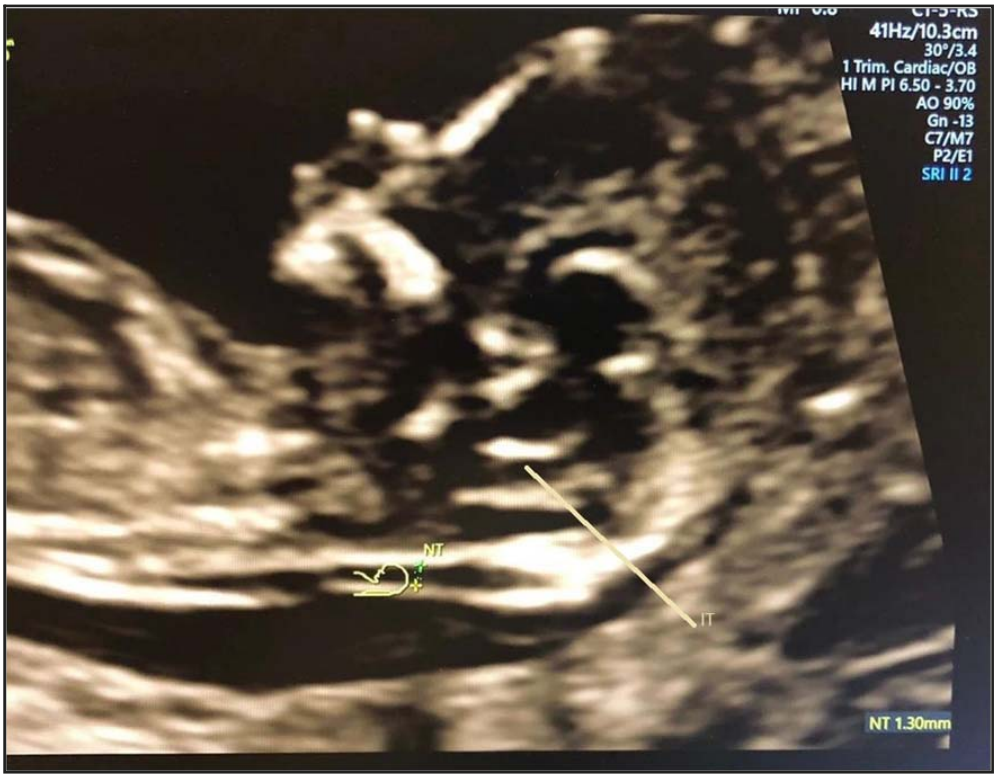

Figure 3 Ultrasound of a normal fetus in the mid-sagittal plane at 12 week gestation, normal nuchal translucency. the normal intracranial translucency of the fourth ventricle (IT) is present (red arrow)

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Discussion

In this prospective study, the ultrasound examinations were done for 200 referred pregnant women in the Maternity Teaching Hospital / Erbil city. All cases have been examined in both first trimester (11-13^{+6} week) and in second trimester. The prevalence rate for OSB in the current study was 1%. We cannot depend on the proportion of OSB found in this study to indicate the prevalence of the disease among the Kurdish population inside Erbil city. This study was hospital-based and conducted in one tertiary referral facility. The substantial majority of OSB needs a population-based study which has been lacking till now.

In the current study, IT was identifiable in 196 out of 200 (98%) first-trimester scans (Fiqure 1). The IT was not seen in 4 out of 200 (2%) scanned fetuses in the first trimester. Two cases out of 200 (1%) were diagnosed as OSB cases (Figure 2), and they gave birth to abnormal infants. At the same time, the two other cases showed no abnormalities during second-trimester scanning. The indirect signs that were detected in the second trimester among OSB cases were lemon-shaped head (100%), ventriculomegaly (50%), and myelomeningocele (100%). A study in Italy compared the indirect sonographic signs among forty-nine cases. The lemon sign was detected in 53%, ventriculomegaly in 81%, and myelomeningocele in 4%.[19]

In the current study, the IT was visualized in 98% of scanned fetuses in the same view done routinely for NT (Fiqure 3). This result was consistent with other earlier studies by Chaoui et all.[18] They were able to visualize the fourth ventricle in all normal fetuses (100%) and were not evident in any of the four cases of OSB.[18] A prospective study was conducted in Greece to diagnose OSB among 2,491 pregnancies using indirect signs between 11-13 weeks of gestation as a routine ultrasound scanning.[20] They concluded that IT was not visible among two out of three OSB cases, which was in line with our findings.

This study showed no difference in maternal age and maternal weight. The gestational age (P ≤0.05) was significantly different between the two groups. Crown-rump length typically ranged between 45–84 mm. A 73.5 (67-80) median was more prominent among the cases than the normal fetuses (59.0, range = 38-84).

The study of the Maternity Teaching Hospital inside Erbil city revealed a significant association between congenital anomalies and maternal characteristics; history of previous abnormalities (10.8%, P ≤0.005) and history of medical conditions (27.3%, P ≤0.005).[21] The previous study finding were inconsistent with our study .

A study in Saudi Arabia did not report any statistically significant differences between the cases and controls concerning gestational events; radiation exposure, folic acid intake, medication intake, diabetes, and hypertension.[22] Most of the risk factors for OSB were not significant in the current study; only the folic acid intake was significant (P = 0.018) (96% were supplemented with folic acid, and only 3.5% did not take any supplementation during pregnancy). Studies reported a significant association between lack of folic acid intake and incidence of OSB. Review studies confirmed the protective effects of folic acid supplementation in neural tube defects.[23]

The sensitivity of ultrasound in detecting OSB cases in the current study was 100%. This indicated that IT was a perfect sonographic marker for diagnosing patients with OSB. The high specificity (98%) means that IT could identify those cases without the disease and test negative as a marker. Value and accuracy were 50%, 100%, and 99%, respectively. This high accuracy means IT as a sonographic marker was a successful tool in differentiating between healthy and unhealthy infants.

A study conducted in India included 341 pregnant ladies scanned in first and second trimester concluded that

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Obliterated IT has reasonable sensitivity for detection of OSB and presence of normal IT excludes OSB and IT could be a useful marker in the early detection of OSB, with sensitivity 100%. And specificity 98%.[24]

A prospective study in Turkey demonstrated high sensitivity (97%) and specificity (99%) for IT in detecting OSB cases in early pregnancy,[25] this in agreement with our study.

Conclusion

Our data showed that the intracranial translucency was obliterated in cases of open spina bifida. The intracranial translucency marker had high accuracy and sensitivity in diagnosing cases of OSB among 11-13+6 weeks pregnant women. More prospective studies need to be conducted in this field with a larger sample size. IT should be integrated into the screening program during antenatal care visits. The damage to the exposed spinal cord is progressive during gestation. Therefore, early diagnosis is recommended before twenty weeks of pregnancy to improve the fetal outcome through intrauterine surgical repair. Unfortunately, this technique is not feasible in this part of the world.

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Competing interests

The authors declare that they have no competing interests.

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