Review Article

Accuracy of Prenatal Ultrasound Scans for Screening Cleft Lip and Palate: A Systematic Review

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Abstract

Children born with clefts encounter various postnatal issues which have a negative impact and long-term psychological effects on both the parents and themselves. This systematic review aims to find the accuracy of two-dimensional (2D)/3D scans for screening cleft lip and palate which would help the parents to be mentally and psychologically prepared to plan for future surgeries. To identify relevant literature, an electronic search was performed using PubMed, Trip database, Cochrane, and Google Scholar database. The search yielded 927 articles, of which 10 fulfilled the eligibility criteria and were included in this systematic review. These studies showed that the combination of 2D and 3D ultrasound scans has increased the specificity and sensitivity in detecting orofacial clefts, as they aid in improved visualization of the fetal face. However, in future, the visualization of the palate can be improved by inventing other modified views as cleft palate diagnosis is more prone to error.

Keywords: Cleft lip, cleft palate, ultrasound

Introduction

Cleft lip and cleft palate are the most common craniofacial birth defect affecting approximately 1–1.5/1000 live births worldwide and between 27,000 and 33,000 clefts per year in India.[1] The cleft children encounter various postnatal disputes that negatively impact their quality of life.[2]

Hence, detection of these clefts using antenatal two-dimensional (2D)/3D ultrasound scans prepares the parents psychologically to plan for postnatal surgery.[3,4] Since there is limited information on the sensitivity and specificity of these ultrasound scans, this systematic review aims to identify the accuracy of prenatal ultrasonographic detection of cleft lip and palate.

Materials and Methods

To obtain, evaluate, and summarize all relevant findings relating to the accuracy of prenatal ultrasound scans for screening cleft lip and palate, a systematic review was conducted as per the PRISMA guidelines. The International Prospective Register of Systematic Reviews was used to register the protocol for this systematic review (ID: 307957).

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Eligibility criteria

The PECO analysis of the articles searched was shown below:

- Population: Pregnant women who have undergone prenatal screening
- Exposure: Prenatal 2D/3D ultrasound scans
- Comparison: Not applicable
- Outcome: Detection rate of fetal cleft lip/palate.

Inclusion and exclusion criteria

Inclusion criteria

1. Cross-sectional, retrospective, and prospective cohort study designs
2. Studies done in the period from January 2012 to January 2022
3. Studies in which children were screened for cleft lip only (cleft lip without cleft palate), cleft lip with or without cleft palate, or cleft palate only (cleft palate without cleft lip) and children having syndromic cleft lip and palate were included

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4. Studies that were written in the English language were only included.

Exclusion criteria

1. Studies that assessed screening other than ultrasound like computed tomography and magnetic resonance imaging were excluded
2. Qualitative studies, reviews, expert opinions, systematic reviews, meta-analyses, and case studies/series
3. Publications with no abstract, conference papers, editorials, and those which were widely out of the scope of the study were excluded.

Search strategy

A broad search of the literature was performed in PubMed, Trip database, Cochrane, and Google Scholar database was performed in the specified time period. The search strategy included the combination of the following terms: "cleft lip," "cleft palate," and "ultrasound." The MeSH terms used in PubMed were "cleft lip," "cleft palate," and "ultrasound." The bibliographies of the selected articles were also searched to ensure that no relevant articles were missed. The relevant studies were sorted out on the basis of their title and abstract. Finally, those studies during which the abstract fulfilled all the inclusion criteria were selected for full-text reading. Further, the full text of all the articles whose abstracts met the inclusion criteria was read. The search strategy for various databases is shown in Table 1. Figure 1 shows the PRISMA flowchart.

Data extraction

Data extraction from the ten included articles was done using a data extraction form. It included the first author's name, year of publication of the article, study design, gestational age of screening in weeks, 2D/3D ultrasound scans, features, outcome, and inferences. Table 2 presents the information extracted from the studies included during this systematic review.

Quality assessment of the included studies

The final analysis included ten cohort studies. The tool used for quality assessment is by Newcastle–Ottawa Quality Assessment Form for cohort studies.[5] The methodological quality of the selected articles which was assessed using the Newcastle–Ottawa Form for cohort studies is summarized in Table 3. For cohort studies, the quality score was based on the following categories: selection, comparability, and outcome. A study is often awarded a maximum of one star for each item in the selection and outcome categories. A maximum of two stars are often given for comparability. Stars have been converted into scores for our convenience. The higher the score, the better the quality of the study. The studies with scores 9–7 are good studies, 5–6 scores are satisfactory studies, and 0–4 scores are unsatisfactory studies. Further, these scores have been categorized into high, unclear, and low risk of bias using Review Manager Software version 5.3. Bias risk assessment results are shown in Figure 2, and the risk of bias summary is shown in Figure 3.

Results

Search results

The search generated a total of 943 articles based on the title from four different electronic databases: PubMed, Trip database, Cochrane, and Google Scholar. PubMed produced 627 articles, Trip database produced 268 articles,

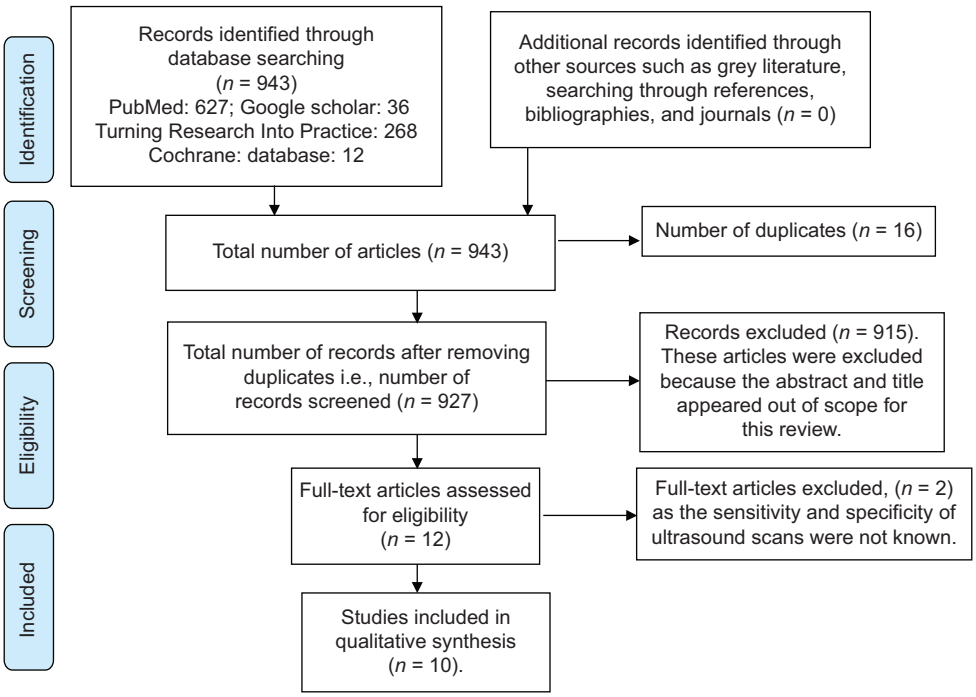

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart

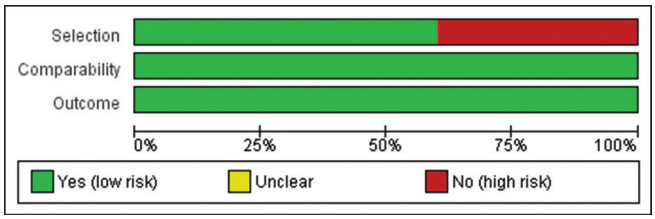

Figure 2: Bias chart

Table 1: Search strategy for systematic review

Database	Search pattern
PubMed	([cleft lip] AND [cleft palate]) AND (ultrasound) filters: Abstract, full text, in the past 10 years, humans, English
Google Scholar	Cleft lip, cleft palate, ultrasound
Trip database	Cleft lip, cleft palate, ultrasound
Cochrane	Cleft lip, cleft palate

Google Scholar produced 36 articles, and 12 articles were found in Cochrane. Among the obtained articles, 16 articles were eliminated due to duplication, 915 articles eliminated after abstract reading, and 2 articles eliminated after full-text reading. Finally, ten articles were selected for the review using a PRISMA flowchart based on inclusion and exclusion criteria. The inter-examiner bias was eliminated. The first two authors (DK and IS) analyzed the studies. The discrepancies between the first two authors were resolved by the consensus from the third author (MK). Out of these, seven articles were rated as good quality, three with satisfactory quality, and none of the articles were rated as poor quality.

Outcome

A study done by Berggren *et al*. on 2D or 3D scans found that the sensitivity of clefts was 43% and specificity of 100% excluding isolated cleft palate. However, additional scanning views of the face need to be followed in those cases in which the fetal face seemed to be impossible to visualize.[6] Loozen *et al.* studied clefts using both 2D and 3D scans. His findings reveal that out of 76.9% of cases, there was an underestimation of clefts in 19.4% and overestimation in 3.7% of cleft cases. 3D reverse face view allows a relatively straightforward evaluation of the fetal palate with a high degree of accuracy.[7] Gindes *et al*.'s study on 3D ultrasound scans on cleft palate found the sensitivity, specificity, positive predicted value, and negative predicted value to be 71.4%, 91.9%, 62.5%, and 94.4%, respectively. Acoustic shadows must be avoided, and at least two different angles of 3D imaging are required for a better diagnostic accuracy of cleft palate.[8] Studies conducted by Martinez-Ten *et al*. using 3D ultrasound scans found that all cases had clefting of the primary palate and 86% of clefts in the secondary palate with a satisfactory false-positive rate. Identification of retronasal triangle in the coronal plane recognizes the primary and secondary palate of a cleft fetus, as it has a resonable degree of certainity.[9] A study done by Lam *et al*. found that the overall accuracy of clefts visualized

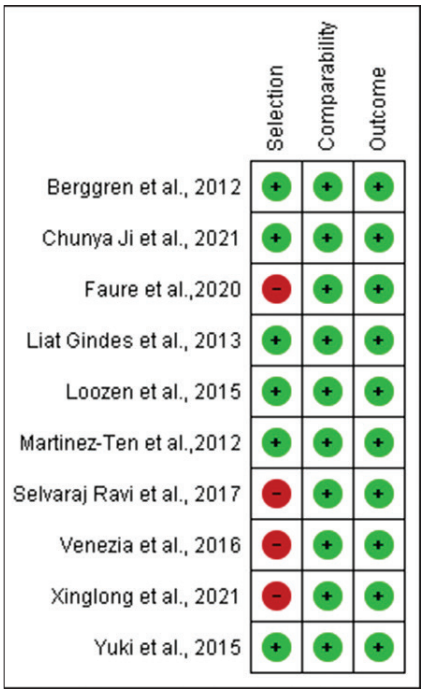

Figure 3: Risk of bias summary

on 2D and 3D scans was 95%. Flipped face and oblique face views allow a higher chance of satisfactory visualization of the secondary palate.[10] The study conducted by Venezia *et al*. on 2D and 3D scans found the sensitivity of 2D and 3D to be 50% and 100%, respectively.[11] Lakshmy *et al*.'s study on 2D and 3D scans found no false-positive results with one missed bifid uvula case. Although 2D axial, sagittal, and coronal views are complementary to one another in detecting cleft palate, a further 3D evaluation would be necessary.[12] Faure *et al*. conducted a study on 2D and 3D ultrasound scans on cleft palate, which found the adjusted kappa coefficient between prenatal and postnatal findings to be 0.88 which corresponds to an excellent agreement. 3D imaging using modes such as tomographic ultrasound imaging or volume contrast imaging offers a realistic visualization of the cleft palate.[13] The sensitivity of 2D and 3D scans with reformatting technique by Ji *et al*. was found to be 80% and 92%. 3D ultrasound reformatting technique using Omniview displays the full extent and severity of the secondary palate, and it could also overcome the shortcomings of other 3D ultrasound technologies.[14] Deng *et al*. found the sensitivity of clefts on 2D and 3D scans to be 36.8% and 89.5%, respectively. 2D ultrasound is mainly affected by the fetal position along with the scanning angle. Hence 3D imaging analyses cleft lip and palate with good reproducibility even at different angles and directions of cleft sites.[15]

Discussion

Cleft lip/palate is due to the disturbance in the growth and fusion of five facial prominences between the 4th and 10th weeks of human intrauterine period of development. In the 5th week, two bilateral nasal pits divide the frontonasal prominence into

Table 2: Study characteristics

Author name and year	Study design	Gestational age (weeks)	2D/3D ultrasound	Features	Outcome	Inference
Martinez-Ten *et al*., 2012[9]	Prospective study	11-13 weeks of gestation	3D	Primary and secondary palate	Out of 240 cases, using offline analysis, the primary palate was intact in 229 (95%), cleft in 9 (4%), and indeterminate in 2 (1%). 7 out of 9 fetuses had the cleft of primary palate confirmed (false-positive rate 0.9% 2/231). The secondary palate was classified intact in 217 (90%), 6 cleft (3%), and indeterminate in 17 (7%). Secondary palate clefts were confirmed in all six cases and missed in one, which was diagnosed at 16 weeks. The visualization rate was affected by the quality of the 3D dataset (P<0.001) and gestational age at evaluation (P<0.01)	All cases having primary palatal clefts and 86% of cases involving the secondary palate were visualized using 3D ultrasound with a satisfactory false-positive rate
Berggren *et al*., 2012[6]	Retrospective study	18-20 weeks and at gestation week 32	2D or 3D	Unilateral and bilateral CL, CP, CLP, CP, and alveolus, isolated CP	44 (31%) of the patients were diagnosed by prenatal ultrasound and 97/144 (67%) were diagnosed at birth. The detection rate was 44/102 (43%) if ICP was excluded. The sensitivity of clefts was 43% if cases of ICP are excluded. The specificity was 100%	The detection rates and accuracy of the prenatal scans can be improved by increased focus on these clefts, standardizing the scan plans and rescan in the cases of incomplete facial view are necessary
Gindes *et al*., 2013[8]	Retrospective study	12-40 weeks +3 days	3D	CP	Among 13 fetuses suspected of cleft palate, 3 had intact palate (false-positive 23%). Sensitivity - 71.4%, specificity - 91.9%, positive predicted value - 62.5%, negative predicted value - 94.4% for detecting palatal clefts	3D is useful in detecting cleft palate in 83% of high-risk cases with 5% false-negative. Due to some technical artifacts, it has a false-positive rate of 23%
Loozen *et al.,* 2015[7]	Retrospective cohort study	24 weeks +5 days	2D and 3D	CL, CLA, CLP, CP	Prenatal diagnosis was in accordance with postnatal findings in 76.9% of cases (103/134) with underestimated clefts in 19.4% (26/134) and overestimated in 3.7% (5/134). No errors in bilateral and unilateral clefts	Prenatal ultrasound is accurate in distinguishing between uni- and bilateral clefts. Although the cleft palate is missed easily, underestimation of cleft extend is frequent
Lam *et al*., 2015[10]	Retrospective study	Before 24 weeks of gestation	2D and 3D	CL, CLA, CLP	Out of 42 cases, 12 were CL, 6 were CLA, and 24 were CLP. Severity of the cleft is overdiagnosed in five cases and underdiagnosed in three cases giving an overall accuracy of 81% with no errors on the concerning side of the cleft. Therefore, the overall accuracy of the presence or absence of clefts was 95% (40/42)	The accuracy of CL was high, but the prediction of alveolar clefts was most prone to error
Venezia *et al*., 2016[11]	Prospective cohort study	Second-trimester screening	2D and 3D	CL, CLA, CP	Of the six cases, three were correctly diagnosed with 2D, whereas the remaining three were obtained with the aid of 3D ultrasound. The sensitivity of 2D was 50%, whereas 3D was 100%	Combining 2D and 3D gives the best results of sensitivity and specificity

Contd...

Table 2: Contd...

Author name and year	Study design	Gestational age (weeks)	2D/3D ultrasound	Features	Outcome	Inference
Lakshmy *et al*., 2017[12]	Prospective study	First trimester followed by second-trimester screening	2D and 3D	Unilateral, bilateral, medial CLP	14 cases, of which 5 were unilateral, 2 median, 4 bilateral cleft lip and palate, and 1 atypical palatine cleft identified. No false-positive results found. One case of bifid uvula was missed	The inclusion of 2D markers in all three planes increases the sensitivity in the identification of palatal clefts
Faure *et al.* 2020 [13]	Prospective longitudinal study	14-40 weeks of gestation	2D and 3D	CP	43 fetuses with suspicion of cleft palate without the primary palate involvement were included. Feasibility of imaging secondary palate was obtained in all 43 cases with no failure. The adjusted kappa coefficient between prenatal and postnatal findings was 0.88 (95% CI: 0.79-0.97) corresponding to an excellent agreement	Using a strictly axial transverse ultrasound view, visualization of the secondary palate enables to diagnose cleft palate without cleft lip
Ji *et al*., 2021[14]	Prospective cohort study	18.3-31.7 weeks of gestation	2D and 3D with reformatting technique	CL, CLA, CLP	The sensitivity of 2D and 3D with reformatting technology for CLA was 80% (20/25) and 92.0% (23/25)	Both 2D and 3D with reformatting technique have high diagnostic accuracy for CL and CLA. However, 3D ultrasound has a much higher diagnostic accuracy for CLP
Xinglong *et al*., 2021[15]	Prospective cohort study	20-32 weeks of gestation	2D and 3D	CL, CP	No significant (P>0.05) difference of two- and three-dimensional ultrasound detection rate of the pure cleft lip; two-dimensional ultrasound cleft palate detection rate was 36.8% (7/19), and three-dimensional ultrasound cleft palate detection rate was 89.5% (17/19). The two methods showed a statistically significant (P<0.05) difference in the detection rate of cleft palate	3D ultrasound can improve the accuracy of the cleft palate

CL: Cleft lip, CP: Cleft palate, CLA: Cleft lip and alveolus, CLP: Cleft lip and palate, ICP: Isolated cleft palate, CI: Confidence interval

lateral and medial nasal processes. By the end of the 7th week, the intermaxillary segment is formed which fuses along the midline together with the maxillary prominences from posterior to anterior. Failure of this development results in the cleft of the lip, alveolar process, and hard palate anterior to the incisive foramen (primary palate). The secondary palate which is located posterior to the incisive foramen is fused by the lateral palatal shelves of the maxilla prominences. Failure of this fusion results in the cleft of the secondary palate.[16]

Children born with cleft lip and cleft palate are at a greater risk of feeding difficulties, language disorders, ear infections, anatomical anomalies, and other postnatal disputes. Families of these cleft children also experience long-term psychological effects.[16] Hence, prenatal ultrasound has been utilized to diagnose these clefts using 2D and 3D methods at an early stage so that the parents would be mentally prepared and plan for postnatal surgeries.[17] The accuracy of ultrasound diagnosis of clefts varies widely and has increased over the years with the improvement of ultrasound equipment. With standard sonography, these facial clefts can be classified by a combination of coronal, sagittal, oblique, and axial scansions.[11] Hence, this systematic review aims to find the accuracy of those prenatal ultrasound scans in detecting cleft lip and palate children.

The diagnosis of cleft lip and palate in the first trimester has been scarcely reported in the literature. Martinez-Ten *et al*. in 2012 conducted a study using 3D ultrasound at the time of 11 to 13 weeks of gestation. The occurence of some false-positive cases in the study illustrated that early prenatal diagnosis of cleft lip and palate has certain limitations. However, a dedicated second-trimester scan for evaluation of the lip and palate should be mandatory in those cases.[9]

In 2012, Berggren *et al*. have concluded that the rate of identifying the facial clefts can be improved by focusing on the standardizing screening plans and rescanning if incomplete facial view is obtained.[6]

Table 3: Quality assessment of the included studies using the Newcastle–Ottawa Scale for cohort studies

	Selection 1 (a/b=1, c/d=0)	Selection 2 (a=1, b/c=0)	Selection 3 (a/b=1, c/d=0)	Selection 4 (a=1)	Comparability 1 (a=1, b=1)	Outcome 1 (a/b=1)	Outcome 2 (a=1)	Outcome 3 (a/b=1)	Score
Martinez-*et al*., 2012	c	a	a	a	a	b	a	a	7
Berggren *et al*., 2012	c	a	a	a	a	b	a	c	6
Gindes *et al*., 2013	c	a	a	a	a	b	a	a	7
Loozen *et al*., 2015	c	a	a	a	a	b	a	a	7
Yuki *et al*., 2015	c	a	a	a	a	b	a	b	7
Venezia *et al*., 2016	c	a	a	a	a	b	b	c	5
Lakshmy *et al*., 2017	c	a	a	a	a	b	a	c	6
Faure *et al*.	c	a	a	a	a	b	a	a	7
Ji *et al*., 2021	c	a	a	a	a	b	a	b	7
Deng *et al*., 2021	c	a	a	a	a	b	a	a	7

The accuracy of ultrasound in determining the type of cleft is not sufficient in much research, and in order to overcome this, Loozen *et al*. in 2015 had conducted a study using both 2D and 3D scans and found that no errors were made in distinguishing unilateral from bilateral clefts. This study is a reliable method to find the type of cleft though cleft palate is easily missed and underestimation of the extent of the cleft is common.[7]

3D ultrasound has an advantage over the 2D ultrasound in the spatial orientation and the third planar image and improves the interpretation of 2D images of clefts. Gindes *et al*. in 2013 had conducted a study on visualizing cleft palate in 2D and 3D scans at 12-40 weeks of gestation. He had found that the misinterpretations were at the second and third trimesters when acoustic shadows are more dominant. The cases during which the palate could not be demonstrated were within the third trimester. In most high-risk cases, detection of the fetal cleft palate during pregnancy is possible with an accuracy of about 90%.[8]

The overall detection rate of facial clefts by midtrimester ultrasound was comparable to that reported in the literature. Lam *et al*. in 2015 evaluated the accuracy of 2D and 3D scans before 24 weeks of gestation. He had found that the most common inconsistency was in the overdiagnosis or underdiagnosis of alveolar clefts, whereas there have been no errors concerning the side of the cleft. The limitations of ultrasound predictions should be explained to parents at the time of counseling.[10]

Systematic screening 2D ultrasound requires at least two scans. The median sagittal scanning allows visualization of the fetal profile and the philtrum protruding. Fore coronal scan of the nose and mouth allows the display of the upper lip and the possible alignment abnormalities of the alveolar processes. Venezia *et al*. in 2016 demonstrated the reliability of the screening of the midtrimester in the diagnosis of facial clefts with 2D and 3D ultrasound concluding the sensitivity of 2D ultrasound to be 50%, while the 3D ultrasound was found to be 100%. Combining ultrasound 2D + 3D is the one that guarantees the best results of sensitivity and specificity.[11]

Screening for palatine clefts starts with a good 2D assessment of bony landmarks of the palate. The sagittal, axial, and coronal views are complementary to every other in suspecting cleft palate (CP), which might need further 3D evaluation. Lakshmy *et al*.'s study in 2017 demonstrated that the evaluation of the palate can be done at the 11–14-week scan based on 2D markers and can also be assessed with 3D sonography. The inclusion of 2D markers in all three planes increases the sensitivity for the detection of palatine clefts.[12]

Faure *et al*. in 2020 had conducted a study by visualizing the fetal secondary palate in 3D plane, starting with 2D axial transverse ultrasound view. He had found the adjusted kappa coefficient between prenatal and postnatal evaluation to be 0.88 (95% confidence interval: 0.79-0.97) corresponding to an excellent agreement. Using a strictly axial transverse ultrasound view, visualization of the secondary fetal palate enables to diagnose cleft palate without cleft lip. This method offers a prenatal anatomic classification of cleft palate with a high level of concordance to postnatal findings.[13]

Reformatting technique such as Omniview can enhance the detection of isolated cleft palate which is difficult to visualize in traditional ultrasound. Any line, curve, or polyline can be drawn with this technology along the structure of the palate to display the entire palate in a single image. Ji *et al*. had conducted a study with both 2D and 3D with reformatting technique and found that 3D with reformatting technique has high diagnostic accuracy for cleft lip and alveolus. However, 3D ultrasound has a much higher diagnostic accuracy for cleft lip and palate.[14]

Currently, 2D ultrasound has been able to successfully diagnose cleft lip deformity, and 3D ultrasound as a screening test has proven to be a feasible screening tool. Deng *et al*. had concluded that there was no significant ($P > 0.05$) difference in the 2D and 3D ultrasound detection rate of the pure cleft lip. 3D ultrasound can show the structure of the palate that is difficult to display with conventional 2D ultrasound, which significantly improves the detection rate of prenatal fetal harelip and palate, especially in the diagnosis of cleft palate, which has greater advantages than 2D ultrasound examination.[15]

In this review, only those articles published in the English language were included. Additional records identified through gray literature were not included. All studies comprised in this review were cohort studies, and further, more longitudinal studies are required to have concrete evidence on the accuracy of 2D and 3D scans in detecting children born with cleft lip and palate.

The success rate of ultrasound scans depends mainly on the fetal position and on the experience of the sonographers. In future, the limitation in the visualization of the palate can be improved by inventing other modified views as cleft palate diagnosis is more prone to error.

Conclusion

2D and 3D ultrasound scans have the same accuracy for cleft lip. However, if a cleft lip is suspected, 3D ultrasound should be used for secondary evaluation after the 2D ultrasound. 3D imaging is simple to implement and it improves the prenatal detection rate of cleft lip and palate, especially those involving the secondary palate. This 3D imaging from different directions and angles of cleft lip and palate was analyzed with good reproducibility. In conclusion, the combination of 2D and 3D ultrasound scans is the best approach to increase both the specificity and sensitivity as it aids in improved visualization of fetal face.

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Conflicts of interest

There are no conflicts of interest.

References

1. Mossey P, Little J. Addressing the challenges of cleft lip and palate research in India. Indian J Plast Surg 2009;42 Suppl: S9-18.
2. Kashyap N, Pradhan M, Singh N, Yadav S. Early detection of fetal malformation, a long distance yet to cover! Present status and potential of first trimester ultrasonography in detection of fetal congenital malformation in a developing country: Experience at a tertiary care centre in India. J Pregnancy 2015;2015:1-9.
3. Gkantidis N, Papamanou DA, Karamolegkou M, Dorotheou D. Esthetic, functional, and everyday life assessment of individuals with cleft lip and/or palate. Biomed Res Int 2015;2015:510395.
4. James JN, Schlieder DW. Prenatal counseling, ultrasound diagnosis, and the role of maternal-fetal medicine of the cleft lip and palate patient. Oral Maxillofac Surg Clin North Am 2016;28:145-51.
5. Newcastle-Ottawa Quality Assessment form for Cohort Studies. Available from: https://www.ncbi.nlm.nih.gov/books/NBK115843/bin/appe-fm3.pdf. [Last accessed on 2022 May 25].
6. Berggren H, Hansson E, Uvemark A, Svensson H, Sladkevicius P, Becker M. Prenatal ultrasound detection of cleft lip, or cleft palate, or both, in southern Sweden, 2006-2010. J Plast Surg Hand Surg 2012;46:69-74.
7. Loozen CS, Maarse W, Manten GT, Pistorius L, Breugem CC. The accuracy of prenatal ultrasound in determining the type of orofacial cleft. Prenat Diagn 2015;35:652-5.
8. Gindes L, Weissmann-Brenner A, Zajicek M, Weisz B, Shrim A, Tzadikevitch Geffen K, *et al.* Three-dimensional ultrasound demonstration of the fetal palate in high-risk patients: The accuracy of prenatal visualization. Prenat Diagn 2013;33:436-41.
9. Martinez-Ten P, Adiego B, Illescas T, Bermejo C, Wong AE, Sepulveda W. First-trimester diagnosis of cleft lip and palate using three-dimensional ultrasound. Ultrasound Obstet Gynecol 2012;40:40-6.
10. Lam YY, To WW. Evaluation of the accuracy of prenatal ultrasound assessment of facial clefts. Hong Kong J Gynaecol Obstet Midwifery 2015;15:46-52.
11. Venezia R, Mocera G, Alletto A, Vitrano G, Ferrara C, Perino A. Accuracy of the second trimester screening in the diagnosis of cleft lip and palate. Giornale Italiano Di Ostetricia E Ginecologia; 2016;38:269-75.
12. Lakshmy SR, Deepa S, Rose N, Mookan S, Agnees J. First-trimester sonographic evaluation of palatine clefts: A novel diagnostic approach. J Ultrasound Med 2017;36:1397-414.
13. Faure JM, Mousty E, Bigorre M, Wells C, Boulot P, Captier G, *et al.* Prenatal ultrasound diagnosis of cleft palate without cleft lip, the new ultrasound semiology. Prenat Diagn 2020;40:1447-58.
14. Ji C, Yang Z, Yin L, Deng X, Pan Q, Lu B, *et al*. The application of three-dimensional ultrasound with reformatting technique in the diagnosis of fetal cleft lip/palate. J Clin Ultrasound 2021;49:307-14.
15. Deng X, He S, Wu Q, Weng Z, Yang M, Liu M. Prenatal diagnosis of fetal cleft lip and palate with three-dimensional ultrasound information technology. Sci Program 2021;2021:1-7.
16. Vyas T, Gupta P, Kumar S, Gupta R, Gupta T, Singh HP. Cleft of lip and palate: A review. J Family Med Prim Care 2020;9:2621-5.
17. Khajanchi MU, Shah H, Thakkar P, Gerdin M, Roy N. Unmet burden of cleft lip and palate in rural Gujarat, India: A population-based study. World J Surg 2015;39:41-6.