THE ROLE OF PRENATAL ULTRASOUND IN THE DETECTION OF FETAL ANOMALIES: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Structural or functional anomalies occur during intrauterine life and they can be identified prenatally, at birth, or sometimes may only be detected later in infancy, such as hearing defects.

Objectives: The study was aimed at reviewing the available literatures on the role of ultrasound in the detection of fetal anomalies, and identify the missing gap in the subject area.

Methods: The study was a systematic review that on the relevant literature on the topic and key words of research. The references were obtained using the database MEDLINE. The search terms used were; fetal anomalies, ultrasound, detection of fetal anomalies, sensitivity of ultrasound on fetal anomalies, prenatal ultrasound on fetal anomalies and pattern of fetal anomalies. High quality published articles from reputable journal were included in the study. The articles of low quality and those published in predatory journals were excluded from the study.

Results: An electronic search using the search terms had identified 196 related published articles, but only 20 articles were considered for the review. Ten of the articles were prospective studies, whereas the other ten were retrospective studies. The prevalence of fetal congenital anomalies in Europe ranged 1.4% - 4,0%, in Asia, 1.14% – 7.6% and in Africa 1.08% – 6.3%. The detection rate of ultrasound on fetal congenital anomalies in Europe ranged 30% - 95.9%, in Asia, 48.8% - 90.6% and in Africa 49% -78.4%. The detection rate was higher in the second semester when compared to the first semester. The most frequently occurring fetal anomaly in the reviewed articles in all the 3 continents was that associated with central nervous system, but the least frequent occurring anomaly was associated with the skeletal system.

Conclusion: The detection rate reported by published articles has proven the potentiality of ultrasound to diagnose fetal congenital anomalies. To obtain high detection rate, ultrasound scan should be performed in the first, second and third trimesters.

Keywords: Fetal, anomaly, ultrasound.

INTRODUCTION

Congenital anomalies are also known as birth defects, congenital disorders or congenital malformations. They are structural or functional anomalies that occur during intrauterine life and can be identified prenatally, at birth, or sometimes may only be detected later in infancy, such as hearing defects. An estimated 303 000 newborns die within 4 weeks of birth every year, worldwide, due to congenital anomalies [1]. They result in an estimated 3.2 million birth defect-related disabilities every year. Literature shows that 2–3% of all births are complicated by congenital anomalies and therefore, they are an important cause of perinatal morbidity and mortality, accounting for 20–30% of perinatal deaths [2]. Congenital anomalies can contribute to long-term disability, which may have significant impacts on individuals, families, healthcare systems, and societies. The most common, severe congenital anomalies are heart defects, neural tube defects and Down syndrome. Although congenital anomalies may be the result of one or more genetic, infectious, nutritional or environmental factors, it is often difficult to identify the exact causes. Some congenital anomalies can be prevented. Vaccination, adequate intake of folic acid or iodine through fortification of staple foods or supplementation, and adequate antenatal care are just 3 examples of prevention methods [1].

Fetal anomalies can be diagnosed before delivery, during delivery or after delivery. During pregnancy, women usually have undergone screening tests to see whether there is an associated increased risk of a fetal anomaly. But, it is important to note that, screening tests are not a formal diagnosis, and once a screening test reveals an abnormality further investigations are

recommended for the patient. Screening tests for pregnant women are usually performed during the first and second trimesters of pregnancy. During the first trimester a blood test is usually performed to measure the human chorionic gonadotropin (hCG) levels and pregnancy associated plasma protein A (PAPP-A). If hCG or PAPP-A levels are too high or low, that can be an indication of a chromosomal disorder, such as Down syndrome. During the second trimester, the blood test, known as a maternal serum screen, can look at three to four different protein levels in the mother's blood to identify an increased risk of certain structural or chromosomal anomalies [3]. The tests for the diagnosis of fetal anomalies include; chorionic villus sampling, amniocentesis and fetal echocardiography. Ultrasound has extensively been used in the screening and diagnosis of fetal anomalies in both first and second trimesters of pregnancy. The advantages of ultrasound over methods include; non-invasiveness, availability, low cost and reveals a lot of information about developing fetus and maternal abdominal organs without known hazardous effect. Detection of fetal abnormalities depends on a number of factors, including the nature or type of abnormality, sophistication of equipment and experience of the operator [4]. Many studies have documented low sensitivity of ultrasound in the low risk pregnancies, however high sensitivity has been recorded in the high risk pregnancies. Furthermore, high sensitivity has been documented by many studies in the second trimester when compared with the first trimester [4]. The study was aimed at reviewing the available literatures on the role of ultrasound in the detection of fetal anomalies.

Methods

The study was retrospective and secondary source of data was used. The references were obtained using the database MEDLINE. The search terms used were; fetal anomalies, ultrasound, detection of fetal anomalies, sensitivity of ultrasound on fetal anomalies, prenatal ultrasound on fetal anomalies and pattern of fetal anomalies. All the related articles with a high quality and published in a reputable journal were included in the study. The articles of low quality, published in un-reputable journals or considered specific anomaly were excluded from the study.

RESULTS

A retrospective study conducted by Katherine *et al* [5] reviewed cases of abnormal US findings in fetuses scanned before or at 14 weeks gestation during the period July 1, 2000, to October 30, 2002. A total of 8,537 fetuses were scanned. The prevalence of fetal anomaly was 2.9%, whereas the detection rate was 42%. One hundred and sixty eight fetuses had cardiovascular system anomalies, 106 with central nervous system, 18 skeletal system, 75 urinary system, and 66 gastrointestinal system. Ferrier *et al.* [6] Conducted a retrospective study, 15 989 cases of fetal anomalies were included from the registries between 2006 and 2014. The prevalence of birth defects was 3.2% and 18% of the cases were associated with a chromosomal anomaly. The most common chromosomal anomaly was Down's syndrome (54.4%). In cases not associated with chromosomal anomalies, 82% were isolated malformations. The overall prenatal detection rate (including cases with and without chromosomal anomalies) of US screening in the study period was 57.0%. A prospective observational study was conducted by Onyambu & Tharamba [7] for a period of three months. Fifteen fetal anomalies were diagnosed in 500 women who came for routine ultrasound (3%) and detection rate of 87.7%. The most frequently observed fetal anomalies involved the head 8 (1.6%). Each of the remaining anomalies affected less than 1% of the fetuses and included anomalies of the spine 2 (0.4%), pulmonary 2 (0.4%), renal and urinary tract 2 (0.4%) and skeletal systems 2 (0.4%). Another prospective study conducted by Akinmoladun *et al*. [8] over the 4-year period, 989 fetuses were evaluated for fetal anomalies. Anomalies were detected in 62 fetuses, giving a hospital prevalence of 6.3% and detection rate of 95.9. Twenty-five (40.3%) of the fetuses had minor anomalies, while 37 (59.7%) were categorized as major anomalies. Central nervous system (CNS) was the most commonly affected system with 9 (24.3%) having anencephaly and severe ventriculomegaly, followed by the genitourinary and the gastrointestinal systems with 6 (16.2%) each. Another retrospective study was conducted by Bardi *et al*. [9] in a primary care US clinic in Rotterdam. US scan was performed between 11+0 and 13+6 weeks of gestation from 2012 to 2016. Anomalies were diagnosed prenatally in 200 (1.8%) fetuses with a detection rate of 30%; 81 (0.7%) were chromosomal and 119 (1.1%) were

structural. A prospective study conducted by Kaur *et al.* [10] reported an incidence of fetal congenital abdominal anomalies of 5.56 per 1000 births with detection rate of 90%. It reported 32 cases of fetal congenital abdominal anomalies with or without other associated anomalies out of 5761 trans-abdominal obstetrics scan performed within a year. Among the fetal congenital abdominal anomalies, fetal urinary tract anomalies were the most common with an incidence of 4.69 per 1000 births. The incidence of Omphalocele, Gastroschisis and Jejuno-ileal atresia was found to be 5.2, 1.7 and 1.7 per 10,000 births respectively. Among fetal congenital abdominal anomalies, fetal urinary tract anomalies (84.38%) were the most common, followed by fetal anterior abdominal wall defects (12.50%) and fetal GI tract anomaly (3.13%). A prospective study conducted by Iliescu *et al*. [11] two-center 2-year study of 5472 consecutive unselected pregnant women examined at 12 to 13+6 gestational weeks. The prevalence of lethal and severe malformations was 1.39%. The first-trimester scan identified 40.6% of the cases detected overall and 76.3% of major structural defects. Another retrospective, observational study was conducted by Kashyap *et al.* [12] from August 2009 to October 2013. A total number of 4080 pregnant women underwent USG and amongst them 312 (7.6%) patients had fetal structural malformation. A retrospective study conducted by Grande et al. [13] of chromosomally normal singleton pregnancies with an 11 – 14-week scan performed during 2002 – 2009. The ultrasound examination included an early fetal anatomy survey and assessment of nuchal translucency, ductus venosus blood flow and nasal bone. Among 13 723 scanned first-trimester pregnancies with no genetic anomalies and complete follow-up, 439 fetuses (3.2%) were found to present with structural anomalies (194 with major anomalies and 245 with only minor anomalies) with detection rate of 49%. Forty-nine percent of major structural anomalies were detected during the first-trimester scan, the highest rates corresponding to acrania (17/17), holoprosencephaly (three of three), hypoplastic left heart syndrome (10/10), omphalocele (six of six), megacystis(seven of eight) and hydrops (eight of nine). Higher than expected detection rates were obtained for skeletal (69%) and cardiac (57%) defects, coincidentally showing the highest presence of an increased nuchal translucency or abnormal ductus venosus blood flow (38% and 52%,respectively). Manegold *et al.* [14] conducted a prospective study of 8074 fetuses at 11 – 14 weeks between 1998 and 200. All fetuses received an examination for fetal anatomy as well as nuchal translucency (NT) measurement for risk assessment of aneuploidy. The overall incidence of fetal malformations was 3.6% (n = 289) with a detection rate of 90%, of which 40% (116/289) were diagnosed at 11 – 14 weeks. The following 2nd trimester scans revealed 102 (35%) new fetal malformations. An additional 44 (15%) structural abnormalities were found in the 3rd trimester. These were mainly abnormalities of the urogenital system (n = 18). There were also anomalies of the cardiovascular system (n = 9), the gastrointestinal system (n = 6) and the central nervous system (n = 4). One of the cases had a previously undiagnosed, abnormal karyotype. Ebrashy *et al*. [15] conducted a prospective study from January 2002 to January 2007, 2876 pregnant women underwent a 13–14-week ultrasound examination. In the early scan, analyzable data for 2876 TAS and 1357 TVS examinations showed that TVS was significantly better in visualizing the cranium, spine, stomach, kidneys, bladder and upper and lower limbs. Complete fetal anatomical surveys were achieved by TAS in 64% of cases versus 82% of the cases in which it was attempted by TVS. The total number of cases in which anomalies were detected was 31 (1.5%). At the first-trimester scan, anomalies were detected in 21 fetuses and in 14 of these cases the parents chose pregnancy termination. At the second-trimester scan, anomalies were detected in 17 fetuses: 10 new anomalous cases along with seven cases already detected in the first-trimester scan. A retrospective study conducted by Abu-Rustum *et al.* [16] chart review of all patients having first-trimester scans between 2002 and 2009. A survey of fetal anatomy is performed at the time of nuchal translucency assessment at 11 weeks to 13 weeks 6 days. A second-trimester scan is done at 20 to 23 weeks and a third-trimester scan at 32 to 35 weeks. The study included 1370 fetuses, six cases of aneuploidy (0.4%) were detected. The first-trimester scan detected 5 of 6 cases of aneuploidy (83%), confirmed by karyotype. There were 36 cases of structural fetal anomalies (2.6%); 20 (1.5%) were major anomalies. The first-trimester scan detected 16 of 36 (44%); 20 (56%) were identified by second- or third-trimester scans.

The first-trimester scan detection rate of major structural anomalies was 14 of 20 (70%). The 5 that were missed by the first-trimester scan were detected by a second-trimester scan. An observational study conducted by Hildebrand *et al.* [17] in five centers in the southeast region of Sweden population. A total of 21,189, unselected pregnant women was studied. The scan was performed at one center in the first trimester and at the remaining four centers in the second trimester. Outcome measures resulting from first trimester scanning were compared with those from the second trimester scanning. In the first trimester scan 13% of all anomalies were detected, and in the second trimester scan 29% were detected. Lethal anomalies were detected at a high level at both times: 88% in the first, 92% in the second. The percentage of chromosomal aberrations discovered at the early scan was 71%, in the later 42% and the prevalence was found to be 4%. A prospective study conducted by Öztekin *et al.* [18] for the period of four years, reported that of 1085 fetuses, 21 (1.93%) had at least one major structural defect considered detectable by routine ultrasound screening and a detection rate of 66.6%. Fourteen (1.29%) were identified at the early screening, and an additional five (0.47%) at the late screening. Two abnormalities were not detected prenatally, and data were obtained from the patients after delivery. Cases detected in the first trimester included four cases of anencephaly, one encephalocele, two cases of cystic hygroma, one omphalocele with increased NT (normal karyotype), one gastroschisis, one anencephaly with spina bifida, one hydrops, one cystic hygroma with intraabdominal cyst, one holoprosencephaly, and one megacystis.. Cranial abnormalities were the most common (7/14) abnormalities detected in the first trimester. Of these, anencephaly was the most common (5/7) cranial malformation detected. Cranial abnormalities were followed by cystic hygroma (3/14), and abdominal wall defects (2/14). Another study conducted by Fadda *et al*. [19]. The patients admitted to the study had effected at least one ultrasound examination within the second trimester of pregnancy (≤ 23 gestational weeks). The examined pregnant women were 42,256 and the period of reference ranged from January 1981 to December 2004. All patients delivered in Gynecologic and Obstetric Clinic of Sassari University, Sassari, Italy. In the considered period were reported 1050/42,256 (2.48%) cases of fetal malformations, of which 974 single and 76 multiple malformations. The cases of malformations diagnosed in prenatal period were 578/1050 (55.05%), of which 65/578 (11.24%) multiple anomalies. The overall sensitivity was 55.05% (95% confidence interval: 52–58%), with a variability from the 32.95% (cardiovascular system) to 81.05% (central nervous system) in relationship to the typology of the examined apparatus. The overall specificity was 99.88% (95% confidence interval: 98–99.9%), the predictive positive value 91.89% (95% confidence interval: 89–93%) and the negative predictive value 98.87% (95% confidence interval: 95–99%). A cross-sectional study was performed by Neto *et al*. [20] to validate diagnostic test results, including all high-risk pregnant women submitted to morphological obstetric ultrasound at the Instituto de Medicina Integral Professor Fernando Figueira (I.M.I.P.), from March 2002 to March 2006. During the period studied, 457 high-risk expectant mothers were recruited. Prenatal ultrasonography led to a diagnosis of congenital anomaly in 289 (63.2%) patients and 257 (56.2%) of these diagnoses were confirmed postnatally. Breaking down the prenatal diagnoses of congenital anomalies by body system, 129 (92.8%) of the 139 central nervous system abnormalities diagnosed postnatally had been diagnosed in advance by intrauterine ultrasound. Postnatal assessments of complications of placenta, cord, and membranes confirmed abnormalities found by ultrasound in 127 (90%) cases. Abnormalities of the genital and urinary (n=70), musculoskeletal (n=46), digestive (n=45) and circulatory (n=42) systems were confirmed postnatally with frequencies varying from approximately 73% to 87%. A prospective and retrospective study conducted by Singh *et al.* [21] on 10890 pregnant women showed that 124 fetuses had major congenital malformations. The average incidence of malformations was 1.14% with the maximum number of malformations 96 (77.4) during the third trimester of pregnancy. Most common anomaly was ventriculomegaly 41 cases (27.33%) followed by anencephaly, 39cases (26.00%). Neural tube defects accounted for more than 50%of the anomalies with the common association with spinal deformities. Polyhydramnios, 28 (71.79%) cases were common association with neural tube defects. Oligohydramnios was associated with 4 (66.66%)

cases of renal anomalies. Fetal malformations had predilection female fetuses with male to female ratio of 1:1.3. Spinal abnormalities were common in male fetuses. Overall mortality of malformed fetuses was 90 (72.58%) cases, however, in anencephaly, diaphragmatic hernia and hydrops fetalis it was 100%. In skeletal dysplasias it was 80%. The most common site of encephalocele was occipital in 18 (94.73%) cases. The most common renal malformation was found to be bilateral hydronephrosis in 4 patients. Skeletal dysplasia was seen in 5 cases with 3 cases had associated pulmonary hypoplasia. Achondroplasia was seen in 3 cases and achondrogenesis in 2 cases. Another study conducted by Munim *et al.* [22] reported an incidence of 2.8% congenital abnormalities of all deliveries. The ultrasound was able to diagnose congenital abnormalities in just under half of the cases (48.8%) whereas in 51.2% (83) malformations could not be diagnosed. The most frequent abnormalities detected by ultrasound scan were of the kidney (19/20) followed by central nervous system (30/36). The ultrasound scan failed to detect any facial defects in the study. Similarly, only a quarter of cardiac defects were diagnosed on the scan. A prospective observational study was conducted by McAuliffe et al. [23] on three hundred twenty-five singleton fetuses (11+0 to 13+6 weeks) and pregnancy outcome was available for 300 (92.3%) of cases. In 89 (24.6%) cases, transvaginal ultrasound was performed. The following fetal structures were seen in 95% of cases: cranium and intracranial anatomy, face, cord insertion, stomach, and all 4 limbs. The bladder was visualized in 89.5% of cases, the cardiac 4 chamber view in 84%, and the spine in only 45% of cases. Complete anatomy was seen in 109 (33%), of a total of 6 congenital defects in this cohort, 1 was detected in the first trimester (neural tube defect), 4 at the 18- to 20-week anatomic scan, and 1 postnatally. A study conducted by Chen *et al.* [24] from February 1998 to March 2001, 3710 pregnant women were referred to the prenatal diagnostic and counseling department of the Tsan Yuk Hospital for advanced maternal age and 2566 were seen before 14 weeks. of these, 1684 consented to take part in the study and were examined by transabdominal and transvaginal sonography between 12 and 14 weeks of gestation. Eighty (4.75%) cases were excluded from the analysis because the outcome of their pregnancy could not be traced. A total of 1609 fetuses of 1604 women, including 1599 singletons and 5 pairs of twins were studied. Twenty-six fetuses with structural abnormalities were found in a total of 1609 fetuses that were viable in the 12- to 14-week ultrasound examination, including 16 (61.5%) structural abnormalities with normal karyotype and 10 (38.5%) structural abnormalities associated with chromosomal abnormalities. The incidence of structural abnormalities was 1.6% (26/1609). Postnatal, post morterm, or fetoscopic examination confirmed the structural abnormalities. Chromosomal abnormalities were diagnosed by a conventional cytogenetic study. Fourteen out of the 26 structural abnormalities were diagnosed at the 12- to 14-week scan, including 7 cases with chromosomal abnormalities (7/14, 50.0%). Five cases suspected of having structural abnormalities at the 12- to 14-week scans were found to be normal on subsequent examination and were not confirmed after birth (including two cases suspected of having a ventricular septal defect; one case of increased nuchal translucency associated with hydropic change; one case of pyelectasis and another case of clubfoot). The detection rate in the first trimester was 53.8% (14/26; 95% CI 44, 64) with a false-positive rate of 0.3% (5/1583; 95% CI 0.16, 0.44). The overall detection rate for structural abnormalities at the first- and second-trimester scan was 76.9% (20/26; 95% CI 68.6, 85.2). There were 16 (61.5%, 16/26) cases of structural abnormalities that were not associated with chromosomal abnormalities: 7 were detected in the first trimester; 4 were detected in the second trimester. One Pena–Shokeir syndrome defaulted routine scan, but was diagnosed in the late second-trimester scan. There were 10 structural abnormalities that were found to be associated with chromosomal abnormalities: 7 detected in the first trimester and 2 in the second trimester. There were 1503 cases with nuchal translucency measurement performed. Twenty-six fetuses had structural abnormalities. In the fetuses with increased nuchal translucency (greater than the 95th percentile for gestational age), structural abnormalities were detected in 29.2% (7/24) of the cases, which was significantly higher than that of the fetuses with normal NT (1.3%, 19/1479) at 12 to 14 weeks gestation. In the 14 abnormalities detected in the first trimester, 7 (50%, 7/14) had increased NT. There were altogether 12 cases of cardiac

abnormalities in the study: 7 (58.3%, 7/12) were detected in the first-trimester scan; 4 (33.3%, 4/12) were detected in the second-trimester anomaly scan; 1 (8.3%, 1/12) was detected in the late second trimester ultrasound examination.

DISCUSSION

Ultrasound examination, with state-of-the-art equipment and in expert hands, can visualize as many structures at 13–14 weeks as it could at 16 weeks 5–10 years previously and at 20–22 weeks 15–20 years previously. The first structural evaluation of the fetus can and should be performed between 11 and 14 weeks. However, the evaluation should also be performed in the second and third trimesters. Ultrasound anomaly screening should be directed to all pregnant women not to a selected population [15]. The gold standard for the accuracy of ultrasound in the diagnosis of fetal congenital anomalies is the neonatal diagnosis of congenital anomalies. This requires follow up throughout the gestation period to the delivery. To have an effective follow up in order to obtain maximum detection rate the study design has to be prospective. However, ten out of the twenty reviewed articles were retrospective studies, which could be a limitation on obtaining accurate detection rate. The studies conducted in Europe include; [5], [6], [9], [12], [13], [16], [17], [18], [19] and [20], in Asia; [10], [11], [14], [21], [22], [23], and [24], in Africa; [7], [8] and [15]. Despite the difference in continents of the reviewed there was no much difference in both the prevalence and the detection rate of the congenital anomalies. However, the highest prevalence was in Asia and the lowest was in Africa, whereas the highest and the lowest detection rate was reported in Europe. To have a maximum and accurate detection rate ultrasound scan should be performed in the first, second and third trimesters based on what was reported by the reviewed articles. Studies conducted by [10], [11], [14] and [21] performed ultrasound scans in the first, second and third trimesters, and reported detection rates of 90.6%, 96%, 95.9% and 77.4%. The studies that performed ultrasound scan in the first and second trimesters were conducted by [5], [6], [7], [9], [16] and [17] reported detection rate of 41.5%, 86%, 87.8%, 30%, 70% and 92%, whereas studies conducted by [13], [15], [18] and [24] performed ultrasound scan between 11-14 weeks of gestation only and reported 49%, 64%, 66% and 53.8% as detection rate. The most frequently occurring fetal anomaly in the reviewed articles in all the 3 continents was that associated with central nervous system, but the least frequent occurring anomaly was associated with the skeletal system. The commonest anomalies detected were independent of the continent where the study was conducted, the study design, the number of ultrasound scans performed on the patient or the trimester when the ultrasound was performed. However, [5] reported cardiovascular system, whereas [10] and [14] urinary tract as the commonest anomalies detected in their studies.

CONCLUSION

The detection rate reported by published articles has proven the potentiality of ultrasound to diagnose fetal congenital anomalies. To obtain high detection rate, ultrasound scan should be performed in the first, second and third trimesters.

REFERENCES

1. WHO (2016), Congenital Anomalies. Available at: https://www.who.int/news-room/fact-sheets/detail/congenital-anomalies. [Accessed, 22nd August, 2019]
2. Onyambu, C. and Tharamba, N. Screening for congenital fetal anomalies in low risk pregnancy: the Kenyatta National Hospital experience. *BMC Pregnancy and Childbirth*, 2018.18 (1): 1-9.
3. Comprehensive Women Health Center (2019). Fetal Anomaly (Birth Defect) Information & Resources. Available at: https://cwhccolorado.com/for-patients/fetal-anomaly-resources/index.html. [Accessed, 22nd August, 2019].
4. Carlos Noronha Neto, Alex Sandro Rolland de Souza, Olímpio Barbosa de Moraes Filho, Adriana Mota Bione Noronha. Validation of ultrasound diagnosis of fetal anomalies at a specialist center. Revista da Associação Médica Brasileira; 2009.55(5):.541-546.
5. Katherine W. Fong, Ants Toi, Shia Salem, Lisa K. Hornberger, David Chitayat, Sarah J. Keating, Fionnuala McAuliffe, Jo-Ann Johnson. Detection of Fetal Structural Abnormalities with US during Early Pregnancy. Pubs.rsna.org. (2019). [Online] Available at: https://pubs.rsna.org/doi/pdf/10.1148/rg.241035027. [Accessed 15 Sep. 2019].

6. Clément Ferrier, Ferdinand Dhombres, Babak Khoshnood, Hanitra Randrianaivo, Isabelle Perthus, Lucie Guilbaut, Isabelle Durand-Zaleski, Jean-Marie Jouannic. Trends in resource use and effectiveness of ultrasound detection of fetal structural anomalies in France: a multiple registry-based study. BMJ; 2018.9: 1-6
7. Callen Kwamboka Onyambu & Norah Mukiri Tharamba. Screening for congenital fetal anomalies in low risk pregnancy: the Kenyatta National Hospital experience. *BMC Pregnancy and Childbirth*; 2018.18 (1): 1-9.
8. Akinmoladun JA, Ogbole GI, O Oluwasola TA. Pattern and outcome of prenatally diagnosed major congenital anomalies at a Nigerian Tertiary Hospital. Niger J Clin Pract; 2018.21(1): 560-5
9. Francesca Bardi, Eric Smith, Maja Kuilman, Rosalinde J.M. Snijders, Caterina Maddalena Bilardo (2018). Early Detection of Structural Anomalies in a Primary Care Setting in the Netherlands
10. Kaur N, Pamnani S, Kaur B. Role of ultrasound in diagnosis of fetal congenital abdominal anomalies: One year prospective study. International Journal of Medical Research and Review; 2017.5 (7)
11. Namrata Kashyap, Mandakini Pradhan, Neeta Singh, and Sangeeta Yadav. 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. Journal of Pregnancy; 2015.1(1): 1-9
12. Iliescu D, Tudorache S, Comanescu A, Antsaklis P, Cotarcea S, Novac L, Cernea N, Antsaklis A. Improved detection rate of structural abnormalities in the first trimester using an extended examination protocol. Ultrasound in Obstetrics & Gynecology; 2013.42 (3): 300-9
13. Grande M, Arigita M, Borobio V, Jimenez JM, Fernandez S, Borrell A. First trimester detection of structural abnormalities and the role of aneuploidy markers. Ultrasound in Obstetrics & Gynecology;2012. 39 (2): 157-63
14. G. Manegold, S. Tercanli, H. Struben, D. Huang, A. Kang. Is a Routine Ultrasound in the Third Trimester Justified? – Additional Fetal Anomalies Diagnosed After Two Previous Unremarkable Ultrasound Examinations. Ultraschall in Med; 2011.32: 381–386
15. A. Ebrashy, A. El Kateb, M. Momtaz, A. El Sheikhah, M. M. Aboulghar, M. Ibrahim, M. Saad. 13–14-Week Fetal Anatomy Scan: A 5-Year Prospective Study. Ultrasound Obstet Gynecol;2010. 35: 292–296.
16. Abu-Rustum RS, Daou L, Abu-Rustum SE. Role of first-trimester sonography in the diagnosis of aneuploidy and structural fetal anomalies. Journal of Ultrasound in Medicine;2010. 29 (10): 1445-52
17. Hildebrand E, Selbing A, Blomberg M. Comparison of first and second trimester ultrasound screening for fetal anomalies in the southeast region of Sweden. Acta Obstetricia Et Gynecologica Scandinavica; 2010.89(11):1412-9.
18. Özgür Öztekin, Deniz Öztekin, Şivekar Tınar, Zehra Adıbelli. Ultrasonographic Diagnosis of Fetal Structural Abnormalities in Prenatal Screening At 11–14 weeks. Journal of Diagnostic And Interventional Radiology; 2009.15 (3): 221-225.
19. Fadda GM, Capobianco G, Balata A, Litta P, Ambrosini G, D'Antona D, Cosmi E, Dessole S. Routine second trimester ultrasound screening for prenatal detection of fetal malformations in Sassari University Hospital, Italy: 23 years of experience in 42,256 pregnancies. European Journal of Obstetrics, Gynecology, and Reproductive Biology;2009. 144 (2): 110-114
20. Carlos Noronha Neto, Alex Sandro Rolland de Souza, Olímpio Barbosa de Moraes Filho, Adriana Mota Bione Noronha. Validation of ultrasound diagnosis of fetal anomalies at a specialist center. Revista da Associação Médica Brasileira; 2009.55 (5): 541-546.
21. S Singh, GS Shergill, A Singh, R Chander. Role of Ultrasound In Detection of Antenatal Fetal Malformations. Ind J Radiol Imag;2006. 16:4:831-834
22. Shama Munim, Salva Nadeem, Nadya Ali Khuwaja. The Accuracy of Ultrasound in the Diagnosis of Congenital Abnormalities. J Pak Med Assoc. 2006. 56(1): 16-18.
23. McAuliffe FM, Fong KW, Toi A, Chitayat D, Keating S, Johnson JA. Ultrasound detection of fetal anomalies in conjunction with first-trimester nuchal translucency screening: a feasibility study. Am J Obstet Gynecol. 2005. 193 (3): 1260-5
24. Min Chen, Yung Hang Lam, Chin Peng Lee, Mary Hoi Yin Tang. Ultrasound screening of fetal structural abnormalities at 12 to 14 weeks in Hong Kong. Prenat Diagn . 2004. 24: 92–97.