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FIRST TRIMESTER ULTRASOUND: ADDITION OF ANATOMICAL SCREENING ADDS VALUE TO THE EXAMINATION: A RETROSPECTIVE CASE SERIES

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ABSTRACT: CONTEXT: First trimester scans have been performed for measurement of crown rump length and nuchal translucency, for combined screening. Now the scanning protocol is broadened to include a full anatomic screening of the fetus. The introduction of cell free DNA (cfDNA) to prenatal diagnosis for aneuploidy raises questions to the continued use of first trimester scanning as this test, has a higher sensitivity and specificity. **AIMS:** The aim of this study was to demonstrate the detection of fetal and maternal findings in first trimester ultrasound, which would influence outcome or alter management of the pregnancy. **SETTINGS AND DESIGN:** The study was a retrospective analysis of the first trimester scans performed in the Fetal Medicine Division of the Obstetrics and Gynecology department of a tertiary referral center for a one year period, from January 1, 2014, to December 31, 2014. **MATERIALS AND METHODS:** All first trimester scans performed in the unit were studied regardless of number of fetuses or maternal factors. A total of 14429 obstetric scans were performed, of which 4421 were between 11–14 weeks gestation. The details and outcome of cases were obtained from the institution database or from the patients telephonically if they delivered at another institution. 38 (0.8%) cases were abnormal. 11(29%) were asymptomatic embryonic demise and 4 were gynaecological problems. 22 cases (58%) were structural anomalies or increased nuchal translucency (>3.5mm). Of these 21 cases in whom follow up was obtained, 19 resulted in termination of pregnancy. In 4 of 6 cases of isolated increased nuchal translucency, karyotype was done and revealed 3 (75%) to be abnormal. In the other case, the karyotype is normal and the pregnancy is now ongoing. One patient who deferred direct testing delivered a neonate confirmed to be trisomy 21. **CONCLUSION:** Use of ultrasound in the first trimester has moved beyond aneuploidy screening with detailed guidelines available for anatomical screening. The first trimester ultrasound continues to be useful despite advances in aneuploidy detection strategies, as it offers an opportunity for the detection of major structural anomalies and enables early termination of pregnancy if required with less morbidity to the mother.

KEYWORDS: First trimester, anomaly, transvaginal scan, Nuchal translucency.

INTRODUCTION: Prenatal imaging has grown in use beyond second trimester diagnosis of fetal anomalies or third trimester diagnosis of fetal well-being and growth. First trimester ultrasound examination has been used for the past 25 years as an adjunct to biochemistry for the detection of aneuploidy commonly the most frequently occurring anomalies such as trisomy 21.¹ First-trimester combined biochemical screening can detect up to 95% of fetuses with trisomy 21 and around 78% to 90% of other trisomies (with a false positive rate of 5%)² As an addition to the imaging of crown rump length and nuchal translucency, the increased use of trans-vaginal scan and the improved resolution of ultrasound machines has increased the detection of anomalies in the first trimester. However, with the introduction and gradual increase in the use of cell free DNA in prenatal diagnosis

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of chromosomal abnormality, there may be questions whether ultrasound examination 11–14 week window period continues to have use.³

MATERIALS AND METHODS: The aim of this study was to see the benefits of first trimester scanning in the detection of fetal and maternal findings, which would influence outcome or alter management of the pregnancy.

This was a retrospective case series of all consecutive patients referred to a tertiary care centre and teaching college, fetal medicine unit for a one year period, from January 1, 2014, to December 31, 2014. In our unit, first trimester scanning is offered to all patients who book prior to 14 weeks gestation. Crown rump length and Nuchal translucency are measured during the scan and in combination with maternal biochemistry BHcG and PAPP-A, used for aneuploidy screening as per standard protocols. In addition to this basic imaging, complete anatomical screening is performed as per ISUOG (2013) guidelines.⁴

Patients were included in the study if there was at least 1 live fetus with a CRL between 44 and 84 mm. The examination was carried out by 4 doctors trained and certified in nuchal translucency measurement. All fetuses were initially scanned transabdominally and transvaginal scans were performed if required to complete anatomic screening.

The scanning sections included the CRL (crown rump length), Nuchal translucency (NT) (Fig. 1) and nasal bone which were used for combined biochemical screening along with maternal β HcG and PAPP-A. The anatomical screening included lateral ventricles and Biparietal diameter plane of the head, both orbits with lens, pre-maxillary triangle,^{5,6} all three segments of the four limbs, hands and feet, the axial sections of the abdomen and thorax for situs, colour interrogation for cardiac ventricles and great vessels. The presence of stomach, bladder, cord insertion and number of cord vessels was also interrogated.⁴ Pulse Doppler was used to look for tricuspid valve for presence of regurgitation, and ductus venosus wave form patterns. These were not included in the estimation of aneuploidy risk. If the NT was greater than 3.5mm or any questionable finding was seen, the senior fetal medicine specialist examined the patient and counseled the family.

The patients who had ductus venosus reversal or tricuspid regurgitation in isolation were reviewed at 16 weeks. A complete examination of the fetus including detailed cardiac evaluation was performed at the time.

All first trimester scans performed in the unit were studied regardless of number of fetuses or maternal factors. The total number of obstetric scans performed was 14429, of which 3421 were First trimester scans between 11 – 14 weeks gestation. The number of cases performed and the details were obtained from the database software Sonocare ® and the primary data collation was done on Microsoft Excel. Pregnancy outcomes of cases determined to be abnormal were obtained from the institution database and from the patients telephonically if they chose to deliver at another institution. In the present analysis, the screen positive cases seen in combined biochemistry and absent nasal bone outcomes were not analyzed.

FINDINGS: The number of cases which were found to be abnormal was 38 (0.8%) and of these 11 (29%) were asymptomatic embryonic demise or anembryonic pregnancies. (Table 1) These women could consult with their doctors and manage the failed pregnancy accordingly. One case was found to be a scar pregnancy, that is, an implantation of pregnancy in the uterine myometrium within the

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caesarean scar. This was diagnosed by the presence of a gestational sac seen embedded within the myometrium in the anterior wall of the uterus and ultrasound guided curettage was performed after uterine artery embolization. The patient made a full recovery.

Of the remaining, four were complicated by gynaecological problems, two of which were large fibroids and one of which was a dermoid cyst. One patient, who had a large fibroid measuring 8 x 8cms, had two episodes of fever and pain suggestive of red degeneration. These were conservatively managed the patient delivered uneventfully at term. A short cervix was diagnosed in one patient (2cms) in the first trimester scan and the patient underwent cervical encirclage. She underwent PPRM (preterm pre-labour rupture of membranes at 28 weeks and was delivered due to signs of chorio-amnionitis. The neonate required intensive care but was discharged well after 6 weeks of preterm care. The fourth patient had an ovarian cyst 10 x 10cms which was clear and suggestive of a simple cyst. The patient declined aspiration and later underwent a laparoscopic resection of the cyst when torsion occurred at 16 weeks. The remainder of the pregnancy was uneventful.

After excluding these cases, 22 cases remained which had an antenatal diagnosis of fetal conditions which would affect pregnancy outcome. The details of the ultrasound findings are listed in Table 2. As mentioned earlier, detailed evaluation of fetal anatomy was carried out as per ISUOG guidelines and trans-vaginal scanning was used if required to ensure completion of anatomical screening.⁴

Neural tube defects are the leading cause of anomalies, and this was seen again in our case series. There were 3 cases of open neural tube defects and one anencephaly (Fig. 2). Open neural tube defects were diagnosed due to the presence of small cystic swelling at the region of the spine in one case, who also had an increased nuchal translucency and obliteration of the intracranial translucency (Fig. 3).⁷ All four cases underwent termination of pregnancy. Ventriculomegaly was suspected in two cases at the 11 – 14 weeks scan with a small choroid plexus seen with large amount of fluid surrounding it, rather than the well-fitting “butterfly” choroid plexus.⁸ Quantification of the choroid plexus was not performed and both patients refused karyotype. Both were called back for and evaluation at 15 – 16 weeks and the findings were confirmed at the time. Both fetuses showed severe ventriculomegaly at second examination at 16 and 20 weeks respectively. The spine and posterior fossa were normal in both cases. Due to the early onset and severe findings both patients opted for termination of pregnancy and, despite counseling, did not opt for further examination which if performed would have aided in establishing aetiology.

Cardiac imaging was performed in all cases, and the images taken were abdominal and cardiac situs followed by cardiac ventricular inflows and arches demonstrated in axial sections of the fetus using colour or power Doppler. Imaging of the two equal inflows into the ventricles during diastole and the outflows which were demonstrated by aortic and ductal arch were carried out by transvaginal or transabdominal scanning depending on crown rump length (CRL) and fetal position. We had 100% detection of cardiac anomalies with no cases which had undergone first trimester scanning being discovered to have a cardiac anomaly later in pregnancy. Of the 3 cardiac cases which were detected, one had an increased nuchal translucency. Increased nuchal translucency is associated with increased risk of cardiac anomalies and a finding of increased NT should prompt a detailed cardiac examination. However our finding of cardiac defects in the face of normal NT argues in favour of routine anatomical screening of fetuses with regard to cardiac screening even in the absence of increased nuchal translucency. Cardiac anomalies detected were counselled regarding the need for

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invasive testing for karyotype and were followed with a scan at 16-17 weeks to confirm the diagnosis. One case of truncus arteriosus and one of tetralogy of Fallot were diagnosed by 16 weeks scan following suspicion at first trimester scan.

Two cases of megacystis were seen. A cystic area seen in the fetal pelvis in the midline with the two umbilical arteries seen on either side was defined as the bladder. One fetus had a very large bladder 20mm in size with echogenic kidney seen on transvaginal examination. As this was evidence of lower urinary tract obstruction (LUTO) diagnosed very early in pregnancy with a poor outcome, termination of pregnancy was opted for. The other patient was a low risk primigravida, who was married (non-consanguineous) for 4 months. There was no history of maternal medical comorbidities. The scan findings were apparently normal on a midsagittal view except for a megacystis measuring 8mm. The anatomical screening revealed that the lower limbs were not moving relative to each other and at the knee joint. 3D transvaginal scanning confirmed the diagnosis of symmelia. Due to the poor prognosis of this condition, the family opted for termination of pregnancy. Post abortal findings confirmed the presence of fused limbs and absent external genitalia. Another case showed bilateral talipes and short long bones with all parameters at less than first centile for the period of gestation. As this was a second degree consanguineous marriage and there had been two previous pregnancy terminations for skeletal dysplasia, a possible genetic association was suspected, which would likely be a recessive condition with 25% chance of recurrence in each subsequent pregnancy. The couple was informed of the facts and elected to terminate the pregnancy. Perinatal examination including fetogram when compared with that of the previous sibling revealed features suggestive of short rib polydactyly syndrome.

Another case which was diagnosed was a large omphalocele, with liver and small bowel as content. As it was a large defect, the possible need for staged repair was discussed. The couple declined invasive testing and opted for termination of pregnancy.

An analysis of cases in whom diagnosis was not made in first trimester and was subsequently made in second trimester was also made. Among all the cases who had undergone scanning, two cases developed findings later. One was a patient with a BMI of 32, in whom an examination at CRL of 54mm showed intracranial translucency was not delineated. Imaging of the spine did not reveal any findings, at the time but an open neural defect was seen on a subsequent scan. Following this, the unit protocol was altered to include trans-vaginal scanning of fetal spine for all patients in whom intracranial translucency could not be seen on the mid sagittal view. Intracranial translucency is the fetal developing fourth ventricle which is seen on mid sagittal section in the 11 – 14 weeks as a hypo-echoic lie seen between the midbrain and the developing cisterna magna. The non- visualization of intracranial translucency has been described as a pointer for the detection of open neural tube defects in first trimester scan.

The other patient had a normal spine at FTS scan and second trimester imaging revealed a sacro-coccygeal teratoma. This is a slow growing tumour which could have developed after the first trimester scan. It was of a purely cystic type and was avascular and less than 20mm in size. The spine was completely normal in the second trimester imaging also. However despite detailing the optimal prognosis the family opted for termination of pregnancy.

Among the 22 cases which showed abnormal fetal findings, 20 (90%) were lethal or severe anomalies which would have posed risk of permanent damage and severe morbidity.

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The cases with increased nuchal translucency were 10 in number. Of these, 4 had associated findings as shown in Table 2. Those (N=6) with isolated increased nuchal translucency (NT) had NT values ranging from 3.6mm to 5.9mm with a median of 4.8mm. The families were counselled regarding the absence of any other anomalies and the possibility of chromosomal, genetic association. Direct testing to assure regarding chromosomal normalcy was recommended followed by early fetal ECHO at 16 weeks and a targeted scan for fetal anomalies at 20 weeks. Of the 6 patients, 4 opted for direct testing, of which two were trisomy 21, and one was trisomy 18. One pregnancy with isolated increased nuchal translucency had a normal karyotype and normal targeted scan and is currently an ongoing pregnancy at 23 weeks at the time of writing. Here, the diagnosis of chromosomal normalcy has enabled the couple to continue on with the pregnancy. Most invasive procedures were performed as chorion villus sampling and in a few cases where the family required more time to decide the course of action an amniocentesis was performed. All other cases with proven aneuploidy underwent termination of pregnancy. Of the two with isolated increased nuchal translucency, one patient who was counselled and deferred invasive testing had delivery of a neonate with trisomy 21 which was confirmed on karyotype. The other patient was lost to follow up.

The vast majority of diagnoses made are of the more severe conditions which are either lethal or severely debilitating, for which reason, the management has tended to be towards termination. This also reflects that when an earlier diagnosis of a structural anomaly is made, the couple has wider options and time for discussion and decision. In addition, diagnosis of some conditions such as symmelia is difficult in later pregnancy as there is anhydramnios or severe oligohydramnios, due to bladder outlet obstruction. In the absence of adequate liquor, limb anomalies may be entirely missed. In an earlier gestational age as the fetal renal contribution to amniotic fluid is relatively less and amniotic fluid formation is due to transudation from the amniotic membranes, the examination of the limbs is facilitated.

DISCUSSION: The diagnosis of fetal anomalies has been studied by several investigators. As early as 1996, Nicholaides et al determined that anencephaly could be detected by ultrasound and that acrania rather than absence of the cranial vault and cerebral hemispheres which is the classical finding of the second trimester should be looked for.⁸ In a similar manner posterior fossa examination of intracranial translucency has been described for the early detection of open neural tube defects.⁷ The detection of sirenomelia which is similar to symmelia seen in our case series has been described in another article.² Increased nuchal translucency is associated with increased incidence of chromosomal anomalies. However, this does not mean that all fetuses with a nuchal translucency within normal limits will be structurally normal. The benefits of a first-trimester anomaly scan including fetal echocardiography performed on fetuses with a “normal” NT was described by Becker et al,⁹ who detected 58.6% of major anomalies in this population of fetuses. In this manner, screening for structural anomalies has been gradually improved upon by various investigators until cardiac screening has also been included in the armamentarium.⁴

In our case series, the detection was more than 90% for major anomalies. In a large study, it was discussed that major anomalies are seen in 1.7% of cases in first trimester screening and hence first trimester screening for anomalies and cardiac anomalies should be performed to benefit the pregnant patient.⁹ One case of open neural tube defect seen at CRL of 55mm was not detected and was seen at the next scan. Following this the protocol was made more stringent to include

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transvaginal examination of all fetuses showing obliteration of the intracranial translucency at the first trimester scan.⁸ There were no other major anomalies missed on first trimester scan. Evolving anomalies such as ventriculomegaly and were also suspected on first trimester scan and confirmed at 16 weeks.

The detection of major anomalies resulted in termination of pregnancy in over 90% of the cases. This lays emphasis on the need for protocol based screening methods for the detection and for the certainty of the diagnosis in this period of gestation.²

CONCLUSION: Ultrasound examination performed in a protocol based manner at the 11 – 14 week period offers an opportunity for early diagnosis and management of many of the major anomalies which can be seen in fetal life. It paves the way for karyotypic diagnosis which changes the pregnancy options when the test is positive, and offers the couple the option of an early termination of pregnancy should they opt for the same. There is a need for continued use of this modality and to improve the anatomical screening of the fetus at this scan. Many of the major anomalies can be thus diagnosed or suspected and confirmed at 16 weeks. Thus in many ways, the anomaly scan can be moved to the 11 – 14 week period for the major and lethal anomalies. This does not negate the importance of the targeted scan at 18 – 20 weeks but is an additional tool both for early diagnosis of major anomalies and for reassurance of the family which may have had such a diagnosis in a prior pregnancy.

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Fig. 1: Nomal Nuchal Translucency

Fig. 2: Anencephaly

Fig. 3: Obliterated IT in open spinal defect

Fig. 4: Megacystis

Fig. 5: Symmelia

Fig. 6: Omphalocele

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Fig. 7: Increased Nuchal Translucency

System	Diagnosis	Number of cases	Increased Nuchal translucency seen associated	Outcome
Central nervous system	Open neural tube defects	3	1	Termination of pregnancy
	Anencephaly	1	0	Termination of pregnancy
	Ventriculomegaly	1	0	Repeat scan at 17 weeks – gross ventriculomegaly – Termination opted
		1	0	Repeat scan 20 weeks ventriculomegaly severe 23mm – Termination opted
Renal system	Bladder outlet obstruction	1	0	Termination of pregnancy
Cardiac	Outflow abnormalities	2	1	Termination of pregnancy – 1
				Post CVS abortion - 1
	AVSD	1	0	Termination of pregnancy
Gastro-intestinal tract	Omphalocele	1	0	Termination of pregnancy
Skeletal	Sirenomelia	1	0	Termination of pregnancy
	Skeletal dysplasia	1	1	Termination of pregnancy
Marker	Increased Nuchal translucency (>3.5mm)	10		Ref. Table 2

Table I: System wise diagnosis of anomalies seen in First trimester scan

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Table 2: Increased Nuchal translucency Cases

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