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Fetal Anatomy on the 1st Trimester of Pregnancy

A Antsaklis, A Souka

INTRODUCTION

First trimester ultrasound scan was initially used to date the pregnancy. In the last 15 years technological progress and in particular the introduction of the transvaginal approach made possible the detailed examination of the fetal anatomy in the first trimester the diagnosis of structural defects.

In the decade a number of studies have shown that nuchal translucency (the accumulation of fluid in the nuchal area) can be measured by ultrasound at 11-14 weeks. Nuchal translucency measuremement is a sensitive and accurate screening test for the diagnosis of chromosomal abnormalties yielding a sensitivity of about 75% for a 5% screen positive rate.[1] The introduction of first trimester biochemical markers free beta-hCG and PAPP-A has increased the sensitivity to about 90% for the same screen positive rate.[2]

Increased nuchal translucency at 11-14 weeks has been associated with structural defects and in particular cardiac defects and a wide range of genetic syndromes.[3] Possible pathophysiological mechanisms include cardiac dysfunction, venous stasis, anomalous or delayed development of the lymphatic vessels of the neck, abnormal collagen biosynthesis, fetal anemia and congenital infections.

The majority of the fetal organs can be visualized in the first trimester and transvaginal scanning has greatly increased our ability to examine the first trimester fetus.

Using ultrasound scanning in the first trimester we can accurately date the pregnancy, establish fetal viability and ascertain chorionicity in multiple pregnancies. At 11-14 weeks we can estimate the risk of chromosomal defect by nuchal translucency measurement and examine fetal anatomy.

THE NORMAL FIRST TRIMESTER FETUS

Several ultrasound studies[4-28] using mainly the transvaginal approach at 4-12 weeks of gestation describe the development of the normal fetus as follows:

The 4th week

The gestational sac is visible from about 4 weeks and 3 days as a hypoechoic, ring-like 2-3mm structure surrounded by a hyperechoic rim. Further details within the sac cannot yet be defined. The sac represents the chorionic cavity and is typically located in the upper part of the decidualised endometrium in an eccentric position.

The 5th week

The yolk sac becomes visible as the first structure within the sac at about 5 weeks and is always present at 5 weeks and 4 days. At the end of the 5th week the fetal pole measuring 2-3mm can be seen by the yolk sac and heart motion may be identified. At this stage the fetal heart rate is about 100 beats per minute.

The 6th week

At 6 weeks the embryo measures (crown-rump-length, CRL) 4-8mm. The fetal pole, the yolk sac and the heart motion are always visible. Heart activity should always be seen in embryos of 5mm (6 weeks and 4 days) or more. The gestational sac contains two fluid-filled cavities: the ceolomic (chorionic) cavity with the yolk sac and the considerably smaller amniotic cavity with the fetal pole. The two cavities are separated by a thin membrane surrounding the embryo, the amniotic membrane. At the end of the 6th week the cavity of the rhombencephalon becomes visible as a small hypoechogenic area at the cephalic part of the fetal pole.

The 7th week

At 7 weeks the crown-rump-length is 9-14mm and the mean heart rate is about 130 beats per minute. The amniotic cavity starts expanding rapidly. The head can be distinguished from the body and hypoechogenic areas (brain vesicles) appear in the developing brain at the cephalic end of the embryo. The cavity of the rhombencephalon that will eventually form the pons and the cerebellum can always be identified at 7 weeks as a rhomboid, hypoechoic area at the cranial pole of the embryo. At this stage the rhombencephalon is larger than the developing hemispheres. The small cavities of the hemispheres originating from the dividing Y-shaped telencephalon, the diencephalon (that will form the thalami, hypothalamus and the 3rd ventricle) and the mesencephalon (that will later form the nuclei and the aqueduct of Sylvius) may be identifiable.

The umbilical cord is short and appears wider and hyperechogenic at the point of the insertion in the abdomen; this is the first sign of bowel herniation into the cord. The lower limb buds can vaguely be depicted.

The 8th week

At 8 weeks the crown-rump-length is 15-22 mm, the brain vesicles are more prominent and the choroid plexuses can be visualised as small hyperechogenic areas. The rhombencephalon is still the largest cavity lying on top of the brain. There is a broad connection between the lateral ventricles, the diencephalon and the mesencephalon. Fetal heart rate is about 160 beats per minute and the heart occupies more than 50% of the thoracic cavity. Atria and ventricles are sometimes visible at the end of the 8th week. The abdominal cavity is fully occupied by the liver anteriorly and the stomach dorsally while the intestine is herniated into the umbilical cord. Fluid in the stomach can occasionally be seen towards the end of the 8th week probably as a product of the gastric epithelium, since swallowing movements only start at 11 weeks. The outlines of the skull, spine and ribs can vaguely be seen. The limbs appear as short echogenic outgrowths and the first body movements become visible during the 8th week.

The 9th week

At 9 weeks the crown-rump-length is 23-31mm. The amniotic cavity is now larger than the coelomic cavity and occupies most of the sac volume. The fetal body becomes ellipsoid with the head being diproportionally big and the soles of the feet touch in the midline. The choroid plexuses are obvious and occupy almost fully the lateral ventricles. The cortex is thin and hypoechoic. The cereberall hemispheres become visible and are clearly separated. The connection between the mesencephalon and the third ventricle becomes narrower. The fetal heart rate reaches a peak of about 175 beats per minute. Bowel herniation is visible in all fetuses. The first ossification centers can be seen at the mandible and clavicle. Limb movements can be identified.

THE POST-EMBRYONIC PERIOD (10-11 WEEKS)

During the post-embryonic period the crown-rump-length is 32-54mm. The fetus aquires human shape and the fetal body becomes longer although the head is still disproportionally large with a prominent forehead and a flat occiput. The cereberall

hemispheres start being detectable during the 9th week. Ossification starts from the occipital bone at 10 weeks. The cortex is about 1mm thick at the end of the first timester. The lateral ventricles occupy completely the anterior part of the head and cover the diencephalon. The mesencephalon gradually moves towards the middle of the brain, the 3rd ventricle, after a transient increase, becomes narrow and the cerebellar hemispheres fuse in the midline 11-12 weeks. Fetal heart rate drops to about 165 beats per minute at the end of the 11th week. The motion of the atrioventricular valves and the atial and ventricular septa may be visible at 10 weeks. All cardiac structures can be visualized at the end of the 11th week. Starting from the end of the 8th week the small bowel herniates into the umbilical cord and gives the sonographic appearance of a hyperechogenic mass at the insertion of the cord. Maximum herniation of the bowel is detectable at the beginning of the 10th week whereas the return of the bowel in the abdominal cavity begins at 10 weeks and 4 days and is usually completed at 11 weeks and 5 days. In 75% of embryos the stomach is visible before the 10th week. The ossification centers of the spine and the long bones start being visible at 10 weeks. The ossification of the spine begins at the level of the cervical vertebrae and spreads caudally to the thoracic and lumbosacral areas during weeks 12 to 13. Ossification of the metacarpals and metatarsals can be identified at 12 weeks. The digits and sometimes the toes become visible from 11 weeks.

FETAL ANATOMY AT 11-14 WEEKS

Although in the general population structural defects are relatively common (3-5%) and cardiac defects the commonest amongst them, few studies have addressed the issue of fetal anatomy in low risk populations as part of the 11-14 weeks scan.[20,29-34] Visualization of the cardiac anatomy at this gestational period has been reported from specialists in fetal echocardiography and has been mainly limited to high risk pregnancies.[35- 45]

Two studies[20,46] examining fetal anatomy at 11-14 weeks have used the following protocol:

1. Skull and brain: examination of the completeness of the skull, the presence of the midline in the brain and the butterfly shape of the choroid plexuses.
2. Face: examination of the orbits and lenses and the view of the fetal profile.
3. Spine: examination of the alignment of the vertebrae and the skin covering the spine.
4. Heart: examination of the four-chamber view and the great vessels.
5. Stomach: visualization of the stomach as a hypoechoic structure at the left upper abdomen.
6. Abdomen: examination of the umbilical cord insertion into the abdominal wall.
7. Kidneys: visualization of the kidneys as hyperechoic structures with a hypoechoic center laterally to the spine.
8. Bladder: visualization of the bladder as a hypoechoic structure in the fetal pelvis.
9. Extremities: examination of the long bones, fingers, toes and the movement and posture of the joints.

In a study of 1,144 fetuses examined by at 11-14 weeks with a combination of the transabdominal and transvaginal route full check of the fetal anatomy was achieved in 48% of the fetuses, whereas non-cardiac anatomy was visualized in 86% of the fetuses.[46] Successful visualization of the fetal organs depended on crown-rump length.. The use of the transvaginal approach increased successful examination of the fetal anatomy from 72% to 86% of the fetuses. Transvaginal scanning was particularly helpful in examining the face, kidneys and bladder.

In a screening study for structural abnormalities at 11-14 weeks using transvaginal ultrasound, fetal anatomy (not including face and heart) was seen in 94% of the cases.[30] Similarly in an anatomical survey of 298 fetuses at 12^{+0} to 13^{+6} weeks of gestation Braithwaite et al were able to complete the examination of the fetal anatomy, including the four-chamber view, in 95% of the fetuses.[20] With the combination of the transabdominal and transvaginal

route the four-chamber view of the heart was seen in 97% of the fetuses, the bladder in 98%, the head, brain and kidneys in 99% and the remaining organs (diaphragm, stomach, abdominal wall, spine and extremities) in 100% of the fetuses. The use of the transvaginal approach increased successful examination of the fetal anatomy from 72% to 95%.[20] In both studies the factors influencing visualization of the fetal organs were gestation, maternal habitus and uterine position and the authors stress the contribution of the transvaginal ultrasound in completing the examination of the fetus.

A few studies have addressed the issue of visualizing the four-chamber view and the outflow tracts at 11-14 weeks.[36-39,44,46,47] Examination of the fetal heart at this early gestation is still mainly restricted to high-risk patients and performed in specialized centers by experts in fetal echocardiography. Visualization rates of the four-chamber view improved with gestation, remaining poor before 11 weeks and increasing to more than 90% during the 12^{th} and 13^{th} week. Similarly visualization of the outflow tracts was achieved in the majority of the fetuses examined between 12^{+0} and 13^{+6} weeks of gestation. Only two studies have examined cardiac anatomy as part of the routine 11-14 weeks scan.[20,46] In the first study of 298 women examination was performed at 12^{+0} to 13^{+6} weeks and the four-chamber view was seen in 76% of fetuses transabdominally, 95% transvaginally and 97% using a combined approach. Outflow tracts were not examined.[20] In the second study 1,144 women were examined at 11-13^{+6} weeks of gestation (CRL 45-82 mm). Complete cardiac anatomy was seen in 50% of fetuses, with visualization of the four-chamber view in 87% of cases and of the three-vessel view in 50% of cases.

STUDIES SCREENING FOR STRUCTURAL DEFECTS BY FIRST TRIMESTER ULTRASOUND

Three studies on a total of 12,327 pregnancies have examined the impact of assessing fetal anatomy in the first trimester on the detection rate of structural defects. The differences in the detection rates can mainly be attributed to differences in protocols, definition and postnatal ascertainment of anomalies. The study with the lowest detection rate reports on all (major and minor) anomalies; if only major anomalies were included the first trimester scan sensitivity would be 50.8% and the overall ultrasound scan sensitivity 78.8%.[34] Detection rates in the two other studies have been calculated excluding nuchal anomalies. The majority of abnormalities diagnosed in the second and third trimester would not be detectable in the first trimester including central nervous system defects (microcephaly, ventriculomegaly, brain atrophy, Dandy-Walker malformation, cerebellar asymmetry), cardiac defects (tetralogy of Fallot, hypoplastic left heart, ventricular septal defects), renal defects (hydronephrosis, multicystic dysplastic kidneys) and gastro-intestinal defects (bowel obstruction). However, it is likely that at least some of the cases of neural tube defects and cardiac defects and probably all cases of abdominal wall defects and limb reduction defects will in the future be diagnosed in the first trimester. These studies have shown that the first trimester scan can detect more than one third of the major structural anomalies, including lethal anomalies or those leading to severe handicap (anencephaly, holoprosencephaly, body stalk anomaly).

In conclusion, examination of the fetal anatomy is feasible during the routine 11-14 weeks scan and the completeness of the examination mainly depends on maternal habitus and gestational age. It is clear that the optimal gestation for examining both cardiac and non-cardiac anatomy starts from the beginning of the 12th week to the end of the 13th week of gestation. Access to the transvaginal approach is important in completing the examination.

With the modern trend of shifting prenatal diagnosis at the earliest possible gestation and the advancing technology, it is not difficult to see the 11-14 weeks scan becoming a first mini-anomaly scan with the aim to diagnose the severest structural anomalies, thus giving the parents earlier reassurance about the well being of their fetus.

STRUCTURAL DEFECTS AT 11-14 WEEKS

Central nervous system defects

Acrania/anencephaly (birth prevalence 1 in 1,000)

The diagnosis of anencephaly in the second and third trimesters of the pregnancy is based on the absence of cranium and cerebral hemispheres. Animal studies have shown that the absence of the skull leads to progressive degeneration and destruction of the brain tissue. Similarly, ultrasound studies have shown that in human embrya acrania progresses to exencephaly and anencephaly.[49-57] Acrania, meaning the absence of the skull (cranium) is the hallmark of anencephaly in the first trimester. The brain may show signs of degeneration or even appear normal. Several authors have described cases of anencephaly from as early as 9 weeks; the appearance of the brain varies from echogenic and disorganized with abnormal shape of the skull and head circumferance smaller than the abdominal circumferance to completely normal.[49,50,54,55,56]. In the four screening studies for structural defects by first trimester ultrasound all cases of anencephaly were diagnosed in the first trimester.[30,32,34,48.] In two screening studies for chromosomal abnormalities by nuchal translucency measurement on a total of 6,861 pregnancies, all 7 anencephalic fetuses were correctly identified in the first trimester.[51,57] In another screening study of about 54,000 pregnancies there were 47 cases of anencephaly.[52] In the first phase of the study the sensitivity of the first trimester scan for diagnosing anencephaly was 74% (23 of 31 cases) but this increased to 100% (16 of 16 cases) in the second phase when sonographers were instructed to look for the specific signs of anencephaly at this early gestation.

Holoprosencephaly (birth prevalence 1 in 5,000)

This rare but severe defect covers a spectrum of conditions where there is a defect in the division of the prosencephalon, the frontal part of the brain. There are 3 types (lobar, semilobar, and alobar holoprosencephaly) depending on the degree of fusion of the prosencephalon. In the lobar type the ventricles and thalami are devided but the cavum septum pellucidum is absent. In the semilobar type the lateral ventricles and thalami are only partially separated and in the alobar type there is complete fusion of the ventricles with a large monoventricle and fused thalami. The defect is strongly related to chromosomal abnormalities (particularly trisomy 13 and 18) and other structural defects (mainly facial clefts). Holoprosencephaly was present in 24% of the 46 fetuses with trisomy 13 at 10-14 weeks described by Snidjers et al.[58] The diagnosis of the alobar type has been reported in the first trimester based on the visualization of a single ventricle and the fusion of the thalami.[59-67] In the earliest report of alobar holoprosencephaly Blaas et al diagnosed the defect at 9 weeks and 2 days (CRL 22 mm).[66] There was a small monoventricular endbrain behind the forhead and a proboscis. The diagnosis was confirmed a week later. In four screening studies for structural defects by first trimester ultasound on a total of about 9,500 fetuses there were four cases of holoprosencephaly and three were diagnosed in the first trimester.[30,33,34,46] Spina bifida (birth prevalence 1 in 1,000) Spina bifida is the result of failed closure of the neural tube normally occurring during the 6th week whereas the ossification of the spine begins at 10 weeks. The hallmarks of the diagnosis of spina bifida in the second trimester are the scalloping of the frontal bones of the skull (lemon sign) and the displacement of the cerbellum (Arnold-Chiari malformation, banana sign).

The diagnosis of spina bifida has been reported in the first trimester from as early as 9 weeks.[68-72] Blaas et al identified the defects in three embryos from high-risk pregnancies at 9 weeks of gestation (CRL 22-28 mm).[71] The authors used a combination of two and three-dimensional transvaginal ultrasound to examine the spine. They note that the scalloping of the frontal bones and the Arnold Chiari malformation did not occur before 12 weeks.

In four screening studies for structural defects by first trimester ultrasound there were 12 cases of spina bifida on a total of about 9,500 fetuses and 6 were diagnosed in the first trimester.[30,33,34,46] It is of interest that at least in some cases the lemon-sign and banana-sign are present in the first trimester.

Heart defects

Congenital heart defects are amongst the commonest structural defects with a birth prevalence of 5-10 per 1,000 births. Approximately one half of those will need medical or surgical treatment (major defects) and the other half will be asymptomatic (minor defects). First trimester diagnosis of several cardiac abnormalities has been reported in the first trimester such as ectopia cordis, common truncus arteriosus, dextrocardia, monoventricular heart, Uhl disease, atrioventricular septal defect and ventricular septal defect.[73-77]

In a screening study of 114 pregnancies at risk for cardiac defects by transvaginal ultrasound at 11-16 weeks of gestation there were 6 abnormal fetuses scanned at 11-14 weeks and the defect was diagnosed in five (sensitivity 83%).[78] Nuchal fluid was increased in four fetuses. In another small study of 15 high-risk fetuses scanned at 12 to 13^{+6} weeks.[79] The first trimester scans were normal in 10 cases and inconclusive in 4 cases; one of the two cardiac anomalies (left isomerism) was identified at 12 weeks and a muscular ventricular septal defect was diagnosed postnatally (sensitivity 83%). Haak et al performed first trimester transvaginal fetal echocardiography in 54 fetuses with increased nuchal translucency and reported sensitivity and specificity 88% and 97% respectively.43 Another study on 241 fetuses with increased nuchal translucency at 11-14 weeks (crown-rump length 40-85mm) identified 28 of the 37 cardiac anomalies in the first trimester (sensitivity 76%).[80]

Screening studies for heart defects have so far been limited to high-risk pregnancies defined by family history, maternal disease (diabetes, epilepsy) or increased nuchal thickness and performed in the setting of fetal echocardiography units by experts in cardiac scanning, thus explaining the high sensitivities reported. There is a strong association of increased nuchal translucency with cardiac defects. A meta-analysis of screening studies reported that the detection rates for heart abnormalities were about 37% and 31% for NT cut-offs of 95th and 99th centiles respectively.[81] Fetal echocardiography, during first trimester if possible, should be included in the routine follow up of the fetuses with increased nuchal fluid.

Abdominal wall defects

Exomphalos (omphalocele, birth prevalence 1 in 4,000)

In exomphalos there is midline defect of the abdominal wall through which intrabdominal viscera herniated into a sac. The umbilical cord inserts at the apex of the sac. Herniation of the small bowel only is a normal step of the embryonic development and occurs between 8 and 10 weeks. The diagnosis of exomphalos is made if the bowel fails to return into the abdominal cavity by 11 weeks or if other viscera are herniated at any gestation.

Exomphalos is commonly associated with chromosomal abnormalities and syndromes. Chromosomal abnormalities, usually trisomy 18, are present in about half of the fetuses with exomphalos in the first trimester, one third of cases in the second trimester and about 15% at birth. Exomphalos may be part of an extended defect in the abdominal wall development. If the abnormality involves the cephalic fold it results in pentalogy of Cantrell (exomphalos, ectopia cordis, cardiac defects, diaphragmatic hernia, sternal cleft). If it involves the caudal fold it results in bladder or cloacal exstrophy, bowel atresia and vertebral defects.

Many cases with exomphalos have been diagnosed in the first trimester, the earliest case being at 11 weeks for exomphalos containing liver.[82-87] Van Zalen-Sprock et al reported on 14 cases with exomphalos at 11-14 weeks.[86] Nuchal fluid was increased in eight fetuses and seven of those were chromosomally abnormal. Exomphalos contained bowel only in fetuses with chromosomal abnormality. Liver was often present in the contents of the sac as well as bowel in the chromosomally normal ones. In a study of 622 high-risk patients there were two cases of exomphalos diagnosed in the first trimester.[31] In four screening studies on a total of about 9,500 patients there were two cases with exomphalos correctly identified in the first trimester. [30,33,34,46]

In a study screening for chromosomal defects at 10-14 weeks by nuchal translucency measurement in about 1,500 patients, the diagnosis of exomphalos was made at this early gestation.[57] Finally in another screening study for chromosomal defects at 11-14 åâäïìÜääò by nuchal translucency measurement, 15,726 fetuses were examined and there were 18 cases of exomphalos.[87] The karyotype was normal in seven fetuses; the remaining eleven fetuses had trisomy 18, 13 or triploidy. This study showed that the prevalence of exomphalos and the risk of chromosomal defects in affected fetuses is increased in the first trimester because of the strong association with lethal chromosomal anomalies.[87]

Gastroschisis (birth prevalence 1 in 4,000)

In gastroschisis there is a small defect of the abdominal wall laterally and usually on the right of the umbilical cord insertion through which herniation of the viscera (usually small bowel) occurs. Although gastroschisis is as common at birth as exomphalos there are few cases reported in the first timester.[88,89] Prenatal diagnosis is based on the visualization of loops of bowel floating in the amniotic fluid. Gastroschisis is rarely associated with chromosomal abnormalities.

Defects of the urinary tract

Megacystis

Dilatation of the urinary bladder in first trimester fetuses has been reported in association with obstructive uropathy (usually with posterior urethral valves or urethral atresia), severe renal abnormalities and prune belly syndrome. [90-97]

Liao et al studied 145 fetuses with bladder diameter more than or equal to 7mm at 10-14 weeks of gestation.[98] Fetuses with mild and moderate megacystis (bladder diameter 7-15mm) were chromosomall abnormal in 24% of cases; in the ones with normal karyotype spontaneous resolution occurred in 90% of cases but in 10% there was progressive evolution to obstructive uropathy and/or echogenic kidneys. Fetuses with severe bladder dilatation (more than 15mm) were chromosomally abnormal in 11% of cases but progression to obstructive uropathy was observed in all of the remaining chromosomally normal cases.

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Meckel-Gruber syndrome (birth prevalence 1 in 10,000)

This is a lethal, autosomal recessive condition with variable phenotypic expression. The typical features include encephalocele, bilateral polycystic kidneys and polydactyly. Other features may be present such as growth deficiency of prenatal origin, microcephaly, cerebral and cerebellar hypoplasia, anencephaly, Dandy-Walker malformation, absence of the corpus callosum, cleft lip and palate, renal agenesis, hypoplastic bladder, obstructive uropathy, syndactyly of the fingers and toes. Phenotype may vary from isolated polydactyly, which may represent the mild expression of the heterozygote state, to the full clinical manifestation of the disease. The diagnosis is based on ultrasound examination demonstrating encephalocele, usually occipital, enlarged, dysplastic, echogenic kidneys and polydactyly.

In three studies on a total of 15 pregnancies from high-risk families all eight affected fetuses were correctly diagnosed in the first trimester.[99-101] Another case of the syndrome from a low-risk couple was identified at 13 weeks in a study screening fro chromosomal abnormalities by nuchal translucency measurement.[100] In four screening studies on a on a total of about 9,500 patients there were two cases with Meckel-Gruber syndrome diagnosed in the first trimester. [30,33,34,46] These studies have shown that the phenotype of Meckel-Gruber syndrome is present from the first trimester and it is likely that the diagnosis is actually easier at this early gestation when amniotic fluid volume is still within normal

range rather than in the second trimester when oligohydramnios hinders detailed ultrasound examination.

Skeletal defects

Caudal regression syndrome (sirenomelia, birth prevalence 1 in 500,000)

This is a rare sporadic defect involving vertebral abnormalities varying from partial sacral agenesis to complete absence of the lumbosacral part of the spine. Sirenomelia, the extreme form of the syndrome presents with variable degrees of hypoplasia and fusion of the lower limbs and is associated with genitourinary, gastrointestinal, and central nervous system defects. Sirenomelia is about 250 more common in mothers with poorly controlled diabetes.

There are five cases of first trimester diagnosis of sirenomelia the earliest being at nine weeks of gestation.[102-105] In one case the mother was a diabetic presenting with ketoacidotic coma.[102] Features of the syndrome identifiable in the first trimester are crown-rump-length shorter than expected for the gestation, inability to visualize independently the lower limbs and abnormal movement of the lower limbs, intrabdominal cyst and increased nuchal tanslucecny.

Body stalk anomaly (birth prevalence 1 in 15,000)

This is a rare sporadic anomaly characterized by anterior wall defect, kyphoscoliosis, limb reduction and a rudimentary umbilical cord. Possible pathogenetic mechanisms included abnormal folding of the trilaminar embryo in the first 4 weeks of gestation, early rupture of the amniotic membrane and abnormal embryonic blood supply. In a study of about 106,000 pregnancies for chromosomal abnormalities by nuchal translucency measurement there were 14 cases of body stalk anomaly and all were diagnosed in the first trimester.[106] In all fetuses the lower part of the body was outside the amniotic sac, in the coelomic cavity, possible because of early rupture of the amniotic membrane. Nuchal translucency was increased in about 70% of cases and the karyotype was normal in all cases. Contrary to this theory, Paul et al presented a fetus with body stalk anomaly at 10 weeks of gestation (CRL 35 mm).[107] There were multiple anomalies including clefting defect of the cranium and brain, anterior wall defect, severe kyphoscoliosis and deformity of the lower limbs. The fetus was inside the amniotic sac, which appeared intact with no sonographic features of rupture. The earliest diagnosis of the defect is at 9 weeks of gestation; the fetus was partly outside the amniotic cavity, there was an abdominal wall defect and the lower limbs could not be seen.108 In four screening studies on a on a total of about 9,500 patients there was one fetus with body stalk anomaly diagnosed in the first trimester. [30,33,34,46]

Skeletal dysplasias

Skeletal dysplasias present with a prevalence of about 1 in 4,000. Although in some skeletal syndromes the clinical picture does not become obvious until the second or even the third trimester, there are skeletal defects that have been diagnosed in the first trimester and the commonest ultrasound features include limb shortening and bowing, limb fractures and hypomineralization of the skul and the spine and increased nuchal translucency.

Achondrogenesis (birth prevalence 1 in 40,000)

Achondrogenesis type II is a lethal, autosomal recessive skeletal dysplasia usually presenting with hydrops, severe shortening of the limbs, narrow thorax, and hypomineralization of the vertebral bodies but normal mineralization of the skull. In the rarer type I of the disease there is hypomineralisation of the skull and rib fractures.

There are two case reports on the first-trimester sonographic diagnosis of achondrogenesis type II in high-risk pregnancies; both fetuses had increased NT and short limbs that were abnormally positioned, with lack of movement.[109,110] There is also a report of fetus with achondrogenesis type I presenting at 13 weeks with increased NT, short limbs, small thorax and deficient ossification of the skull, vertebral bodies and pelvic bones.[111]

Hypophosphatasia (birth prevalence 1 in 100,000)

Hypophosphatasia is a rare skeletal disease which is clinically classified according to the age of onset of symptoms. The most severe type is perinatal hypophosphatasia, which has an autosomal recessive mode of inheritance. The perinatal form of the disease is due to abnormalities in the tissue-non-specific isoenzyme of alkaline phosphatase (TNS-ALP).

Souka et al reported on three pregnancies of a high-risk family. In the two affected pregnancies the diagnosis was made at 12 and 14 weeks and the features were marked hypomineralization of the skull and spine, narrowing of the chest with short ribs, shortening of all the long bones, bilateral talipes and increased nuchal translucency.

Osteogenesis imperfecta type II (birth prevalence 1 in 60,000)

This is a lethal skeletal dysplasia with the majority of cases are new mutations of the genes encoding collagen type I. Recurrence (6–7%) is usually due to parental mosaicism (somatic or germ-line), although, in a small number of families, autosomal recessive inheritance has been observed. In the second trimester, the characteristic sonographic features are short limbs and ribs with multiple fractures and hypomineralization of the skull.

Makrydimas et al, reported on an affected fetus presenting at 11 weeks with obvious shortening of all long bones and ribs and increased nuchal translucency.[113]

Roberts syndrome

This is a rare, autosomal recessive condition characterized by symmetrical limb defects of variable severity (tetraphocomelia), facial cleft, hypertelorism, microcephaly and growth retardation.

In a fetus with Roberts syndrome, from a high-risk family, the sonographic findings at 11 weeks were increased NT and tetraphocomelia.[114]

Short-rib polydactyly syndrome

This is a rare, autosomal recessive, lethal skeletal dysplasia, characterized by short limbs, narrow thorax and post-axial polydactyly.

In a fetus with short-rib polydactyly syndrome type I, from a high-risk family, the sonographic findings at 13 weeks were increased NT, narrow chest, short limbs and polydactyly.[115]

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