First trimester fetal anatomy study and identification of major anomalies using 10 standardized scans

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Abstract

Objective: to validate the use of the first trimester scan not just as a screening tool for chromosomal anomalies, but also as a method to identify the major anatomic anomalies using 10 standardized scans.

Methods: five years of prospective study analyzing the fetal anatomy of 5924 patients with a singleton pregnancy during the first trimester screening for chromosomopathies. A check list of 10 predetermined scans had been used. The follow up consisted of two more scans in the second and third trimester, according to the local protocol, and a final evaluation of neonatal outcome at birth.

Results: in the 5924 examined patients, the percentage of major malformations is 0.74%, most of all discovered in the first trimester (47.7%). The Detection Rate for the malformations related to the nervous system is about 50% and for the malformations of the abdomen, heart and skeleton is slightly lower (43.5%).

Conclusions: first trimester ultrasound using 10 standardized scans is a valid screening method for chromosomopathies and also an effective method to identify many of the major fetal anatomical anomalies.

Key words: malformations, check list, chromosomopathies, fetal medicine.

Introduction

In recent years the first trimester scan has played a crucial role not just for evaluating the fetal viability and determining the gestational age, but also as a screening tool for the identification of chromosomal anomalies measuring the fetal nuchal translucency thickness (NT) (1). Furthermore several studies showed the capacity of the first trimester scan to identify more than the 80% of the major fetal malformations not related to chromosomopathies, with a sensitivity between 12.5 and 83.7% (2, 3). It has also been described how some sonographic markers used for the combined test (like an increased NT, reverse flow in the ductus venosus, tricuspid regurgitation, the absence of internal translucency) might be correlated with the presence of anatomical malformations. In 2007 we started a prospective observational study on the fetal anatomy during the local screening program for chromosomal anomalies.

The aim of this study is to validate the possibility to use the first trimester scan not only as a screening for chromosomal anomalies, but also for as a valid method for the identification of major fetal malformations. We used a checklist of 10 standardized scans, the same used for the investigation of chromosomopathies, during the combined test.

Methods

A five-year prospective study, from August 2007 to September 2012, carried out at Misericordia Hospital in Grosseto involving 5924 patients with a singleton pregnancy.

The Ethics Committee of the hospital approved the research protocol. Each patient was required to sign an informed consent form before their scan.

The anatomy study had been done during the research of sonographic markers for the screening of chromosomopathies, so no additional human and time resources were required for the Fetal Medicine Unit.

First of all during the visit it was done an accurate maternal medical history. The gestational age requested as inclusion criteria of the study was between 11⁺⁰ and 13⁺⁶ weeks and had to be confirmed by a CRL between 4.5 and 8.4 cm.

Four operators, all accredited with the Fetal Medicine Foundation of London, carried out all the transabdominal scans using a Voluson E8 (GE Medical Systems) device. Occasionally it was necessary the

use of transvaginal scan for patients with high BMI, unfavorable fetal position and just in case that anatomical anomalies were discovered transabdominally. Each operator was trained to minimize the execution time using 30 minutes.

In case of incomplete visualization of anatomic structures for early gestational age, the patient was scheduled for a later appointment within the 13⁺⁶ weeks.

For the simultaneous studies of the chromosomopathies' markers and the fetal anatomy we added to the 9 bidimensional scans routinely used, an additional approach in 3D/4D because it provided an easier and quicker image of all four fetal extremities. The use of this method was already been applied in case of diagnosis of malformation in order to confirm and optimize the counselling. In fact it gives a more realistic picture for the parents understanding (Fig. 1).

As follow-up there were provided one scan between the 19th and the 22nd week and another one between the 30th and the 33rd week (according to the local pregnancy booklet), both carried out following the SIEOG guidelines (Italian society of obstetric and gynecological sonography).

In case of fetal malformation a counselling with a multidisciplinary team composed of gynecologists, geneticists and neonatologists was planned for the patient in order to explain and decide a shared management.

A careful neonatal examination for babies born alive was offered to confirm the diagnosis of malformation. Anomalies non diagnosable in utero, i.e. hip dysplasia, metabolic disorders, skin injuries and phimosis

were not included as outcomes for the study.

If the patient decided for a voluntary termination of pregnancy or a miscarriage occurred, an anatomopathological examination for the diagnosis was done. Data collection (characteristics and maternal history, gestational age, digital images, follow-up) was done and stored using View Point.

Para-physiological conditions, such as moderate pyelectasis or single umbilical artery were not considered as major malformation in this study; the increased NT and the cystic hygroma as well.

We did not discover any malformation caused by infections.

The major malformations that we have taken into account are those described by the Royal College of Obstetricians and Gynecologists.

Results

During the period between August 2007 and September 2012, 5924 patients with singleton pregnancy were examined. The average of the maternal age was 32.2 years old (range 16 - 47). The 30.9% had an age greater than 35 years old. In the 98% of cases, they were caucasian women. The average of the BMI was 27.6kg/m². The first trimester scan took an amount of time between 15 and 50 minutes depending on fetal position. Most of the time, however, the exam was carried out in less than 30 min. For those cases with an anatomical malformation a longer time was required because of the need of transabdominal,

Combined test	Scan	Anomalies
CRL		Body stalk anomalies, severe scoliosis
NT, NB, mandibular angle, IT		Anomalies of the profile, neural tube
DBP, CC		Holoprosencephaly, anencephaly
FHR, 4 cardiac chambers, thoracic wall		Situs inversus, ectopia cordis
AC, stomach		Gastroschisis, omphalocele
Bladder, vessels of the umbilical cord		Megacystis
Upper limb, humerus		Skeletal anomalies
Lower limb, femur		Gastroschisis, omphalocele
Ductus venosus		Skeletal anomalies
3/D 4/D view four limbs		

Figure 1. Check list of the 10 standard US scans in the 1st trimester fetal study, simultaneously used for the screening of chromosomopathies and for the identification of major fetal anomalies.

transvaginal and 3D/4D scan.

In order to complete the full checklist for the study of the anatomy a transvaginal approach was used just in the 1.9% of the cases. This approach was used particularly in case of high maternal BMI or in case of persistent fetal position unfavorable. In 2% of the cases it had been necessary to repeat the scan because the images' quality was not satisfactory.

In Table 1 are reported all the structural anomalies highlighted either in the first trimester and in later gestational ages, the relative nuchal translucency, the outcome and the karyotype.

The Table shows that the percentage of major malformations observed was 0.74% (44/5924).

The prevalence of structural neurological anomalies was 45.4% (20/44) which represents the 0.34% (20/5924) of the examined population, while severe morphologic anomalies of the trunk (40.9%; 18/44), the heart (6.8%; 3/44) and the skeleton (4.5%; 3/44) are present with a percentage of 52.3% (23/44).

Many of the major morphological anomalies were observed in the first trimester (47.7%; 21/44) and they represent the 0.35% (21/5924). During the second trimester, the percentage of major malformations observed was 3.8% (14/44) which represents the 0.24% (14/5924).

It is important to highlight that during the first trimester, for the malformations related to nervous system a Detection Rate (DR) of the 50% (10/20) was obtained, while for the trunk, the heart and the skeleton the DR was slightly lower (45.3%; 10/23).

In our population we found a percentage of 5.7% (338/5924) of fetuses with a NT >95th percentile, with a prevalence of major malformations of 1.48% (5/338). We have also identified 28 cases of chromosomopathies (26 diagnosed at the first trimester screening and 2 false-negative cases).

In 17 cases, the detection of anatomical malformations had determined the execution of the karyotype test to make diagnosis of the presence/absence of chromosomopathy. None of patients who had received a diagnosis of fetal malformation decided to decline the invasive exam. We hadn't any case in which it was strongly suspected an anatomic malformation and it was not confirmed by an anatomicopathological exam.

The number of images stored for each test was 12, because in addition to the 10 planned by our checklist, we also stored the images of the three different measurements of NT.

Discussion

Our study shows that using 10 standardized scans in the first trimester scan, besides being an effective method of screening for chromosomopathies, it is possible to identify more than half of anatomical anomalies, according to the studies by Souka, 2006 and Economides and Braithwaite, 1998 (4, 5). Moreover, the use of this checklist helps the study of the

fetal anatomy, making it more systematic and without the need of longer time than that required for the combined test.

The study also agrees in confirming the distinction, already made by Syngelaki et al. (6), of the anomalies of the first trimester into two groups:

1. anomalies that should always be highlighted;
2. anomalies that could potentially be highlighted.

In the first group there are acrania, alobar holoprosencephaly, abdominal wall defects, megacystis, limb body stalk anomaly. All these anatomical anomalies were properly highlighted in the first trimester.

According to the work by Syngelaki, our results confirm the difficulty to highlight anomalies of the second group, such as holoprosencephaly, agenesis of the corpus callosum, duodenal atresia and hydronephrosis, detectable later than the first trimester. Among these anomalies potentially detectable such as palatoschisis, renal agenesis, multicystic kidney, the lethal skeletal dysplasia, diaphragmatic hernia, open spina bifida, our results are in line with the literature and particularly for the palatoschisis that is part of a poly malformative context.

We hadn't found any possibility to detect the open spina bifida earlier.

Re-evaluating retrospectively all the images stored of fetuses with this pathological condition, usually diagnosed in the second trimester, it appeared possible to have a diagnosis of open spina bifida in the first trimester according to new evidence in the literature regarding the Internal Translucency.

Actually new evidences suggest an abnormal posterior cranial fossa in the scan used to measure NT and NB (7, 8). The open spina bifida is associated with dislocation of the brainstem and compression of the fourth ventricle and cisterna magna in the confined space between the occipital bone and the sphenoid bone.

Looking at our mid-sagittal scans used for the measurement of fetuses' NT with open spina bifida highlighted in the second trimester, in all cases it was observed an internal translucency absent (Fig. 2).

Figure 2. Internal nuchal translucency absent.

Table 1. Fetal malformations highlighted per anatomical segment; presence / absence of NT> 95th; time of diagnosis; outcome; karyotype divided into not run / abnormal / normal.

Fetal malformation	TOT	Diagnosis					Outcome			Karyotype	
		NT> 95 th	11-13 w	20-24 w	> 24 w	NV	IVG	Miscarriage	Not run	A	N
Neural tube	10	0	6	4	0	2	8	0	7	1	2
Acrania	6		6				6		3	1	2
Encephalocele	1			1			1		1		
Open spina bifida	2			2		1	1		2		
Sacroccygeal teratoma	1			1		1	1		1		
Brain	10	2	4	5	1	3	7	0	6	2	2
Agnesia corpus callosum	2			2		2			2		
Severe ventriculomegaly	1			1			1				1
Holoprosencephaly	4	2	4				4		2	2	
Cerebellar hypoplasia	3			2	1	1	2		2		1
Face	1	1	1	0	0	0	1	0	0	0	1
Labialpalatoschisis	1	1	1				1				1
Lungs	1	0	0	0	1	1	0	0	1	0	0
Diaphragmatic hernia	1				1	1			1		
Heart	3	0	0	3	0	1	2	0	2	0	1
Hypoplastic left heart	2			2		1	1		2		
Tetralogia of Fallot	1			1			1				1
Torso and abdomen	5	1	5	0	0	1	4	0	1	0	4
Ectopia cordis	1	1	1				1				1
Gastroschisis	2		2			1	1				2
Omphalocele	2		2				2		1		1
Gastrointestinal tract	1	0	0	0	1	1	0	0	1	0	0
Intestinal obstruction	1				1	1			1		
Kidneys	8	1	2	1	5	5	1	0	4	0	2
Megacystis	2	1	2			1	1				2
Hydronephrosis	3				3	3			3		
Multicystic kidney	2				2						
Syndrome Potter	1			1		1			1		
Skeleton	2	0	0	1	1	1	1	0	1	0	1
Acondrodysplasia	2			1	1	1	1		1		1
Others	3	0	3	0	0	0	1	2	2	1	0
Body stalk anomaly	1		1					1	1		
Fetal hydrops	2		2				1	1	1	1	
TOTAL	44	5	21	14	9	15	25	2	25	4	13

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