Ultrasound evaluation of fetal gender at 12–14 weeks

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Aims. The aim of this study was to assess the feasibility and accuracy of fetal gender assignment by transabdominal ultrasound at 12–14 weeks of gestation.
Methods. Fetal gender assessment was performed in 1222 singleton pregnancies. In all fetuses the crown–rump length (CRL) was measured and the genital area of the fetus was examined in the mid–sagittal plane. The result of ultrasound examination was compared to the phenotypic sex of the newborn after delivery.
Results. The feasibility as well as accuracy in determining gender increased with growing fetal CRL. At CRL < 50 mm (gestational age < 11+4) the feasibility was 39.1% and accuracy 30.5% (40.9% in male gender vs 24.3% in female gender). At CRL 50–54.9 mm (gestational age 11+4 to 12+0) the feasibility was 63.5% and accuracy 75.0% (89.1% in male gender vs 66.7% in female gender). At CRL 55–59.9 mm (gestational age 12+0 to 12+2) the feasibility was 90.5% and accuracy 96.6% (99.1% in male gender vs 93.5% in female gender). At CRL ≥ 60 mm (gestational age ≥ 12+2) the feasibility was 97.4% and accuracy 100.0% (100.0% in male gender vs 100.0% in female gender).
Conclusions. Fetal gender may reliably be determined when CRL ≥ 60 mm (gestational age ≥ 12+2). Male gender may already be reliably determined when CRL ≥ 55 mm (gestational age ≥ 12+0). If CRL < 50 mm (gestational age < 11+4) the gender cannot be reliably predicted.

Key words: fetal gender, fetal sex, first trimester, ultrasonography

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INTRODUCTION

During screening for Down syndrome in the I. trimester of pregnancy, parameters with values dependent on fetal gender (fetal nuchal translucency measured by ultrasound, free β-hCG and PAPP-A levels in maternal serum) are evaluated when calculating "individual risk" of incidence of trisomy in the fetus[1-4].

Reliable non-invasive determination of fetal gender in the monitored time period could enable modification of normal values of these parameters based on fetal gender and make the algorithm for calculating "individual risk" more accurate. A more accurate calculation of the "individual risk" of incidence of trisomy in the fetus could lead to a decrease in the number of invasive procedures (chorionic villus sampling, amniocentesis) indicated to determine the karyotype of the fetus and thus minimalize possible fetal complications associated with these examinations. Also, it would not be necessary to perform invasive procedures if there was suspicion of sex-linked genetic disease of the fetus[5-7].

Information about fetal gender is currently not used in clinical practice for the correction of calculation of „individual risk" for fetal trisomy. In contrast, if there is suspicion of sex-linked genetic diseases, reliable information about fetal gender already plays a significant role in current clinical practice.

To date, only a few studies regarding fetal gender assignment in early pregnancy by ultrasound have been published, and these are usually of an older date and describe only a small sample of patients[8-20].

The aim of this study was to assess the feasibility and accuracy of fetal gender assignment by transabdominal ultrasound at 12-14 weeks of gestation, during which combined screening for the most common fetal chromosomal anomalies is performed.

MATERIALS AND METHODS

Ultrasound examination aimed at determining fetal gender was performed during the first trimester of pregnancy at 12-14 weeks (CRL, 45-82.4 mm). All examinations were performed by one examiner (M.L.). From January 2005 to February 2010, a total of 1222 fetuses were examined, all were from a single pregnancy without established morphological or chromosomal abnormalities in the fetus or newborn. All the scans were performed transabdominally using 5-MHz transducers (GE Voluson E8 Expert ; GE Voluson 730 Expert, GE Healthcare Technologies, Zipf, Austria). The crown-rump length (CRL) was measured in all fetuses. The genital area of the fetus was examined in the mid-sagittal plane, in the neutral position of the fetus (without the presence of hyperflexion or hyperextension). When determining fetal gender, the method described by Efrat et al.[13] was

used. The angle between the genital tubercle axis and a horizontal line through the lumbosacral skin surface was measured. Angles >30° established the gender to be male (Fig. 1), if the axis of the genital tubercle ran parallel (<10°) or convergent to the horizontal line, gender was established as female (Fig. 2), if the angle was intermediate (10–30°) gender was not determined. The result of ultrasound examination was compared to the phenotypic sex of the newborn after delivery.

Statistical analysis was performed using the $\chi 2$ test, or Fisher's exact test when appropriate. Values of $P < 0.05$ were considered statistically significant.

RESULTS

The possibility of determining fetal gender during ultrasound examination based on the crown–rump length (CRL) is presented in Table 1, 2. It was possible to establish gender in 1025 of a total of 1222 fetuses (84%). In 197 fetuses (16%) it was not possible to determine gender during ultrasound examination. The most common cause was an intermediate angle (10–30°) between genital tubercle axis and the horizontal line (78%), followed by unfavorable fetal position (12%) and maternal habitus (10%). In 51 of 1025 fetuses (5%) it was not possible to perform a comparison of gender assignment by ultrasound examination with phenotypic sex of the newborn after delivery. In the remaining 974 fetuses, gender was correctly established in 92.5% of cases (901/974), male gender in 96.3% (471/489), female gender in 88.7% (430/485) (Table 3).

The feasibility and accuracy in determining gender during ultrasound examination increased with growing crown–rump length (CRL) of the fetus (Table 2, 3, 4, 5, 6). The difference between male and female gender was not statistically significant.

The feasibility of gender determination during ultrasound examination was 39% at CRL 45–49.9 mm, 64% at CRL 50–54.9 mm, 90% at CRL 55–59.9 mm and 97.4% at CRL 60–82.4 mm. The difference was statistically significant (P=0.012 for CRL 45–49.9 mm vs. CRL 50–54.9 mm, P=0.021 for CRL 50–54.9 mm vs. CRL 55–59.9 mm, and P<0.0001 for CRL 45–54.9 mm vs. CRL 55–82.4 mm)

The accuracy in determining male gender was 41% at CRL 45–49.9 mm, 89% at CRL 50–54.9 mm, 99% at CRL 55–59.9 mm and 100% at CRL 60–82.4 mm. The difference was statistically significant (P=0.023 for CRL 45–49.9 mm vs. CRL 50–82.4 mm).

The accuracy in determining female gender was 24% at CRL 45–49.9 mm, 67% at CRL 50–54.9 mm, 94% at CRL 55–59.9 mm and 100% at CRL 60–82.4 mm. The difference was statistically significant (P=0.014 for CRL 45–49.9 mm vs. CRL 50–54.9 mm, P=0.00013 for CRL 45–49.9 mm vs. CRL 50–82.4 mm, P=0.00036 for CRL 45–54.9 mm vs. CRL 55–82.4 mm, and P=0.015 for CRL 45–59.9 mm vs. CRL 60–82.4 mm).

At CRL < 50 mm (gestational age < 11+4) feasibility was 39.1% and accuracy 30.5% (40.9% in male gender vs 24.3% in female gender). At CRL 50–54.9 mm (gestational age 11+4 to 12+0) the feasibility was 63.5% and accuracy 75.0% (89.1% in male gender vs 66.7% in female gender). At CRL 55–59.9 mm (gestational age 12+0 to 12+2) the feasibility was 90.5% and accuracy 96.6% (99.1% in male gender vs 93.5% in female gender). At CRL ≥ 60 mm (gestational age ≥ 12+2) the feasibility was 97.4% and accuracy 100.0% (100.0% in male gender vs 100.0% in female gender).

DISCUSSION

According to our results, it was possible to reliably determine the fetal gender by transabdominal ultrasound (feasibility 97.4%, accuracy 100%) at CRL ≥ 60 mm (gestational age ≥ 12+2). At CRL ≥ 55 mm (gestational age ≥ 12+0) the feasibility was 95.5% and accuracy 99.1% (99.8% in male gender vs 98.4% in female gender). At

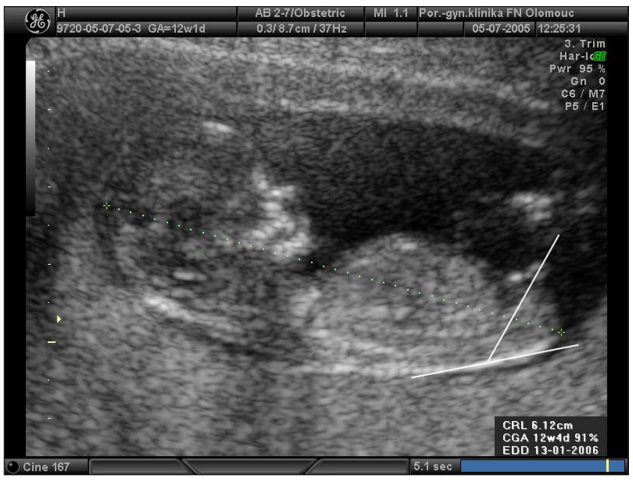

Fig. 1. Ultrasound examination established gender to be male if the angle between the genital tubercle axis and a horizontal line through the lumbosacral skin surface was >30°.

Fig. 2. Ultrasound examination established gender to be female if the axis of the genital tubercle ran parallel (<10°) or convergent to the horizontal line.

Table 1. Gender identification at ultrasound examination according to crown–rump length (CRL).

CRL	Gestational age	Patients	Gender indetified by ultrasound		Gender verified	Lost to follow-up
(mm)	(weeks)	(n)	(n)	(%)	(n)	(n)
45.0–49.9	11+1 to 11+4	156	61	39	59	2
50.0–54.9	11+4 to 12+0	170	108	64	100	8
55.0–59.9	12+0 to 12+2	242	219	90	208	11
60.0–64.9	12+2 to 12+5	291	283	97	268	15
65.0–69.9	12+5 to 13+1	238	232	97	222	10
70.0–74.9	13+1 to 13+3	58	57	98	56	1
75.0–79.9	13+3 to 13+5	43	42	98	41	1
80.0–82.4	13+5 to 13+6	24	23	96	20	3
Total		1222	1025	84	974	51

Table 2. Gender feasibility by ultrasound according to crown–rump lenght (CRL).

CRL (mm)	Gestational age (weeks)	Feasibility (%)					
45.0–49.9	11+1 to 11+4	39,1	51.8	83.9	90.4	95.5	97.4
50.0–54.9	11+4 to 12+0	63,5					
55.0–59.9	12+0 to 12+2	90,5	95.2				
60.0–64.9	12+2 to 12+5	97,3					
65.0–69.9	12+5 to 13+1	97,5					
70.0–74.9	13+1 to 13+3	98,3	97.6				
75.0–79.9	13+3 to 13+5	97,7					
80.0–82.4	13+5 to 13+6	95,8					

Table 3. Accuracy of sonographic fetal gender assignment according to crown–rump length.

CRL (mm)	Gestational age (weeks)	Total accuracy		Male accuracy		Female accuracy	
		(n)	(%)	(n)	(%)	(n)	(%)
45.0–49.9	11+1 to 11+4	18/59	31	9/22	41	9/37	24
50.0–54.9	11+4 to 12+0	75/100	75	33/37	89	42/63	67
55.0–59.9	12+0 to 12+2	201/208	97	114/115	99	87/93	94
60.0–64.9	12+2 to 12+5	268/268	100	135/135	100	133/133	100
65.0–69.9	12+5 to 13+1	222/222	100	121/121	100	101/101	100
70.0–74.9	13+1 to 13+3	56/56	100	29/29	100	27/27	100
75.0–79.9	13+3 to 13+5	41/41	100	18/18	100	23/23	100
80.0–82.4	13+5 to 13+6	20/20	100	12/12	100	8/8	100
Total		901/974	93	471/489	96	430/485	89

Table 4. Total accuracy of sonographic fetal gender assignment according to crown–rump length.

CRL (mm)	Gestational age (weeks)	Total accuracy (%)					
45.0–49.9	11+1 to 11+4	30.5	**58.5**	**92.5**	**96.5**	**99.1**	**100**
50.0–54.9	11+4 to 12+0	75					
55.0–59.9	12+0 to 12+2	96.6	**99**				
60.0–64.9	12+2 to 12+5	100					
65.0–69.9	12+5 to 13+1	100					
70.0–74.9	13+1 to 13+3	100	**100**				
75.0–79.9	13+3 to 13+5	100					
80.0–82.4	13+5 to 13+6	100					

Table 5. Male accuracy of sonographic fetal gender assignment accoridng to crown–rump length.

CRL (mm)	Gestational age (weeks)	Male accuracy (%)					
45.0–49.9	11+1 to 11+4	40.9	**71.2**	**96.3**	**98.9**	**99.8**	**100**
50.0–54.9	11+4 to 12+0	89.1					
55.0–59.9	12+0 to 12+2	99.1	**99.7**				
60.0–64.9	12+2 to 12+5	100					
65.0–69.9	12+5 to 13+1	100					
70.0–74.9	13+1 to 13+3	100	**100**				
75.0–79.9	13+3 to 13+5	100					
80.0–82.4	13+5 to 13+6	100					

Table 6. Female accuracy of sonographic fetal gender assignment accoridng to crown–rump length.

CRL (mm)	Gestational age (weeks)	Female accuracy (%)					
45.0–49.9	11+1 to 11+4	24.3	**51**	**88.7**	**94**	**98.4**	**100**
50.0–54.9	11+4 to 12+0	66.7					
55.0–59.9	12+0 to 12+2	93.5	**98.2**				
60.0–64.9	12+2 to 12+5	100					
65.0–69.9	12+5 to 13+1	100					
70.0–74.9	13+1 to 13+3	100	**100**				
75.0–79.9	13+3 to 13+5	100					
80.0–82.4	13+5 to 13+6	100					

CRL ≥ 50 mm (gestational age ≥ 11+4) the feasibility was 90.4% and accuracy 96.5% (98.9% in male gender vs 94.0% in female gender). At CRL ≥ 45 mm (gestational age ≥ 11+1) the feasibility was 83.9% and accuracy 92.5% (96% in male gender vs 88.7% in female gender).

Efrat et al.[13] describe the feasibility of determining fetal gender using transabdominal ultrasound as 92.6% (CRL ≥ 55.4 mm; n=656), Chelli et al.[10] 89.7% (CRL ≥ 45 mm; n=312), Hsiao et al.[11] report the feasibility as 88.9% (CRL ≥ 45 mm; n=496) and 96% (CRL ≥ 57 mm; n=400), Mazza et al.[14] 87.5% (BPD 18–29 mm; n=385). In the last two studies, however, the same method was not used to determine gender and in the last study a different biometric parameter was used (BPD; biparietal diameter of the head). It is also difficult to compare the results due to the small sample size of patients as well as the improved imaging of new ultrasound devices.

Efrat et al.[13] present the accuracy of determining fetal gender to be 98.5% (CRL ≥ 55.4 mm), 99.6% in male gender vs 97.4% in female gender. Chelli et al.[10] describe at CRL ≥ 45 mm an accuracy of 85.7% (in male gender 87.9% vs 83.3% in female gender). Hsiao et al.[11] report an accuracy of 91.8% (CRL ≥ 45 mm), 92.5% in male gender vs 91.2% in female gender. Mazza et al.[14] at BPD 18–29 mm describe an acucuracy of 87.5% (male gender 91.5% vs 95.9% female gender) and at BPD ≥ 23 mm report an accuracy of 100%.

At CRL < 50 mm (gestational age < 11+4) fetal gender assignment by transabdominal ultrasound in our patient set was possible in only 39% of fetuses (61/156). In most cases gender was determined to be female (63%). The assignment accuracy was in indirect proportion between the sexes, male gender was successfully determined in 41% of cases (9/22) and female in only 24% of cases (9/37). Therefore in total, reliable gender assignment was possible in only 11.7% (18/154) of the examined fetuses. Efrat et al.[12] at CRL 43.4–55.3 mm present reliability of gender assignment to be 92.5% (37/40) and accuracy to be 70.2% (26/37), 44.4% in male gender assignment (8/18) vs 94.7% in female gender assignment (18/19). However, this study used a different method for determining fetal gender and a different CRL was evaluated. At a similar CRL of 45–54.9 mm the feasibility of gender determination in our set was 51.8% (169/326) and accuracy was 58.5% (93/159), 71.2% in male gender assignment (42/59) vs 51.0% in female gender assignment (51/100).

Pedreira et al.[21] described a change in the orientation of the genital tubercle during examination (CRL 44.7–72.6 mm) on a set of 11 fetuses (6 fetuses of male gender and 5 fetuses of female gender). Determination of fetal gender in the first trimester of pregnancy by transabdominal ultrasound necessitates considerable erudition of the examiner and a sufficient timeframe for the examination, because the most difficult as well as most important is the imaging of the fetus in the required reference plane. According to our results, at CRL < 50 mm (gestational age < 11+4) the fetal gender cannot be reliably predicted using this method.

Cowans et al.[1] demonstrated the significant influence of fetal gender on values of nuchal translucency (delta NT) and level of free ß–hCG and PAPP–A in maternal serum during screening for chromosomal aneuploidies in the first trimester on a set of 56024 normal singleton pregnancies and in 722 pregnancies where the fetus had trisomy 21. Normal female fetuses had levels of nuchal translucency (delta NT) which were 9.4% lower, and maternal serum levels of free ß–hCG and PAPP–A were higher (by 14.7% and 6.3% respectively) compared to fetuses of male gender. Female fetuses with trisomy 21 had 12% lower values of nuchal translucency (delta NT) and higher levels of free ß–hCG (by 20.8%) and PAPP–A (by 5.7%). Larsen et al.[3] describe higher levels of free ß–hCG (by 15%) as well as PAPP–A (by 7%) in maternal serum in cases of female fetuses in a set of 2637 normal single pregnancies. Lam et al.[2] on a set of 12189 pregnancies between week 10–14 presented 5% lower values of nuchal translucency (delta NT) in fetuses of female gender. Reliable determination of fetal gender by transabdominal ultrasound in week 12–14 of gestation could serve as an additional marker to allow for more accurate calculation of the individual risk of incidence of trisomy 21 in the fetus.

Fetal gender may also be determined non–invasively in the first trimester by analyzing free fetal DNA obtained from the plasma of maternal peripheral blood. The method allows assignment of genotypic sex of the fetus and sensitivity and specificity of this method is nearly 100% (ref.[5]). During ultrasound examination, only the phenotypic sex of the fetus may be assessed, which may differ from genotypic sex (testicular feminization, severe hypospadia, etc.). However, ultrasound examination is less invasive, less expensive and easily feasible. The possibility of reliably and non–invasively determining fetal gender already in the first trimester, however, incurs the risk of misuse of fetal gender selection for non–medical purposes.

CONCLUSIONS

Fetal gender may reliably be determined by transabdominal ultrasound when CRL ≥ 60 mm (gestational age ≥ 12+2). Male gender may already be reliably determined when CRL ≥ 55 mm (gestational age ≥ 12+0). If CRL < 50 mm (gestational age < 11+4) gender cannot be reliably predicted. It is always necessary to take into account the maternal habitus, the position of the fetus and the imaging possibilities of the ultrasound device. The experience and erudition of the examiner are very important.

ABBREVATIONS

BPD, Biparietal diameter; CRL, Crown–rump length; hCG, Human chorionic gonadotropin; NT, Nuchal translucency; PAPP–A, Pregnancy associated plasma protein – A.

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