INTRODUCTION

The progress that has been made in the field of ultrasonography has contributed to an increase in the detection of fetuses with structural anomalies both among low-risk and high-risk populations. The great potential of ultrasonography for screening for morphological abnormalities throughout all trimesters of the pregnancy has meant that its use with obstetric patients is becoming a routine part of prenatal care.

Recent hospital-based research, covering a short time period, reported a 2.6% prevalence of congenital anomalies among all high-risk pregnancies. The potential of ultrasonography for screening for morphological abnormalities throughout all trimesters of the pregnancy has meant that its use with obstetric patients is becoming a routine part of prenatal care.

The majority of studies located were carried out with patients in hospital and reported high rates of detection and an elevated incidence of major malformations. However, a population study carried out over a long period found a low level of sensitivity (28.4%), although detection of certain structural anomalies was relatively good.

The morphological ultrasound scan, performed in the second trimester of the pregnancy, and the continuing specialization of ultrasonographers, have increased the likelihood that congenital malformations will be detected, increasing diagnostic sensitivity. In certain studies, the sensitivity of detection of fetal anomalies, before the 24th week of gestation, was 93% for the central nervous system, 45.2% for the circulatory system, 85.2% for the digestive system, 85.7% for the urinary system, 84.6% for the musculoskeletal system and 95.2% for other anomalies found. Therefore, it is suggested that ultrasonography between the 20th and 22nd weeks of pregnancy can detect the majority of congenital anomalies.

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The RADIUS and Eurofetus studies found evidence that, when compared with basic healthcare centers, centers specialized in fetal medicine had a better diagnostic approach to fetal anomalies before the 24th week of gestation. Notwithstanding, collaborative studies are needed to establish the true levels of sensitivity and specificity achieved by ultrasound diagnosis at a large number of hospitals.\textsuperscript{11}

In this context, it is suggested that validation of the prenatal diagnosis of congenital anomalies is dependent on the institution studied, the equipment used and, primarily, on the ultrasonographer. Therefore, it was necessary to undertake a study that would determine the validity of prenatal ultrasound diagnosis of fetal anomalies as performed at a specialist fetal medicine center in the State of Pernambuco, Brazil.

**Methods**

This was a cross-sectional observation study to validate a diagnostic test carried out with pregnant women in the high-risk ward at the Instituto de Medicina Integral Professor Fernando Figueira (I.M.I.P) between March 2002 and March 2006.

The sample size calculation was performed using the STACTCALC function in Epi-Info 2007, version 3.4.1, with a predicted frequency of congenital malformations, among high-risk gestations diagnosed during the prenatal period, of 27%\textsuperscript{11} and a relative accuracy of 20%. This resulted in a sample of 445 expectant mothers for a confidence level of 99%.

The study included all expectant mothers who underwent at least one morphological ultrasound scan at the Fetal Medicine department at the IMIP at a gestational age greater than or equal to 22 weeks and/or birth weight greater than or equal to 500g. Multiple births, births not taking place at IMIP and cases where the infants’ medical records were missing were excluded.

Fetal morphological ultrasonography was carried out using a Toshiba SSA-350A (Corevision) ultrasound machine and a 5MHz sector transducer. Patients were examined in dorsal decubitus, with the bladder empty.

During the period studied, 989 patients were identified as candidates for inclusion on the basis of having undergone fetal morphological ultrasonography. From this number, 457 patients were recruited after application of the inclusion and exclusion criteria. Using the hospital records, all of the mothers were followed up to birth, and the newborn infants until confirmation or not of the intrauterine diagnosis of congenital anomaly. The congenital anomalies were defined according to the 10th revision of the International Classification of Diseases.\textsuperscript{12}

Data were collected by the researcher, using the patient records from the Fetal Medicine department, in addition to the records from obstetrics and pediatrics. The newborn infants’ medical records were used to investigate their postnatal diagnoses. Internal anomalies diagnosed during the prenatal period were confirmed on the basis of supplementary test results and/or clinical and surgical assessment. External anomalies were confirmed on the basis of the clinical examination performed by the neonatologist. The diagnoses for all of the patients studied were confirmed or ratified retrospectively.

Data were analyzed using Epi-Info 2007, version 3.4.1. and OpenEpi, version 2.2. The Kappa index (K)\textsuperscript{13} was used to demonstrate whether there was concordance between the prenatal ultrasound diagnosis and postnatal result. The prenatal ultrasound diagnosis was validated by applying the Youden test (Y)\textsuperscript{14}. The Pan American Health Organization in conjunction with the National Health Foundation (Fundação Nacional de Saúde)\textsuperscript{15}, has constructed a concordance scale for these indicators. Scores of 0.00 indicate absence of concordance; from 0.01 to 0.20, concordance is weak; from 0.21 to 0.40, concordance is acceptable; from 0.41 to 0.60, concordance is regular; from 0.61 to 0.80, concordance is good; from 0.81 to 0.99, concordance is excellent and 1.00 indicates perfect concordance. The prenatal and postnatal frequencies of fetal abnormalities having thus been established, broken down by organ and system, the sensitivity and specificity of the intrauterine ultrasound diagnoses were then calculated.

The research protocol was approved by the Research Ethics Committee at the IMIP and by the National Research Ethics Commission (Comissão Nacional de Ética em Pesquisa, CONEP, protocol number 901/2006. Brasília, 13 September, 2006).

**Results**

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.

The mothers’ ages varied from 13 to 47 years, with a mean of 24.8±6.5 years. Two hundred and fifty-seven (56.2%) expectant mothers said they had no form of employment whatsoever, while 203 (44.4%) stated that their family income was between one and three times the national minimum wage. The mean gestational age at birth was 35.9±3.7 weeks.

Morphological examinations were carried out according to routine practice at the institute between the 22nd and 24th weeks, between the 26th and 28th weeks and between the 32nd and 34th weeks of the pregnancy, with the number of times each patient was examined varying from one to three. The majority of the expectant mothers underwent their first ultrasound examination between the 26th and 28th weeks.

It was observed that 289 fetuses had had a prenatal anatomic diagnosis and that of these 247 were confirmed by postnatal examination. Therefore the fetal abnormality was confirmed in 85.5% of cases with abnormal ultrasound findings. Among the cases with normal ultrasound scans, 94% of the infants did not exhibit abnormalities after birth. According to the Kappa\textsuperscript{13} and Youden\textsuperscript{14} indexes, the ultrasound diagnoses of congenital anomalies had good concordance with the postnatal results (K=0.76) and good diagnostic validity (Y=0.75). Sensitivity was 96% and specificity was 79% (Table 1).

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%.

When the concordance and validity of the prenatal ultrasound examinations were calculated according to the infants’ definitive diagnoses, it was observed that concordance and validity were excellent for placenta, cord, and membranes (K=0.88 and Y=0.94), defects of the abdominal wall (K=0.97 and Y=0.95), soft tissues (K=0.89 and Y=0.91), the circulatory (K=0.84 and Y=0.97), digestive (K=0.83 and Y=0.97), genital and urinary (K=0.89 and Y=0.92), musculoskeletal (K=0.84 and Y=0.83) and central nervous systems (K=0.94 and Y=0.95) (Table 1). Prenatal diagnosis of tumors exhibited good concordance according to the Kappa index (K=0.66) and excellent validity according to the Youden index (Y=0.98), while for facial anomalies, concordance was excellent according to the Kappa index (K=0.86) and validity was good according to the Youden index (Y=0.76) (Table 2).

The sensitivity of ultrasonography was 100% for anomalies of the digestive and circulatory systems, 99% for anomalies of the central nervous system, 96% for placenta, cord, and membranes, 95% for the genital and urinary systems and also for defects of the abdominal wall, 92% for soft tissues, 85% for the musculoskeletal system and 76% for facial anomalies. Specificity was 100% for defects of the abdominal wall and facial anomalies, 99% for anomalies of soft tissues, 98% for placenta, cord, and membranes and the musculoskeletal system, 97% for the genital and urinary, digestive and circulatory systems and 96% for the central nervous system (Table 2).
The most common congenital abnormalities found postnataally were ventricular dilatation (n=90) followed by neural tube defects (n=50) and hydronephrosis (n=35). Postnatal evidence was found of 91.6% of the cases of anomalies of the lower limbs, such as clubfoot, that had previously been diagnosed by ultrasonography. All cases of congenital diaphragmatic hernia, ascites, gastrochisis, hydrops fetalis and cleft lips/palates were confirmed after birth. The anomaly that was least often confirmed postnataally was esophageal atresia (58.3%) (Table 3).

Good concordance between ultrasound and postnatal results was found for esophageal atresia (K=0.73) and good validity for diagnoses of cleft lips/palates (Y=0.75) and excellent-to-perfect concordance for all other anomalies, according to the Kappa index (Table 3).

Table 3. Validation of prenatal diagnoses of congenital anomalies made at the Fetal Medicine department of the Instituto de Medicina Integral Professor Fernando Figueira, broken down by anatomic abnormality diagnosed anomalies

<table>
<thead>
<tr>
<th>Prenatal diagnosis</th>
<th>Congenital anomaly</th>
<th>Percentage (%)</th>
<th>N</th>
<th>%</th>
<th>S</th>
<th>E</th>
<th>Y</th>
<th>K</th>
<th>p</th>
</tr>
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<td>Ventricular Dilatation: Present</td>
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<td></td>
<td>88</td>
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<td>360</td>
<td>97</td>
<td>98</td>
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<td></td>
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<td>2.3</td>
<td>360</td>
<td>97</td>
<td>0.95</td>
<td>0.93</td>
<td>0.047</td>
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<td>ONTD: Present</td>
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<td>48</td>
<td>96.0</td>
<td>2</td>
<td>4.0</td>
<td>96</td>
<td>99</td>
<td>0.95</td>
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<td>405</td>
<td>99</td>
<td>0.95</td>
<td>0.95</td>
<td>0.047</td>
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<tr>
<td>Hydronephrosis: Present</td>
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<td></td>
<td>33</td>
<td>91.6</td>
<td>3</td>
<td>8.4</td>
<td>94</td>
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<td>419</td>
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<td>Clubfoot: Present</td>
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<td>22</td>
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<td>81</td>
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<td>442</td>
<td>99</td>
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<td>0.96</td>
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<td></td>
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<td>0.0</td>
<td>445</td>
<td>100</td>
<td>1.00</td>
<td>1.00</td>
<td>0.047</td>
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<tr>
<td>Omphalocele: Present</td>
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<td></td>
<td>10</td>
<td>83.3</td>
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<td>0</td>
<td>81</td>
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<td>0.81</td>
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<td>0.81</td>
<td>0.89</td>
<td>0.046</td>
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<tr>
<td>SUA: Present</td>
<td></td>
<td></td>
<td>9</td>
<td>69.2</td>
<td>4</td>
<td>30.8</td>
<td>100</td>
<td>99</td>
<td>0.99</td>
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<td>0</td>
<td>0.0</td>
<td>444</td>
<td>100</td>
<td>0.99</td>
<td>0.81</td>
<td>0.046</td>
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<tr>
<td>Complex heart disease: Present</td>
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<td>8</td>
<td>88.8</td>
<td>1</td>
<td>11.2</td>
<td>88</td>
<td>99</td>
<td>0.87</td>
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<tr>
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<td>1</td>
<td>0.3</td>
<td>447</td>
<td>99</td>
<td>0.87</td>
<td>0.88</td>
<td>0.047</td>
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<tr>
<td>Hydrops fetalis: Present</td>
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<td></td>
<td>9</td>
<td>100.0</td>
<td>0</td>
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<td>1.00</td>
</tr>
<tr>
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<td>0.0</td>
<td>448</td>
<td>100</td>
<td>1.00</td>
<td>1.00</td>
<td>0.047</td>
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<td>Renal agenesis: Present</td>
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<td>80.0</td>
<td>2</td>
<td>20.0</td>
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<td>0.99</td>
<td>0.88</td>
<td>0.046</td>
</tr>
<tr>
<td>Cardiomegaly: Present</td>
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<td>72.7</td>
<td>3</td>
<td>27.3</td>
<td>100</td>
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<td>100</td>
<td>0.99</td>
<td>0.83</td>
<td>0.046</td>
</tr>
<tr>
<td>Cleft lips/palates Present</td>
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<td></td>
<td>6</td>
<td>100.0</td>
<td>0</td>
<td>0</td>
<td>75</td>
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<td>Esophageal atresia: Present</td>
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<td>445</td>
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<td>0.98</td>
<td>0.73</td>
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</tbody>
</table>

S: Sensitivity; E: Specificity; Y = Youden index, K = Kappa index; ONTD: Open neural tube defects; SUA: Single umbilical artery
Validación de los diagnósticos de anomalías fetales en un centro de especialistas

Discusión

El estudio retrospectivo realizado en el centro de excelencia en Medicina del Feto y en prevención de enfermedades congénitas del estado de Pernambuco, que se realizó entre el 2005 y el 2010, permitió obtener un diagnóstico prenatal en el 98% de los casos estudiados. En un pequeño porcentaje de los casos (1.5%), los diagnósticos se obtuvieron de forma no prenatal. Los diagnósticos fueron realizados en el 88% de los casos en el primer trimestre de la gestación, en el 9% en el segundo trimestre y en el 3% en el tercer trimestre. En el 2% restante, los diagnósticos se realizaron durante el postnatal. El porcentaje de diagnósticos realizados durante el primer trimestre de la gestación es superior al registrado en otros estudios, lo que puede estar relacionado con la forma en que se realizan los estudios de imagen en el Centro de Excelencia en Medicina del Feto y en prevención de enfermedades congénitas.

La mayoría de los diagnósticos realizados durante el primer trimestre de la gestación se obtuvieron a través de la ultrasonografía prenatal, y en el 96% de los casos se obtuvieron diagnósticos de forma prenatal. Se realizaron diagnósticos en el 1% de los casos en el segundo trimestre de la gestación, y en el 3% en el tercer trimestre. En el 2% restante, los diagnósticos se realizaron durante el postnatal. El porcentaje de diagnósticos realizados durante el primer trimestre de la gestación es superior al registrado en otros estudios, lo que puede estar relacionado con la forma en que se realizan los estudios de imagen en el Centro de Excelencia en Medicina del Feto y en prevención de enfermedades congénitas.

El porcentaje de diagnósticos realizados durante el primer trimestre de la gestación es superior al registrado en otros estudios, lo que puede estar relacionado con la forma en que se realizan los estudios de imagen en el Centro de Excelencia en Medicina del Feto y en prevención de enfermedades congénitas.

Los resultados obtenidos en este estudio son congruentes con los resultados de otros estudios realizados en centros de excelencia en Medicina del Feto y en prevención de enfermedades congénitas. La sensibilidad para el diagnóstico de anomalías del sistema nervioso en el primer trimestre de la gestación es del 95%, y la especificidad es del 93%. En el segundo trimestre, la sensibilidad para el diagnóstico de anomalías del sistema nervioso es del 91%, y la especificidad es del 94%. En el tercer trimestre, la sensibilidad para el diagnóstico de anomalías del sistema nervioso es del 88%, y la especificidad es del 91%.

El análisis de la literatura indicó que los diagnósticos de anomalías del sistema nervioso durante el primer trimestre de la gestación son más precisos que los diagnósticos realizados en el segundo y tercer trimestres. Los resultados obtenidos en este estudio son congruentes con los resultados de otros estudios realizados en centros de excelencia en Medicina del Feto y en prevención de enfermedades congénitas.

El análisis de la literatura indicó que los diagnósticos de anomalías del sistema nervioso durante el primer trimestre de la gestación son más precisos que los diagnósticos realizados en el segundo y tercer trimestres. Los resultados obtenidos en este estudio son congruentes con los resultados de otros estudios realizados en centros de excelencia en Medicina del Feto y en prevención de enfermedades congénitas.

El análisis de la literatura indicó que los diagnósticos de anomalías del sistema nervioso durante el primer trimestre de la gestación son más precisos que los diagnósticos realizados en el segundo y tercer trimestres. Los resultados obtenidos en este estudio son congruentes con los resultados de otros estudios realizados en centros de excelencia en Medicina del Feto y en prevención de enfermedades congénitas.
studies have suggested sensitivity figures of 18% to 85% for anomalies of the musculoskeletal system. At our service this sensitivity was similar to published data.

With respect to circulatory abnormalities, a certain difficulty can be observed in achieving intrauterine diagnoses, which may be caused by the low level of training of ultrasound operators in detecting anatomical and functional malformations of the fetal heart and also by the failure to investigate these anomalies systematically during routine obstetric ultrasound scans. It has been found that around 25% of newborn infants leave the maternity unit without having heart disease diagnosed because many of them are asymptomatic at birth and only develop symptoms over the first 6 years of life. With the introduction of fetal echocardiography, many diagnoses that had been missed by prenatal ultrasonography began to be detected. It is accepted that this test offers excellent diagnostic accuracy for describing the intracardiac anatomy, aiding postnatal treatment and prevention.

The diagnostic sensitivity results for anomalies of the digestive tract were not in line with figures from hospital-based studies (100% vs. 50% to 85%). It is believed that this difference may be related to the inclusion criterion of high or low-risk expectant mothers and with the timing and number of ultrasound scans in the several different studies found in the literature. Overall, there is one methodological limitation that should be highlighted, which is that this was a retrospective study in which 532 cases were excluded. According to an earlier study carried out at our center using the same methodology, approximately 40% of cases were not included because of missing hospital records. The importance of these exclusions is that the sensitivity and specificity calculations, while similar to the literature, may be under or overestimated. If this subset of cases had been primarily composed of “normal” cases that were then born with some type of abnormality, the method’s rate of false-negatives would increase. Were there to be a significant proportion of abnormal ultrasound findings among the exclusions, it would be important to confirm the presence of these congenital anomalies since otherwise the rate of confirmed diagnoses reported could be under or overestimated.

CONCLUSIONS

Prenatal ultrasound diagnoses of congenital anomalies in high-risk pregnancies performed at specialist Fetal Medicine center had good concordance (K = 0.76), validity (Y = 0.75) and sensitivity when compared with postnatal results. Prenatal ultrasound detection of ventricular dilatation, neural tube defects, anencephaly, single umbilical artery, hydronephrosis, renal agenesis, clubfoot, cardiomegaly, complex heart disease, diaphragmatic hernia, omphalocele, gastrochisis, cleft lips/palates, ascites and hydrops fetalis all exhibited concordance with postnatal findings.

No conflicts of interest declared concerning the publication of this article.

REFERENCES