



ORIGINAL ARTICLE

**Prediction of fetal sex in the first quarter ultrasound screening: ecuadorian experience**

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**Received:** November 27, 2025

**Accepted:** December 9, 2025

**Published:** December 11, 2025

**Citar como:** Padilla-Barragán DE, Moreno-Vargas JA, Moreno-Vargas OM. Predicción del sexo fetal en el screening ecográfico del primer trimestre: experiencia ecuatoriana. Rev Ciencias Médicas [Internet], 2025 [citado: fecha de acceso]; 29(S1): e6949, Disponible en: <http://revcmpinar.sld.cu/index.php/publicaciones/article/view/6949>

**ABSTRACT**

**Introduction:** early prediction of fetal sex constitutes a relevant support in first-trimester screening, especially in contexts where genetic testing is not accessible and ultrasound represents the main diagnostic resource available.

**Objective:** to determine the accuracy of first-trimester ultrasound in predicting fetal sex through sagittal evaluation of the genital tubercle and its anatomical orientation.

**Methods:** descriptive, multicenter, prospective longitudinal study conducted on an intentional sample of 105 pregnant women attended at two specialized centers between 2021 and 2023. Ultrasound sex determination was based on the angle of the genital tubercle relative to the lumbosacral line, compared with confirmatory results from the second trimester or at birth. Descriptive and inferential statistical methods were employed.

**Results:** initially, 52,4 % of fetuses were estimated to be female. Male prediction reached an accuracy of 94 %, while female prediction obtained 83,6 %. The overall effectiveness of the protocol was 88,5 %, with statistically significant associations between the initial assignment and the definitive sex.

**Conclusions:** the orientation of the genital tubercle is a reliable predictor of fetal sex during the first trimester, demonstrating high accuracy in this Latin American population. These findings support the usefulness of the ultrasound approach as an accessible alternative in clinical contexts where early genetic testing is not available.

**Keywords:** Prenatal Diagnosis; Pregnancy; Pregnancy Trimester, First; Ultrasonography, Prenatal.

## INTRODUCTION

Although fetal DNA testing can now determine the sex of a fetus early on, this is far from becoming a routine test in developing countries due to its high cost. This makes ultrasound an important tool for this purpose, as early sex identification by ultrasound can help prevent unnecessary invasive procedures such as chorionic villus sampling or amniocentesis in patients at risk of X-linked diseases.<sup>(1)</sup>

During embryological development, the urogenital system develops from intermediate mesenchyme, derived from the dorsal body wall of the embryo. During embryonic folding, this mesenchyme shifts ventrally, and the urogenital ridge forms on each side of the aorta. The portion of the ridge that gives rise to the urinary system is the nephrogenic cord, and the portion that gives rise to the genital system is the gonadal ridge. This gonadal ridge is the primordium of development in both males and females.<sup>(2,3,4,5)</sup>

The differentiation of the external genitalia is initially determined by the chromosomal makeup of the fetus (XY, XX) and subsequently by the hormones secreted by the gonads dependent on this genetic differentiation (testes and ovaries). These gonads will begin to differentiate from the seventh week of pregnancy.<sup>(4)</sup> During the ninth week, internal differentiation occurs, but the similar appearance of the external genitalia in embryos of both sexes may persist.<sup>(2)</sup>

From the tenth week of gestation, microscopic differentiation of the external genitalia begins, when the genital tubercle starts to elongate to form the penis in male fetuses and the clitoris in female fetuses. At this stage, the female tubercle may elongate more than the male, which can lead to diagnostic errors in the first trimester. By week 12, the anatomy becomes clearer: the female tubercle is oriented horizontally, while the male tubercle adopts a more vertical position. This difference in sagittal orientation forms the anatomical basis for early ultrasound prediction of fetal sex.<sup>(1,5)</sup>

The most relevant difference in these early stages lies in the fact that the urethral fold of the male fetus is in the process of closing, while in the female it remains unfused, constituting the primordium of the labia minora; similarly, the labioscrotal swellings also do not show complete fusion, as they will form the labia majora, a process that concludes around the fifth month of gestation. This lack of fusion in the female fetus can be observed in the first trimester as a "double notch" in the sagittal view of the genital tubercle, a useful marker, along with its angle, for predicting sex. In this context, the literature reports that an angle greater than 30° indicates male sex and a parallel or convergent angle (<30°) corresponds to female sex.<sup>(4)</sup>

In more routine clinical practice, knowing the early sex of a fetus could help increase the sensitivity and specificity of the combined test for trisomy 21 detection, if it is also adjusted for the fetal sex factor, since an increase in free human chorionic gonadotropin and pregnancy plasma protein A (PAPPA) has been observed in the female fetus.<sup>(6)</sup>

In recent years, there has been significant progress in the resolution of ultrasound equipment used to study fetal anatomy and screen for malformations during the first trimester of pregnancy. Part of this ultrasound protocol involves the accurate measurement of the fetal crown-rump length (CRL) in the sagittal plane, where the presence of the genital tubercle (GT) can be clearly visualized at the pelvic level and its characteristics determined. With this in mind, the present research was conducted to determine the accuracy of first-trimester ultrasound in predicting fetal sex through the sagittal evaluation of the genital tubercle and its anatomical orientation.

## METHODS

A prospective, multicenter, longitudinal, observational study was conducted on pregnant women attending the Center for Maternal-Fetal Medicine and Gynecology (CEMAFEG), as well as the FETALIS AMBATO Perinatal Care Center, for the first trimester screening during the period from 06/11/2021 to 17/11/2023.

A sample of 105 pregnant women was selected using a probabilistic, purposive sampling method. These women met the inclusion criteria (single-parent pregnancy, a viable fetus without congenital anomalies, and a crown-rump length between 45 and 84 mm) and the exclusion criteria (which included patient refusal to undergo sex prediction, congenital anomaly, or inability to subsequently confirm fetal sex). Each pregnant woman was evaluated using the correct algorithm for fetal sex determination, after obtaining her informed consent. Examinations were performed using a Voluson S8T ultrasound machine via the transvaginal route.

### Statistical processing

Data processing was performed using SPSS version 26 for Windows, employing descriptive and inferential statistical methods. Absolute frequencies and percentages were analyzed as descriptive statistics to represent the univariate behavior of the categorical variables. Inferential statistics were used for the bivariate analysis, specifically Pearson's chi-squared test, with p-values <0.05 considered statistically significant for statistically significant differences. The results are presented in tables.

### Ethical parameters

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki regarding the design and application of research involving human subjects, thus adhering to the principle of autonomy established in the International Code of Bioethics for research involving human subjects. The institution's Ethics Committee was consulted before the study was conducted, confidentiality of information was guaranteed, each patient was fully informed about the study's objectives and characteristics, and their written informed consent was obtained.

## RESULTS

Table 1 shows a high degree of agreement between first-trimester ultrasound sex prediction and final sex. Of the 50 fetuses initially classified as male, 94,0 % were confirmed as such, demonstrating high accuracy for this group. In contrast, the female sex prediction reached an accuracy of 83,6 %, as 46 of the 55 cases were indeed female. In total, 93 of the 105 fetuses were correctly classified, reflecting high overall accuracy, although with better performance for male sex identification.

**Table 1.** Comparison of the screening of the ssex in the first trimester versus definitive sex.

Sex in the first trimester	Ultimate sex				Total	
	Male		Female		No.	%
	No.	%	No.	%		
Male	47	94,0	3	6,0	50	47,6
Female	9	16,4	46	83,6	55	52,4
Total	56	53,3	49	46,7	105	100

Pearson's X2 test: 63,426 (p<0,01)

## DISCUSSION

Fetal sex determination from the first trimester has been the subject of research for several decades, allowing for the evaluation of multiple ultrasound predictors with varying degrees of accuracy. Sipahi et al.,<sup>(7)</sup> identified the anogenital distance (AGD) measurement as a relevant predictor for female sex, with a reported accuracy of 97,1 %; however, its performance for male sex was considerably lower, reaching only 76,7 %. The largest study based on this methodology was published in 2021 by Alfuraih et al.,<sup>(8)</sup> who evaluated 313 pregnant women and reported an overall accuracy between 64-70 %, suggesting limited diagnostic value.

Another line of research has examined the usefulness of fetal heart rate as an early marker of sex. However, a recent systematic review analyzing 223 publications, conducted by Nouri et al.,<sup>(9)</sup> in 2023, concluded that there is no statistically significant association to support this approach as a predictive tool. Similarly, Kurban et al.,<sup>(10)</sup> evaluated the distance between the yolk sac and the embryonic pole, obtaining a sensitivity of 70 % for predicting female sex in the first trimester, which demonstrates moderate accuracy.

Three-dimensional reconstruction of the genital tubercle has also been explored as a diagnostic alternative. Bogers et al.,<sup>(11)</sup> studied 112 pregnant women using 3D technology and calculated the orientation angle of the tubercle, obtaining a predictive efficacy of only 56 %, which limits its clinical applicability.

Among the methodologies described, measuring the orientation angle of the genital tubercle has proven to be the most reliable. The study with the largest sample size, conducted by González et al.,<sup>(3)</sup> in 2314 pregnant Latin American women, reported an overall accuracy of 90,1 %, a result consistent with our findings, in which a prediction rate of 88,6 % was achieved ( $p < 0,001$ ). These data reinforce the notion that the angle between the genital tubercle and the fetal spine is the most robust ultrasound indicator for determining sex in the first trimester. Similarly, Manzanares et al.,<sup>(12)</sup> studying 672 fetuses in a Hispanic population, also found an accuracy of 87.5%, corroborating the reproducibility of this method.

## CONCLUSIONS

Early determination of fetal sex in the first trimester not only avoids invasive procedures but also improves risk assessment for trisomies, especially trisomy 21. Measuring the angle between the genital tubercle and the fetal spine using sagittal ultrasound, preferably transvaginal, is the most reliable method. This study confirms its validity in the Ecuadorian population, with results consistent with international research. The technique showed an accuracy of nearly 90%, so its inclusion in first-trimester ultrasound screening (weeks 11.5 to 13.6) is recommended, integrating fetal sex into the risk analysis.

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