ORIGINAL PAPER

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Intrauterine growth restriction according to Peruvian customized curves: validation and diagnostic accuracy study

Restricción de crecimiento intrauterino según curvas personalizadas peruanas: estudio de validación y precisión diagnóstica

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ABSTRACT

Introduction: There is no consensus on the growth curve to be used to assess fetal growth. Objectives: To validate customized curves and study their performance in the detection of neonates with intrauterine growth restriction (IUGR), as well as their diagnostic accuracy. Methods: Initially, customized curves were designed with 2,792 singleton fetuses from low-risk pregnancies; the optimal weight at 40 weeks = 1,496.202 + (64.379 x fetal sex) + (831.362 x maternal length) + (9.567 x pregestational weight) was calculated and combined with a standard proportionality function to adjust the weights according to gestational age. Subsequently, its performance was evaluated by applying it in a retrospective cohort of neonates aged 24–40 weeks born between 2018-2022 in a tertiary hospital in Lima-Peru. Twins and congenital anomalies were excluded. Results: A total of 6,598 neonates were studied. Customized curves showed good agreement with INTERGROWTH-21 (IG21) (kappa = 0.68; 95%CI = 0.62-0.74). They detected 2.8% of IUGR (184/6,598), similar to the 3.1% for IG21 (205/6,598). They showed high specificity and negative positive value (NPV) (97% and 98%; 95%CI = 97-98% and 98-99%, respectively). The risk for perinatal death (RR = 7.2; 95%CI = 4.6-11) and accuracy (96; 95%CI = 95-96%) were higher than those of the Fetal Medicine Foundation (FMF) (RR=3.6; 95%CI = 2.5-5.2 and accuracy= 89%; 95%CI = 88-89%, respectively). Conclusion: The customized Peruvian curves were reliable in assessing IUGR. Their detection capacity and diagnostic accuracy were similar to other international curves, although somewhat higher than those of the FMF.

Key words: Perinatal care, Fetal growth retardation, Fetal development, Ultrasonography, prenatal, Fetal research, Perinatal mortality

RESUMEN

Introducción. No existe consenso sobre la curva de crecimiento a utilizar para evaluar el crecimiento fetal. Objetivos. Validar unas curvas personalizadas y estudiar su rendimiento en la detección de neonatos con restricción de crecimiento intrauterino (RCIU), así como su precisión diagnóstica. Métodos. Inicialmente se diseñó unas curvas personalizadas con 2,792 fetos únicos de embarazos de riesgo bajo; se calculó el peso óptimo a las 40 semanas = 1,496.202 + (64.379 x sexo fetal) + (831.362 x talla materna) + (9.567 x peso pregestacional), ecuación que se combinó con una función de proporcionalidad estándar para ajustar los pesos según su edad gestacional. Posteriormente se evaluó su rendimiento aplicándola en una cohorte retrospectiva de neonatos de 24 a 40 semanas nacidos entre 2018 y 2022 en un hospital de tercer nivel de Lima, Perú. Se excluyeron gemelos y anomalías congénitas. Resultados. Se estudió 6,598 neonatos. Las curvas personalizadas mostraron buena concordancia con INTERGROWTH-21 (IG21) (kappa = 0,68; IC95% = 0,62 a 0,74). Se detectó un 2,8% de RCIU (184/6,598), similar al 3,1% de IG21 (205/6,598). Las curvas mostraron alta especificidad y valor positivo negativo (VPN) (97% y 98%; IC95% = 97 a 98% y 98 a 99%, respectivamente). El riesgo para muerte perinatal (RR =7,2; IC95% = 4,6 a 11) y su exactitud (96; IC95% = 95 a 96%) fueron superiores a los de la Fundación de Medicina Fetal (FMF) (RR = 3,6; IC95% = 2,5 a 5,2 y exactitud = 89%; IC95% = 88 a 89%, respectivamente). Conclusión. Las curvas peruanas personalizadas resultaron fiables para evaluar la RCIU. Su capacidad de detección y su precisión diagnóstica fueron similares a otras curvas internacionales, aunque algo superiores a las de la FMF.

Palabras clave. Atención perinatal, Restricción del crecimiento fetal, Desarrollo fetal, Ultrasonido, Investigación fetal, Mortalidad perinatal

Introduction

Intrauterine growth restriction (IUGR) occurs when a fetus is unable to reach its genetically determined growth potential[1]. The importance of its detection lies in its association with feto-neonatal morbidity and mortality[1]. According to the recommendations of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), IUGR is diagnosed when the ultrasound-measured fetal weight or abdominal circumference is below the 3rd percentile[1]. However, the determination of this percentile depends on the fetal growth curve or table used, with discrepancies between the results[2].

Reference tables have been designed since past decades, such as the Hadlock table, which was carried out with a white population in the USA[3], the Fetal Medicine Foundation (FMF) English table with a mostly white population[4], or the World Health Organization (WHO) growth standard designed with low-risk women to express the normal growth of a fetus under optimal conditions[5]. The Intergrowth-21st project differs from the former by not using femur length in the calculation of fetal weight[6], while the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) developed tables for specific ethnicities without adjusting for other factors[7]. There are also customized growth curves, whose formulas include maternal and fetal characteristics such as length, pregestational weight, parity, and fetal sex. Several studies have justified their use[8-10], but others disagree with these considerations[11,12]. Therefore, there is disagreement among clinicians as to which of the curves should be used to classify fetal growth[13].

In Peru, efforts have been made to design curves for the Peruvian population[14,15]. However, there are no validated personalized curves, so in many hospitals international curves are used, and doubts persist as to whether their results reflect the real growth of Peruvian fetuses. Furthermore, it is not clear whether the international curves overdiagnose or underestimate Peruvian fetuses with IUGR. There is no information on their diagnostic accuracy or performance in predicting perinatal death in this country. There is also no information on whether a Peruvian curve would have greater detection and accuracy compared to international curves when applied to the Peruvian population. For this reason, in this study we designed customized intrauterine growth curves for the Peruvian population, which were validated by demonstrating their performance in the detection of neonates with IUGR and their diagnostic accuracy when compared with the most widely used international curves in the world.

Methods

In a first stage, a personalized Peruvian model was constructed. The personalized growth curve was developed by one of the authors (OTR). Ultrasound fetal weights were prospectively calculated for 2,792 fetuses of low-risk pregnant women, i.e. women who did not have hypertension, preeclampsia, diabetes, congenital anomalies, premature rupture of membranes, symptoms of preterm labor, intrauterine growth restriction and who were not hospitalized during pregnancy. They were attended at the Alberto Sabogal Sologuren (n=1,350) and Edgardo Rebagliati Martins (n=1,442) national hospitals in Lima, Peru. They had singleton fetuses at 40 weeks of gestation (calculated by ultrasound at 11 0/7 - 13 6/7 weeks). The study was performed by gynecologists with more than three years of experience in ultrasonography, who used Samsung HS70A ultrasound scanners. Fetal weights were calculated based on biparietal diameter, head circumference, abdominal circumference and femur length, according to Hadlock's formula[3]. An optimal weight at 40 weeks (280 days) was calculated (mean = 3,421.8; standard deviation = 306.5), obtaining a coefficient of variation (CV) of 9%. Then, a linear regression was developed obtaining the following regression equation: optimal weight = 1496.202 + (64.379 x fetal sex) + (831.362 x maternal height) + (9.567 x pregestational weight). F = 170.76 p = 0.00 (ANOVA). R2 = 15,5. Likewise, the equation was combined with a standard proportionality function to adjust the ultrasound weights for gestational age and to consider weight variations during pregnancy, as described by Gardosi[9]. Finally, the Z-scores (observed weight-expected weight/standard deviation) were calculated and their percentiles were determined. The calculator to perform these assessments is available free of charge on the web page https://oswaldotipiani.com/

In the second stage, the personalized curves were validated. Their detection capacity was tested by studying a cohort of neonates who were assumed to have IUGR when their birth weight percentile was less than 3. The diagnostic accuracy of the IUGR condition determined by the Peruvian curves (independent variable) for diagnosing perinatal death (output variable) was also studied. These results were compared with those obtained by the standards/reference tables of the World Health Organization (WHO), Fetal Medicine Foundation (FMF), Hadlock, INTERGROWTH-21st Project (IG21) and the US National Institute of Child Health and Human Development (NICHD).

We then conducted a retrospective observational cohort study in which we reviewed the obstetric and neonatal records of deliveries between 24-40 weeks attended at the Alberto Sabogal Sologuren National Hospital (HNASS) of the Social Security of Peru (EsSalud), in Lima-Peru, from January 2018 to December 2022. The entire population was studied. Neonates with congenital anomalies according to their medical records, multiple pregnancies, incomplete maternal weight and height data, and atypical data (maternal age outside 13-50 years, body mass index greater than 46 or less than 15 kg/cm2, and neonates weighing > 5,500 g or < 500 g) were excluded.

For the statistical analysis, since there is no curve worldwide that is considered a gold standard, reliability was determined by studying the strength of agreement between the diagnosis of IUGR (neonatal weight percentile < 3) provided by the Peruvian curves and the diagnosis of IUGR given by each international standard/table. Cohen's Kappa was used (slight agreement: 0.01-0.20; acceptable: 0.21-0.40; moderate: 0.41-0.60; good or substantial: 0.61-0.80 and almost perfect: 0.81-1). Also, McNemar's test was used to evaluate the discordances between curves, with the null hypothesis that the discordances are uniformly distributed.

On the other hand, 2 x 2 cross-tabulations were used, taking IUGR condition as the independent variable given by each growth curve and perinatal death as the output variable, defined as the presence of intrauterine death (stillbirth) or neonatal death within the first 28 days of birth. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy (sensitivity + specificity/total), false positives and positive (LR+) and negative (LR-) likelihood ratios were calculated, with their respective confidence intervals using Wilson's method. SPSS version 24 and R were used. Statistical significance was set at 0.05. The recommendations of the STARD guidelines for diagnostic validity studies were followed.

Regarding ethical aspects, the research was approved by the HNASS Ethics Committee on September 22, 2022 (Registration Code 684-2022-598). The study was governed by the applied clinical research regulations and the personal data protection laws in force in Peru.

Results

Of 7,250 potentially eligible pregnant women, 6,598 met the selection criteria. Figure 1 shows the flowchart.

Table 1 displays the characteristics of the population studied. 33.8% of the patients were of advanced maternal age and the majority were multiparous with a normal body mass index (BMI). Only 6.5% had short stature. The incidence of diabetes was 2.3%. High percentages of preeclampsia, prematurity and cesarean sections were found. Perinatal death occurred in 129 cases (2%).

Regarding the characteristics of the personalized curves, the estimated weights for each gestational age showed normal distribution (Kolmogorov-Smirnov or Shapiro-Wilk > 0.05), obtaining a coefficient of variation of 12.4 at 40 weeks, which increased as gestational age decreased until a value of 18 at 25 weeks.

Regarding the reliability of the Peruvian curves, considering the minimum value of the confidence interval, good (substantial) agreement was found for the diagnosis of IUGR between the Peruvian curves and IG21 (minimum value of the Kappa CI = 0.62), moderate agreement with Hadlock, NICHD and WHO (0.56 and 0.58 and 0.47, respectively) and acceptable agreement only with FMF (Kappa = 0.34). Likewise, in the study of discordances, it was observed that McNemar's *p* value was > 0.05 when compared with IG21 (Table 2).

Table 1. Maternal and perinatal demographic characteristics.

Features	n = 6,598	
	Mean or n	± SD or (%)
Maternal age (years)	31.5	6.6
> 35 years	2,229	(33.8)
< 19 years old	234	(3.5)
Pregestational weight	64.8	12.7
Nulliparous	2,289	(34.7)
Gestational age	37.4	2.7
Prematurity (<37 weeks)	1,535	(23.3)
Body mass index (kg/m2)	26.7	4.8
BMI ≥ 30 kg/m2	1,401	(21.2)
BMI < 18.5 kg/m2	72	(11)
Maternal size (meters)	1.56	0.6
Maternal height < 1.48 meters	430	(6.5)
Female fetus	3,193	(48.4)
Birth weight (grams)	3,116.5	747.3
Term neonate < 2,500 g	216	(4.3)
Term neonate > 4,000 g	504	(9.9)
Preeclampsia	1,074	(16.3)
Diabetes	155	(2.3)
Premature rupture of membranes	541	(8.2)
Cesarean section	4,798	(73)
Perinatal death	129	(2)
Stillbirths	44	(0.7)
Neonatal death	85	(1.3)

BMI: body mass index; SD: standard deviation

In terms of detection capability, the Peruvian curves identified 184 neonates with IUGR (184/6,598 = 2.8%), a percentage similar to the 3.1% of IG21 (205/6,598) (p=0.309), but significantly lower than the other curves (Hadlock: 370/6,598; NICHD: 320/6,598 and WHO: 458/6,598). The FMF chart was significantly higher than the rest of the curves (694/6,598 = 10.5%) (p<0.001) (Figure 2).

Regarding their measures of effect, the RR for perinatal death, given by IUGR status according to the custom curves, was 7.2 (95%CI = 4.6-11.1), which remained significant after adjusting for prematurity. In the stratified analysis this risk showed homogeneity with Hadlock, IG21, NICHD and WHO (p=0.592), obtaining a combined RR = 6.8 (95%CI = 5.7-8.1; p<0.001). When comparing this combined risk with FMF, the homogeneity test yielded a Chi-square = 8 (p=0.004) (Figure 3).

Concerning measures of diagnostic accuracy, Table 3 shows that the various growth curves had sensitivities ranging from 17%-32%, with specificities 90%-97%. They also noted low PPVs (6%-14%) and high NPVs (98%-99%). LR+ ranged from 3-8.3, but with high LR- values (0.7-0.8). FMF curves showed the highest levels of false positives (10%). Diagnostic accuracy exceeded 90% for most curves.

Figure 1. Participant selection flowchart.

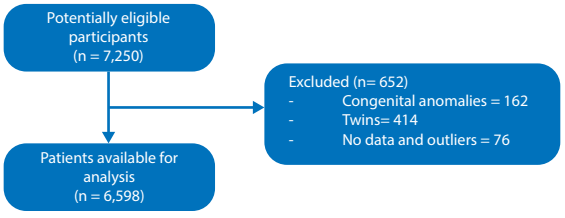
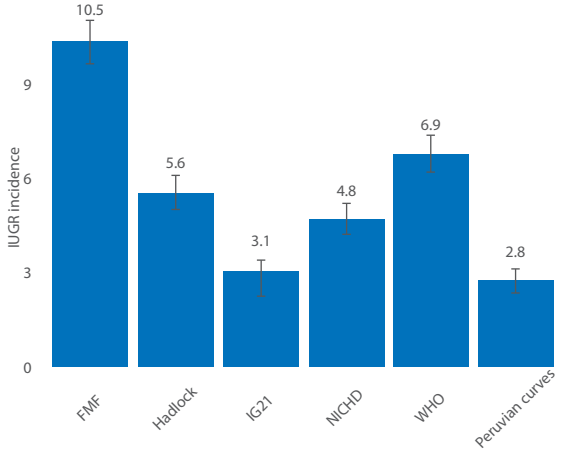


Figure 2. Incidence of intrauterine growth restriction (IUGR) according to growth curves.



FMF: Fetal Medicine Foundation, IG21: INTERGROWTH-21st Project, NICHD: US National Institute of Child Health and Human Development, WHO: World Health Organization

Table 2. Concordance between Peruvian custom curves and other standards/growth curves for the diagnosis of IUGR.

Growth curve/standard	Cohen's Kappa value (95% CI)	Percentage of agreement value (95% CI)	McNemar's test (p-value)
Peruvian curves	Ref.	Ref.	Ref.
Hadlock	0.61 (0.56-0.67)	96.9 (96.4-97.3)	< 0.01
FMF	0.39 (0.34-0.44)	92.2 (91.6-92.9)	< 0.01
IG21	0.68 (0.62-0.74)	98.2 (97.8-98.5)	0.07
NICHD	0.63 (0.58-0.68)	97.3 (96.8-97.7)	< 0.01
WHO	0.52 (0.47-0.58)	95.5 (95-96)	< 0.01

Ref: reference, FMF: Fetal Medicine Foundation, IG21: INTERGROWTH-21st Project, NICHD: US National Institute of Child Health and Human Development, WHO: World Health Organization

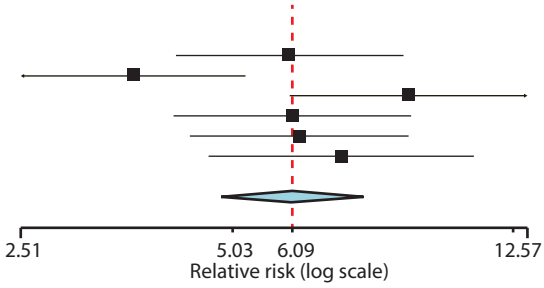
Table 3. Diagnostic accuracy measures of IUGR status according to standards/growth curves for perinatal death.

	Peruvian curves	Hadlock	FMF	IG21	NICHD	WHO
Sensitivity	17 (11-25)	26 (19-35)	30 (22-39)	22 (16-31)	24 (17-32)	32 (24-41)
Specificity	97 (97-98)	95 (94-95)	90 (89-91)	97 (97-98)	96 (95-96)	94 (93-94)
PPV	12 (8-18)	9 (6-13)	6 (4-8)	14(10-20)	10 (7-13)	9 (7-12)
NPV	98 (98-99)	98 (98-99)	98 (98-99)	98 (98-99)	98 (98-99)	99 (98-99)
LR +	6.8 (4.5-10.3)	5.1 (3.7-6.9)	3 (2.2-3.9)	8.3 (5.8-11.8)	5.4 (3.9-7.5)	4.9 (3.8-6.5)
LR -	0.8 (0.8-0.9)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.7 (0.7-0.8)
False positives	3 (2-3)	2 (1-2)	10 (9-11)	3 (2-3)	4 (4-5)	6 (6-7)
Accuracy	96 (95-96)	93 (93-94)	89 (88-89)	96 (95-96)	94 (94-95)	92 (92-93)

PPV: Positive predictive value, NPV: Negative predictive value, LR+: Likelihood ratio positive, LR-: Likelihood ratio negative, FMF: Fetal Medicine Foundation, IG21: INTERGROWTH-21st Project, NICHD: US National Institute of Child Health and Human Development, WHO: World Health Organization

Figure 3. Relative risk for perinatal death from IUGR condition according to growth standards/curves.

Curve	RR (95% C.I.)	Death/IUGR	Death/No IUGR
Hadlock	6 (4.1;8.8)	34/370	95/6228
FMF	3.6 (2.5;5.2)	39/694	90/5814
IG21	8.9 (6;13.1)	29/205	100/6293
NICHD	6.1 (4.2;9)	31/320	98/6180
OMS	6.3 (4.4;8.9)	41/458	88/6140
Peruvian charts	7.2 (4.6;11.1)	22/184	107/6414
Overall	6.1 (4.8;7.8)	196/2231	578/37069
(I^2=57.71%, *p*=0.037)			



FMF: Fetal Medicine Foundation, IG21: INTERGROWTH-21st Project, NICHD: US National Institute of Child Health and Human Development, WHO: World Health Organization

Discussion

Good concordance was found between the Peruvian and IG21 personalized curves. Their diagnostic performance was similar to the rest of the curves studied. However, when compared with FMF, the customized curves had a lower false positive rate, expressed the risk of perinatal death more strongly than FMF, showed a LR that was twice that achieved by FMF and their diagnostic accuracy was also superior.

As for the characteristics of the custom curves, Gardosi's assumption of normality[9] was demonstrated for the estimated weights for each gestational age. In contrast, their coefficients of variation were high at very early gestational ages, which may be explained by the small sample number (less than 30 cases at gestational ages less than 28 weeks). However, the CV of 12.4% obtained at 40 weeks (n = 1,086) is similar to the 12% found by Hocquette[16] for each gestational age at term studied, although somewhat higher than that obtained by Gardosi (11%)[17].

As regards reliability, the concordance for IUGR status provided by the Peruvian curves was good (substantial) when compared with IG21. McNemar's test had a *p* value > 0.05, so the null hypothesis that discordances are uniformly distributed due to chance could not be rejected, unlike the comparison with the rest of the curves. This means that, if we consider IG21 as a golden test, we would be demonstrating the reliability of the customized Peruvian curves. On the other hand, we speculate that the low concordance with FMF could be due to the phenotypic difference between the populations studied, since FMF included in its design a mostly white English population[4].

In relation to its ability to detect neonates who suffered IUGR, it was observed that its percentage (2.8%) was very similar to IG21 (3.1%), but significantly lower than the rest of the standards/tables. These findings are in agreement with other studies, such as that of Fernandez[18] who, using IG21 in a sample of 5,442 singleton pregnancies, detected 106/5,442 (2.0%, 95% CI 1.7-2.4%) IUGR newborns. Moreover, in a study with a large Latin American population (n= 67,968), Miranda[19] found a prevalence of IUGR of 2.1% under the IG21 criteria and 6.2% according to WHO, results very close to ours (3.1% and 6.9% for IG21 and WHO, respectively), raising the question of whether the WHO standard detects more IUGR in Latin America or whether it overdiagnoses them. What does seem to be clear is the

overdiagnosis of IUGR when FMF is used, since its detection rate (10.5%) is significantly higher than the other standards/tables and is similar to the worldwide prevalence of small for gestational age (SGA) characterized by < 10th percentile[20]. This finding was also observed by another study, in which, using various growth curves to detect SGA, FMF found a prevalence of 24.4%, which is much higher than 6.8% for NICHD, 11.6% for WHO, 13.2% for IG21 and 16.2% for Hadlock[20].

In regards to risk estimation, there was an overlap of the confidence intervals of the RRs, so that all curves expressed significantly higher risk of perinatal death when detecting IUGR. A meta-analysis comparing the risk of perinatal death when using custom versus population-based curves also found an overlap of the confidence intervals of their risks (OR = 5.8; 95%CI = 3.8-7.8 and OR = 4; 95%CI = 2.8-5.1 for custom and population-based curves, respectively)[21]. Of note again, FMF was the curve whose RR was significantly lower than that of the other curves, which showed homogeneity among them. These findings are similar to those of Kabiri et al.[20] who, when studying adverse perinatal outcomes in SGA fetuses, obtained high RR scores with NICHD (2.46; 95%CI = 1.9-3.1) but low with FMF (1.47; 95%CI = 1.2-1.8).

As for the diagnostic accuracy measures of the Peruvian curves, they were very similar to the rest of the standards/tables, showing good values of diagnostic accuracy, low sensitivities and PPVs, but high specificities and NPVs, which shows the usefulness of the growth curves as tools that communicate reassurance to the physician and the patient when the weight of a fetus is above the 3rd percentile, since the probability of perinatal death is very low. However, none of the curves could be used as a screening test, as the sensitivities and PPVs are poor. These findings are compatible with those found by Grantz[22] when, when studying neonatal morbidity in SGA fetuses using 3 models of customized curves, he found sensitivities and specificities of 13-15% and 89-93%, respectively, as well as PPVs and NPNs of 5.6-7.2% and 96.3%, respectively. Likewise, Kabiri, when studying SGA fetuses in relation to perinatal death, found sensitivities from 25%-40% and specificities from 84%-93%; as well as PPVs from 1-2% and NPVs of 100%[20]. On the other hand, the Peruvian curves indicated that an IUGR result is 6.8 times more likely to come from a fetus that will suffer perinatal death than from one that will not (LR+), showing strong evidence to confirm the diagnosis. However, LR- did not support these scores, as they did not reach the ideal value for any growth curve (LR- ideal: < 0.2). These findings are similar to those described by Melamed et al.[10], who observed that among SGA fetuses the LR+ were significantly higher for detecting placental abnormalities with the use of customized curves (LR+ = 3.4) rather than population standards, but, also without reaching ideal LR- (LR- = 0.8).

It is also noteworthy that the Peruvian curves showed one of the lowest false positive rates (3%) compared to WHO (6%) and FMF (10%). These findings could clarify the differences in detection rates between these curves and the interpretation of these curves: the WHO and FMF curves show higher IUGR detection rates than the customized curves, but with higher false positives. This would also explain the finding in Miranda's study[19] that OMS apparently detected more SGA neonates than using IG21, but with higher diagnostic yield of IG21 for low Apgar score and low ponderal index. We must remember that false positives can lead to unnecessary interventions and anxiety for patients[20].

Based on these results we can affirm that the Peruvian custom curves are reliable in their assessment of IUGR. That their measures of detection and diagnostic accuracy were similar to IG21, a standard that showed one of the best diagnostic performances when evaluating a considerable number of neonates in the Peruvian population. That its performance was somewhat superior to FMF and that, due to its high negative predictive value, it is a table that provides reassurance when its percentiles rule out IUGR.

The main strength of the study is its sample size, which allows us to evaluate perinatal mortality with adequate statistical power. Another strength is the comparison of the Peruvian curves with five of the most widely used standards/tables in the world, which also allows us to know their results in the evaluation of neonates in the Peruvian population. However, it also presents weaknesses, such as using intrauterine growth curves to evaluate neonatal weights. However, since the outcome of interest (perinatal death) is a postnatal variable, the exposure of interest was weight < 3rd percentile at

birth, this being an acceptable indicator[10]. Likewise, because all the curves were studied under the same conditions, the comparative findings are valid to study concordances and differences between them[19]. On the other hand, we defined IUGR based solely on fetal weight, without including abdominal circumference, which is also accepted and recommended for this purpose[1]. Likewise, this study was performed in a tertiary level center that concentrates cases of high maternal and perinatal morbidity, so the results should also be validated in low-risk health centers.

Conclusion

The customized Peruvian curves were reliable in their assessment of IUGR. Their detection ability and diagnostic accuracy were similar to other international standards/tables, but somewhat superior to the FMF.

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References

1. Lees CC, Stampalija T, Baschat A, da Silva Costa F, Ferrazzi E, Figueras F, et al. ISUOG Practice Guidelines: diagnosis and management of small-for-gestational-age fetus and fetal growth restriction. Ultrasound Obstet Gynecol. August 2020;56(2):298–312. doi: 10.1002/uog.22134
2. Visser GHA, Nicholson WK, Barnea ER, Ramasauskaite D, Nassar AH, FIGO Safe Motherhood, Newborn Health Committee. FIGO position paper on reference charts for fetal growth and size at birth: Which one to use? Int J Gynaecol Obstet. February 2021;152(2):148–51. doi: 10.1002/ijgo.13500
3. Hadlock FP, Harrist RB, Carpenter RJ, Deter RL, Park SK. Sonographic estimation of fetal weight. The value of femur length in addition to head and abdomen measurements. Radiology [Internet]. February 1984 [cited 10 December 2022];150(2):535–40. https://pubs.rsna.org/doi/10.1148/radiology.150.2.6691115
4. Nicolaides KH, Wright D, Syngelaki A, Wright A, Akolekar R. Fetal Medicine Foundation fetal and neonatal population weight charts. Ultrasound Obstet Gynecol. July 2018;52(1):44–51. doi: 10.1002/uog.19073
5. Kiserud T, Piaggio G, Carroli G, Widmer M, Carvalho J, Neerup Jensen L, et al. The World Health Organization Fetal Growth Charts: A Multinational Longitudinal Study of Ultrasound Biometric Measurements and Estimated Fetal Weight. PLoS Med. January 2017;14(1):e1002220. doi: 10.1371/journal.pmed.1002220
6. Odibo AO, Nwabuobi C, Odibo L, Leavitt K, Obican S, Tuuli MG. Customized fetal growth standard compared with the INTERGROWTH-21st century standard at predicting small-for-gestational-age neonates. Acta Obstet Gynecol Scand. November 2018;97(11):1381–7. doi: 10.1111/aogs.13394
7. Buck Louis GM, Grewal J, Albert PS, Sciscione A, Wing DA, Grobman WA, et al. Racial/Ethnic Standards for Fetal Growth, the NICHD Fetal Growth Studies. Am J Obstet Gynecol [Internet]. October 2015 [cited 11 November 2022];213(4):449.e1-449.e41. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4584427/
8. Hugh O, Williams M, Turner S, Gardosi J. Reduction of stillbirths in England from 2008 to 2017 according to uptake of the Growth Assessment Protocol: 10-year population-based cohort study. Ultrasound Obstet Gynecol. March 2021;57(3):401–8. doi: 10.1002/uog.22187
9. Gardosi J, Francis A, Turner S, Williams M. Customized growth charts: rationale, validation and clinical benefits. Am J Obstet Gynecol. February 2018;218(2S):S609–18. doi: 10.1016/j.ajog.2017.12.011
10. Melamed N, Hiersch L, Aviram A, Keating S, Kingdom JC. Customized birth-weight centiles and placenta-related fetal growth restriction. Ultrasound Obstet Gynecol. March 2021;57(3):409–16. doi: 10.1002/uog.23516
11. Papageorghiou AT, Kennedy SH, Salomon LJ, Altman DG, Ohuma EO, Stones W, et al. The INTERGROWTH-21st fetal growth standards: toward the global integration of pregnancy and pediatric care. Am J Obstet Gynecol. February 2018;218(2S):S630–40. doi: 10.1016/j.ajog.2018.01.011
12. Iliodromiti S, Smith GCS, Lawlor DA, Pell JP, Nelson SM. UK stillbirth trends in over 11 million births provide no evidence to support effectiveness of Growth Assessment Protocol program. Ultrasound in Obstetrics & Gynecology [Internet]. 2020 [cited 15 December 2022];55(5):599–604. https://onlinelibrary.wiley.com/doi/abs/10.1002/uog.21999
13. Kajdy A, Filipecka-Tyczka D, Muzyka-Placzyńska K, Modzelewski J, Sys D, Baranowska B, et al. Fetal Growth Diagnosis and Management among Perinatal Medical Professionals: A Survey of Practice and Literature Review. Fetal Diagn Ther. 2021;48(5):342–52. doi: 10.1159/000514504.
14. 14. Ticona-Rendón M, Huanco-Apaza D. Curva de referencia peruana del peso de nacimiento para la edad gestacional y su aplicación para la identificación de una nueva población neonatal de alto riesgo. Rev peru med experim salud publica [Internet]. October 2007 [cited 7 December 2023];24(4):325–35. http://www.scielo.org.pe/scielo.php?script=sci_abstract&pid=S1726-46342007000400002&lng=es&nrm=iso&tlng=es
15. Tipiani O, Malaverry H, Páucar M, Romero E, Broncano J, Aquino R, et al. Curva de crecimiento intrauterino y su aplicación en el diagnóstico de restricción del crecimiento intrauterino. Rev peru ginecol Obstet [Internet]. 2011 [cited 25 October 2022];57(2):69–76. http://51.222.106.123/index.php/RPGO/article/view/188
16. Hocquette A, Monier I, Blondel B, Dufourg MN, Heude B, Zeitlin J. Testing the assumptions of customized intrauterine growth charts using national birth studies. Acta Obstet Gynecol Scand. April 2022;101(4):405–16. doi: 10.1111/aogs.14335

17. Gardosi J, Mongelli M, Wilcox M, Chang A. An adjustable fetal weight standard. Ultrasound Obstet Gynecol [Internet]. 1995 [cited 23 September 2023];6(3):168–74. https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1469-0705.1995.06030168.x

18. Fernandez-Rodriguez B, Alba C de, Galindo A, Recio D, Villalain C, Pallas CR, et al. Obstetric and pediatric growth charts for the detection of late-onset fetal growth restriction and neonatal adverse outcomes. J Perinat Med [Internet]. 1 February 2021 [cited 25 September 2023];49(2):216–24. https://www.degruyter.com/document/doi/10.1515/jpm-2020-0210/html

19. Miranda J, Maestre N, Paternina-Caicedo Á, Parra-Saavedra M, Caradeux J, Sepulveda-Martinez Á, et al. Performance of the INTERGROWTH-21st and World Health Organization fetal growth charts for the detection of small-for-gestational age neonates in Latin America. Intern J Gynecol Obstet [Internet]. 2023 [cited 23 September 2023];161(3):1083–91. https://onlinelibrary.wiley.com/doi/abs/10.1002/ijgo.14657

20. Kabiri D, Romero R, Gudicha DW, Hernandez-Andrade E, Pacora P, Benshalom-Tirosh N, et al. Prediction of adverse perinatal outcome by fetal biometry: comparison of customized and population-based standards. Ultrasound Obstet Gynecol [Internet]. 2020 [cited 11 November 2022];55(2):177–88. https://onlinelibrary.wiley.com/doi/abs/10.1002/uog.20299

21. Chiossi G, Pedroza C, Costantine MM, Truong VTT, Gargano G, Saade GR. Customized vs population-based growth charts to identify neonates at risk of adverse outcome: systematic review and Bayesian meta-analysis of observational studies. Ultrasound Obstet Gynecol [Internet]. 2017 [cited 27 September 2023];50(2):156–66. https://onlinelibrary.wiley.com/doi/abs/10.1002/uog.17381

22. Grantz KL, Hediger ML, Liu D, Buck Louis GM. Fetal growth standards: the NICHD fetal growth study approach in context with INTERGROWTH-21st and the World Health Organization Multicentre Growth Reference Study. Am J Obstet Gynecol. February 2018;218(2S):S641-S655.e28. doi: 10.1016/j.ajog.2017.11.593