Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2025**; 52(11): 39182
https://doi.org/10.31083/CEOG39182

Systematic Review

Prevalence of Fetal Structural Anomalies and Genetic Testing in Fetuses With Increased Nuchal Translucency: A Single-Center Cohort Study and Systematic Review With Meta-Analysis Comparing Latin America and Other Regions

Tania T. Herrera[1,2,*], Idalina Cubilla-Batista[1,2,3,4], Amador Goodridge[2,3], Yovani Chávez-Rodriguez[1,2], Anthonier Hinestroza-Newball[1], Jorge Mendéz-Ríos[5,6], Ameth Hawkins-Villarreal[7,8,9]

[1]Center for Medical Research, Pacífica Salud, Hospital Punta Pacífica, 0816 Panama City, Panama
[2]Sistema Nacional de Investigación, Secretaria Nacional de Ciencia y Tecnología, Senacyt, Ciudad del Saber, Panama
[3]Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT-AIP), Ciudad del Saber, Panama
[4]Docencia e Investigacion, Hospital Dr. Rafael Estevez, Caja de Seguro Social, 02038 Aguadulce, Cocle, Panama
[5]Molecular Diagnostics Laboratory, Centre Hospitalier Universitaire Laval, 2705 Quebec City, Canada
[6]Department of Genetics, School of Medicine, Universidad Interamericana de Panamá, 0818 Panama City, Panama
[7]BCNatal-Fetal Medicine Research Center (Hospital Clínic and Hospital Sant Joan de Déu), Universitat of Barcelona, 08028 Barcelona, Spain
[8]Obstetrics Department, Hospital Santo Tomás, University of Panama, 0801 Panama City, Panama
[9]Iberoamerican Research Network in Obstetrics, Gynecology, and Translational Medicine, 11560 Mexico City, Mexico
*Correspondence: taniah30@gmail.com (Tania T. Herrera)
Academic Editor: Paolo Ivo Cavoretto
Submitted: 21 March 2025 Revised: 14 June 2025 Accepted: 30 July 2025 Published: 26 November 2025

Abstract

Background: Chromosomal microarray analysis (CMA) is the recommended genetic test for fetuses with increased nuchal translucency (NT); however, its use in Latin America remains limited. The objective of this study was to determine the prevalence of genetic testing in fetuses with increased NT in Panama and across Latin America. **Methods**: We conducted a retrospective cohort study of 1512 women who underwent first-trimester screening in Panama, along with a systematic review and meta-analysis of studies reporting genetic testing in Latin America. A comprehensive literature search was conducted across MEDLINE (via PubMed), Epistemonikos, LILACS, BRISA, SciELO, and Google Scholar, covering studies from inception to June 2023 was updated to December 2023. The extracted data included population, setting, timing, and genetic testing methods. The Joanna Briggs Tool was used to assess the risk of bias. Pooled prevalence estimates were calculated using random-effects models. **Results**: Among 1236 fetuses in the Panamanian cohort, 77 (6.23%) had NT $\geq$95th percentile. The systematic review included 11 studies encompassing 842 fetuses diagnosed with increased NT. The overall proportion of fetuses undergoing invasive testing was 0.31 (95% confidence interval [CI]: 0.28–0.33). Anomalies were found in 63% of cases with increased NT. CMA was not reported in any of the studies. **Conclusions**: Most patients in Latin America do not undergo invasive testing, and conventional karyotyping remains the most frequently performed method. To date, no studies have reported the use of CMA in this context. Therefore, the findings of this study highlight significant gaps in access to genetic testing, emphasizing the need for strategic initiatives to improve test availability and build capacity for implementing microarray analysis in the region. **Registration**: The study has been registered on https://www.crd.york.ac.uk/prospero/ (registration number: CRD42023398899; registration link: https://www.crd.york.ac.uk/PROSPERO/view/CRD42023398899).

Keywords: prenatal screening; nuchal translucency; chromosomal microarray analysis; genetic testing; Latin America; fetal anomalies; prenatal diagnosis

1. Introduction

Nuchal translucency (NT), a first-trimester sonographic marker characterized by a subcutaneous accumulation of fluid behind the fetal neck [1–4], has been studied for over three decades. Increased fetal NT is associated with chromosomal abnormalities, congenital heart defects, and structural anomalies. Defined by the 95th and the 99th percentiles, NT $\geq$3 mm increases the risk of severe malformations by 15-fold, while NT $\geq$3.5 mm raises it by 40-fold [4,5]. Increased NT has also been linked to microdeletion syndromes and single-gene disorders.

1.1 Genetic Testing and International Guidelines

Despite standardized NT measurements, international guidelines for managing increased NT vary. For instance, the Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends genetic counseling, chromosomal microarray analysis (CMA), and a detailed second-

trimester ultrasound for NT >3.5 mm [6]. The American College of Obstetricians and Gynecologists (ACOG) advises similar measures, including fetal echocardiography, for NT >3.0 mm or above the 99th percentile [7]. In countries with universal healthcare, CMA is routinely offered for NT >99th percentile. Additionally, cell-free DNA testing is offered as an alternative for patients who do not consent to invasive procedures [8,9].

1.2 Challenges in Latin America

In Latin America, only one national prenatal screening program has been established [10–12]. However, significant barriers to accessing this program include a lack of genetic counselors, limited reimbursement policies, and inadequate medical genetics training. Moreover, the absence of national guidelines for prenatal genetic diagnosis has led to limited data on the availability and use of genetic and genomic testing for high-risk subgroups, such as fetuses with increased NT.

1.3 Objectives

This study aimed to determine the prevalence of fetal structural anomalies in pregnancies with increased NT and the proportion of women who underwent invasive prenatal diagnosis due to increased NT in Latin America and other countries.

2. Materials and Methods

2.1 Panamanian Cohort

This retrospective study selected women who underwent sonographic examination at the Hospital Punta Pacifica, Panama (November 2005–September 2018). Informed consent was obtained from all participants. Singleton and multiple pregnancies were included in the sample, with the maternal and fetal data collected using questionnaires and ultrasound assessments. NT measurements, recorded as the highest of three values, were considered to have increased if they were above the 95th percentile using established reference ranges [13]. Patients with a Down syndrome risk >1/250 were offered counseling and diagnostic tests (chorionic villus sampling or amniocentesis) using rapid FISH or quantitative fluorescence polymerase chain reaction (QF-PCR). Since 2014, noninvasive prenatal tests (i.e., Harmony, Nova Screen, Verify, and Panorama) have become available. Birth outcomes, including live births and adverse events (e.g., intrauterine death, miscarriage, or chromosomal anomalies), were retrieved from clinical records. The study followed ethical guidelines (RESEGIS 2397) and received IRB exemption (CBI-21-104).

2.2 Statistical Analysis

Quantitative variables were tested for normality using the Shapiro-Wilk test. Moreover, normally distributed variables were compared using the *t*-test (mean $\pm$ SD), whereas non-normally distributed variables were compared using the Mann-Whitney U test (median, interquartile range [IQR]). Qualitative variables were analyzed using the chi-square or Fisher's exact test, and significance was set at $p < 0.05$. Further, data were analyzed using STATA version 14.1 (College Station, TX, USA) and R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

2.3 Systematic Review

This systematic review followed the PRISMA guidelines [14] (**Supplementary Table 1**) and was registered on https://www.crd.york.ac.uk/prospero/ (registration number: CRD42023398899; registration link: https://www.crd.york.ac.uk/PROSPERO/view/CRD42023398899). Searches were conducted using databases such as MEDLINE (via PubMed), Epistemonikos, LILACS, BRISA, SciELO, and Google Scholar, without date restrictions, focusing on Spanish and Portuguese studies related to increased NT, genetic anomalies, and Latin America. The initial search (June 2023) was updated to December 2023.

Retrospective and prospective cohort studies on pregnant patients in Latin America were included in the review, whereas case series (<four cases) and pediatric studies without maternal data were excluded. Notably, the data were extracted using a pre-piloted Google Forms sheet by two independent reviewers, covering study details, sample size, inclusion criteria, diagnostic methods, and genetic findings. References were cross-checked, and discrepancies were resolved by consensus. Methodological quality was assessed using the Joanna Briggs Institute checklist for prevalence studies.

2.4 Data Synthesis and Statistical Analysis

Statistical analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria), while a meta-analysis of proportions was conducted using the "meta" and "metafor" packages. A random-effects model was applied using the restricted maximum likelihood (REML) estimator to account for between-study variability.

Heterogeneity was assessed using the τ^2, χ^2 (Cochran's Q), and I^2 statistics. The results are presented as forest plots [15,16]. For outcomes with low heterogeneity, a fixed-effects model was reported for comparison, and funnel plots and Egger regression tests were used to assess potential publication bias. Further, to ensure robustness, pooled estimates and heterogeneity metrics were independently confirmed using Stata version 14.1 (StataCorp, College Station, TX, USA) with the metaprop command. All results were presented with 95% confidence intervals (CIs), and significance was determined using a two-tailed *p*-value threshold of <0.05.

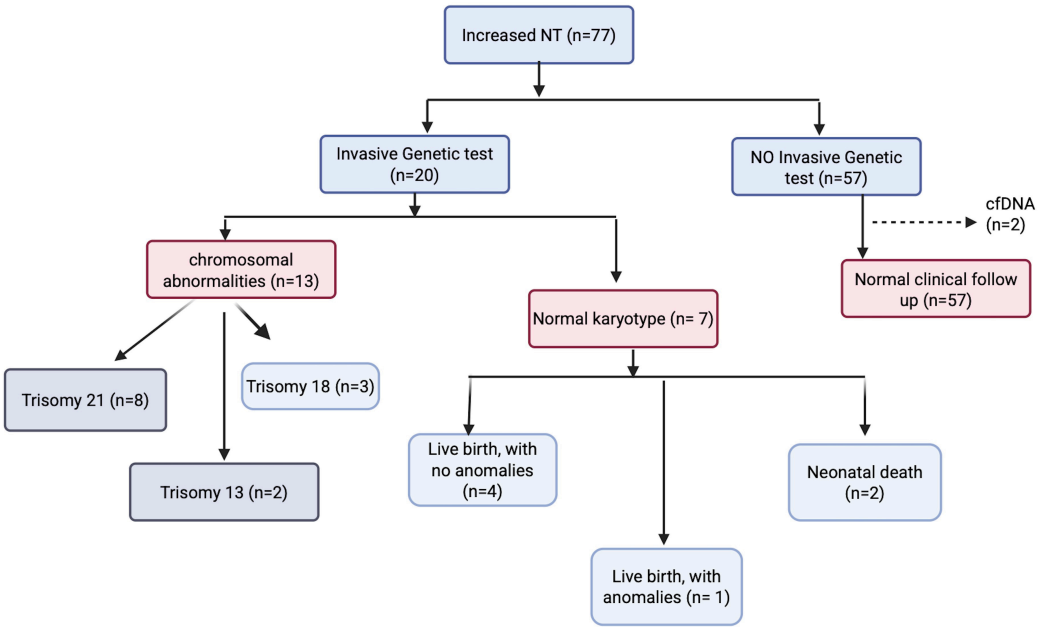

Fig. 1. Flow chart of a Panamanian cohort of increased nuchal translucency (NT). cfDNA, cell free DNA.

3. Results

3.1 Panamanian Cohort

A total of 1512 obstetric ultrasound examinations (of 1652 fetuses) were performed. After excluding patients who were lost to follow-up, pregnant at the time of data extraction, or had incomplete information, 1236 fetuses were included in the final analysis. The mean maternal age of the participants was 31.9 $\pm$ 5.2 years, the mean gestational age at the time of the scan was 13 weeks, and the median NT measurement was 1.76 mm (interquartile range: 0.90–9.80 mm). In 77 fetuses (6.23%), the NT measurement was equal to or above the 95th percentile, while 140 fetuses (13.4%) had an NT measurement equal to or above the 90th percentile (Fig. 1).

As regards pregnancy outcomes, 998 fetuses (96.1%) resulted in live births, while 40 fetuses (3.9%) had a composite adverse perinatal outcome. Additional findings included abnormal nasal bone in 11 fetuses (0.9%), abnormal ductus venosus flow in 10 fetuses (0.8%), and abnormal tricuspid flow in nine fetuses (0.7%). The characteristics of the study population are presented in **Supplementary Table 2**.

3.2 Fetuses With Increased NT

In 77 fetuses (6.23%), 58 had live birth without anomalies (75.3%): 25 had adverse outcomes (32.5%). 4 termination of pregnancy (TOP), one stillbirth and two neonatal death lacked karyotype results. Structural abnormalities were noted in adverse outcomes, which are detailed in Table 1.

Invasive diagnostic procedures such as chorionic villous sampling (CVS) or amniocentesis were performed in 20 cases (23.5%), while two cases (2.3%) underwent cell-free DNA (cfDNA) testing, both leading to healthy live births. Among the TOP cases, one had trisomy 21, one stillbirth was linked to severe oligohydramnios, and two neonatal deaths involved complex congenital heart defects, including a complete atrioventricular canal and double outlet right ventricle with anomalous pulmonary venous connection.

3.3 Fetuses With Normal NT

Adverse outcomes occurred in 24 fetuses with normal NT (<2.5 mm). Six (25%) patients had MC, including two monochorionic and one dichorionic twin pregnancies. Two of these MC were due to cervical incompetence; one followed intra-amniotic infection after cerclage, while the other occurred post-amniocentesis complications. The cause was unknown in 13 cases (54%). Additionally, two stillbirths were recorded: one in an obese patient with hypertension and preeclampsia and another in a patient with low body mass index (BMI) and chronic anemia in **Supplementary Table 3**.

3.4 Systematic Review

The present systematic literature search identified 306 citations related to increased NT, genetic testing, and chromosomal anomalies in Latin America. After removing duplicates, 39 full-text studies were assessed, of which 11 met the inclusion criteria Fig. 2 (Ref. [14]). Collectively, these 11 studies included 842 fetuses with increased NT. Among them, nine studies applied the fetal medicine foundation (FMF) guidelines and NT measurements to evaluate the risk of Down syndrome and other aneuploidies [11,17–24]. One

Table 1. Aneuploidy-adjusted risk, structural abnormalities, soft sonographic markers, karyotype results, and perinatal outcomes in 29 cases with increased NT.

Case number	NT (mm)	Sonographic markers	Risk 1/	Structural abnormalities	Karyotype	Perinatal outcome
314	3.2	Absent nasal bone, tricuspid regurgitation	140	Hypoplastic left heart syndrome	No	Intrauterine death
132	4.4	Absent nasal bone	3	Cystic hygroma, upper extremity distal transverse disruptive syndrome	No	Missed abortion
300	3.0	Nasal bone present, abnormal ductus venosus, tricuspid regurgitation	29	No anomalies	No	Live birth
411	4.5	Normal nasal bone	2	Complete atrioventricular canal, cystic hygroma	Trisomy 18	Missed abortion
437	4.8	Normal nasal bone, normal ductus venosus	44	Cystic hygroma	Normal	TOP
1178	2.7	Oligohydramnios	518	Isolated left clubfoot	No	Live birth, surgical repair
133	4.6	Normal nasal bone, normal ductus venosus, tricuspid valve normal	10	Holoprosencephaly, fetal megacystis, polydactyly	Trisomy 13	Missed abortion
542	5.6	Normal nasal bone, normal ductus venosus, tricuspid valve regurgitation	8	Cystic hygroma, hypoplastic left heart syndrome	Normal karyotype	TOP
600	8.9	Absent nasal bone, normal ductus venosus, normal tricuspid valve flow	5	Cystic hygroma	Trisomy 18	Spontaneous abortion
699	2.7	Normal nasal bone, abnormal ductus venosus, tricuspid regurgitation	3	Exomphalos, complete atrioventricular canal	Trisomy 21	Spontaneous abortion
732	6.6	Absent nasal bone, tricuspid regurgitation, abnormal venous ductus	4	Cystic hygroma	Trisomy 21	Missed abortion
771	8.2	Absent nasal bone, tricuspid regurgitation, abnormal four-chamber heart, absent bladder	10	Exomphalos	Trisomy 18	Missed abortion
789	6.5	Absent nasal bone, tricuspid regurgitation, abnormal four chambers of the heart	2	Bilateral ulnar deviation	Trisomy 21	Missed abortion
626	7.3	Absent nasal bone, tricuspid regurgitation, abnormal four chambers	159	Holoprosencephaly, exomphalos	Trisomy 13	Missed abortion
794	8.6	Absent nasal bone, abnormal tricuspid Doppler	2	Cystic hygroma, hydrops fetalis, ascites, bilateral pleural effusion, mitral atresia, interventricular septal defect	No	Missed abortion
630	8.7	Cystic hygroma, absent nasal bone	34	Atrioventricular defect	46, XY	Cesarean section, neonatal death
1069	3.5	Absent nasal bone, abnormal ductus venosus	4	Bilateral ulnar deviation, abnormal four chambers	Trisomy 21	Missed abortion
1204	3.3	Absent nasal bone	54	None	Trisomy 21	TOP
1108	1.8	Absent nasal bone, abnormal ductus venosus	18	Twin pregnancy discordant for anomaly, clenched hands, abnormal four-chamber view	No karyotype	Intrauterine death of one fetus
805	14.3	Absent nasal bone	3	Cystic hygroma, ectopia cordis	No karyotype	Missed abortion
855	2.9	Normal markers	3680	Absent left lower extremity	No karyotype	Missed abortion
958	7.6	Absent nasal bone	3	Cystic hygroma	No karyotype	Missed abortion
1135	3.3	Tricuspid regurgitation	3	Abnormal four-chamber view	No karyotype	Live birth

Table 1. Continued.

Case number	NT (mm)	Sonographic markers	Risk 1/	Structural abnormalities	Karyotype	Perinatal outcome
1167	3.3	Abnormal nasal bone	3	Double right ventricle outflow tract, abnormal pulmonary vein connection, imperforate anus with perianal fistula, left renal agenesis	46, XY, negative for 22q11 deletion	Neonatal death, neonatal exam: micropenis, scrotalized lips, left and right microtia
1393	9.2		3	Atrioventricular septal defect	No karyotype	Spontaneous abortion
627	6.2		3	Tricuspid atresia, levocardia	Normal	TOP
1325	1.9	Normal markers	9659	None		Live birth, normal follow-up
698	9.8	Absent nasal bone, intestinal hyperechogenicity	6	Renal agenesis	Trisomy 21	Missed abortion
1378	10		3	Cystic hygroma	Trisomy 21	Missed abortion

MC, miscarriages; TOP, termination of pregnancy. “/” indicates a ratio or risk value (e.g., 1/140 or ½).

study used maternal age as the sole screening criterion [25], while another employed the "Fetal Test" software for risk assessment [22].

The main characteristics of the studies included in the systematic review are presented in Table 2 (Ref. [11,17–27]).

3.5 Geographical Distribution of Studies

Four studies were conducted in Brazil and Mexico at academic university hospitals [17–20]. Three studies from Cuba were conducted in provincial centers affiliated with the National Center of Medical Genetics at the Medical University of Havana [7,21,25]. The studies carried out in Peru, Chile, and Colombia were conducted in various settings, including *in vitro* fertilization clinics [22,26], private genetic laboratories [23], and private clinics [24]. Invasive testing options included CVS and amniocentesis, although 36.6% of the patients did not undergo karyotype analysis.

3.6 Methodological Quality of Studies

The methodological quality assessment using the Joanna Briggs Institute (JBI) checklist revealed variability in study quality (Table 3, Ref. [11,17–26]).

Three studies were classified as having a low risk of bias, one had a moderate risk, and seven exhibited a high risk of bias. Common limitations of high-risk studies include inadequate sample sizes, unclear sampling methods, and a lack of response rate reporting. Conversely, low-risk studies demonstrated robust study designs, appropriate statistical analyses, and comprehensive reporting of study settings and participants.

3.7 Prevalence of Increased NT

Fig. 3 illustrates the pooled proportion of fetuses with increased NT identified across the four studies. The overall proportion of increased NT cases was found to be 0.03 (95% CI: 0.03–0.04). Individual study estimates ranged from 0.02 (95% CI: 0.02–0.03) in Vázquez in 2008 to 0.04 (95% CI: 0.03–0.04) in Saldanha in 2009 [18,23].

There was evidence of substantial statistical heterogeneity ($I^2 = 87.40\%$) and statistically significant Cochran's Q test ($p < 0.001$). Egger's test for funnel plot asymmetry was also conducted, resulting in z value in 0.33 and a p-value of 0.7374. This indicates no significant evidence of publication bias ($p > 0.05$). The expected effect size as the standard error approached zero was estimated to be 0.0306, with a 95% CI of 0.0105 to 0.0506. This finding suggests that the underlying effect size is likely unaffected by publication bias (**Supplementary Fig. 1**).

3.8 Prevalence of Invasive Testing

Fig. 4 presents a forest plot of the proportion of fetuses undergoing invasive testing. The pooled proportion of invasive testing was 0.31 (95% CI: 0.28–0.33), with individual study estimates ranging from 0.29 to 0.39. Heterogeneity was moderate ($I^2 = 36.65\%$), with a non-significant Q-test ($p = 0.11$), indicating that the variability across studies was not statistically significant.

3.9 Prevalence of Fetal Anomalies

A meta-analysis was conducted to determine the proportion of anomalies in cases with increased NT. The pooled estimate under the common-effect model indicated that 0.63 (95% CI: 0.59–0.68) of cases with increased NT were associated with anomalies. Similarly, the random-effects model yielded a proportion of 0.63 (95% CI: 0.52–0.73), albeit with a wider CI due to study variability (Fig. 5).

3.10 Risk of Cardiac Anomalies in Fetuses With Increased NT

The pooled proportion of cardiac anomalies was estimated to be 0.42 (95% CI: 0.1–0.73). The proportion of cardiac anomalies varied across studies, with Saldanha *et al*. (2009) [18] reporting 2.4%, Vieira *et al*. (2013) [19] reporting 7.0%, and the Panamanian cohort reporting 0.36%. The random effects model was used to account for heterogeneity, yielding a conservative estimate.

3.11 Comparison With Other Regions

A total of 1512 pregnancies (1236 fetuses) from the Panamanian cohort and 842 fetuses from 11 Latin American studies were analyzed. The prevalence of NT $\geq$95th percentile varied across regions, ranging from 3.6% to 62% in Latin America, 4%–6% in Europe, and higher in selected Asian studies. Congenital heart defects (CHD) were the most frequent structural anomalies in all regions, with rates between 10.4% and 20%, followed by cystic hygroma and hydrops fetalis (Table 4, Ref. [28]).

The aneuploidy detection rate was 33% among MC with karyotyping in Panama and varied from 10.5% to 62% across Latin America. In contrast, North American and European studies reported aneuploidy rates of 34.35%–51.3% in fetuses with NT $\geq$3.5 mm. Turner syndrome, trisomy 21, and trisomy 18 are the most commonly identified aneuploidies.

The invasive testing uptake was significantly lower in Latin America (31%) than in North America and Europe (close to 100%). Notably, CMA has not been reported in any Latin American study, despite it being the recommended genetic test in developed countries. Pregnancy termination rates were lowest in Latin America (7.1%–7.8%), in contrast to 46.9% in Canada and 66.1% in Turkey, likely reflecting legal and cultural differences in prenatal decision-making.

4. Discussion

4.1 Principal Findings

This study highlights the low uptake of invasive genetic testing for fetuses with increased NT in the context of Latin America, despite its importance in detecting chro-

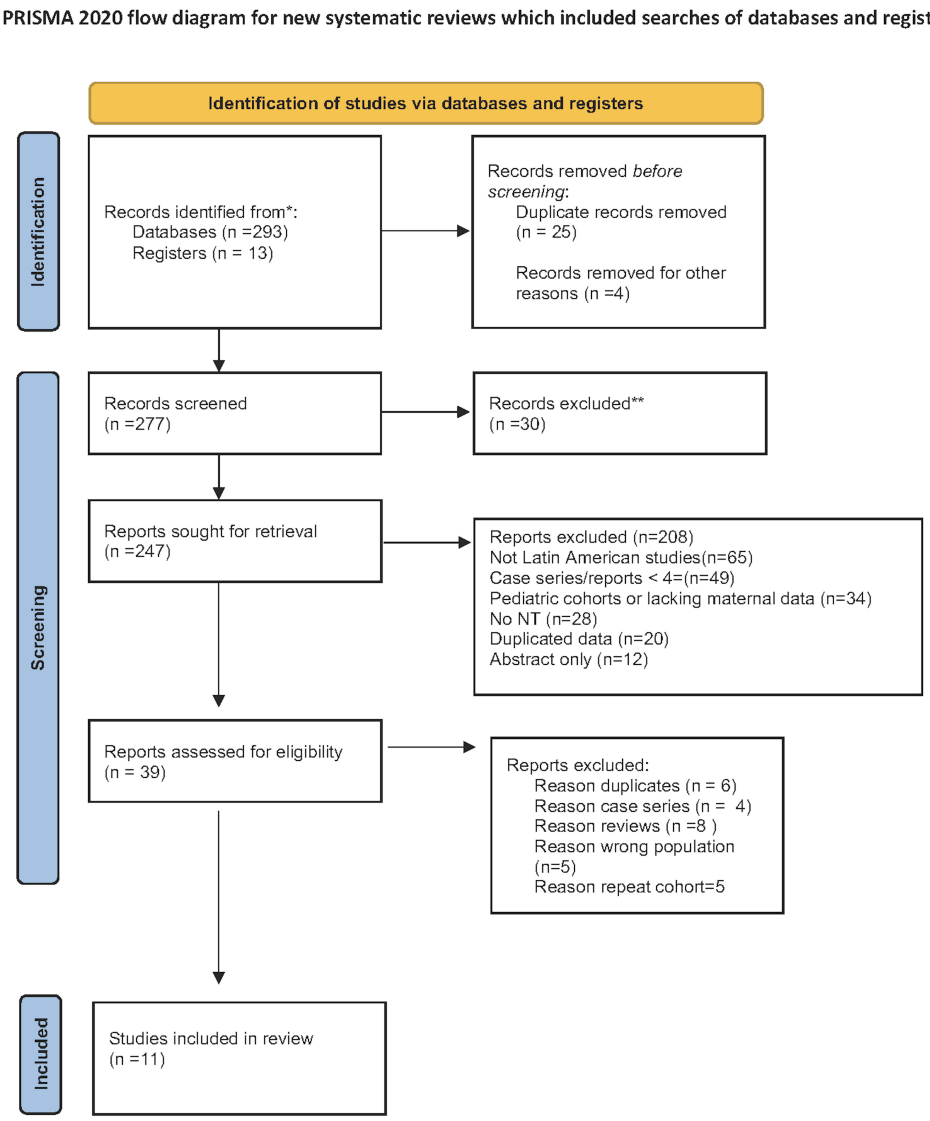

Fig. 2. PRISMA 2020 flow diagram for new systematic reviews that included searches of databases and registers only. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). **If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. For more information, visit: http://www.prisma-statement.org/.

mosomal and structural abnormalities. In the Panamanian cohort, only 23.5% underwent invasive testing, while a systematic review of 842 fetuses across 11 Latin American studies found a rate of 0.31 (95% CI: 0.28–0.33). These figures contrast sharply with those of North America and Europe, where nearly all high-risk pregnancies receive invasive testing [1–3].

Congenital heart defects (10.4%) and cystic hygroma with hydrops fetalis (13%) were found to be the most frequent fetal abnormalities in our cohort, aligning with global data showing structural anomalies in 30–50% of fetuses with increased NT [4–6]. However, unlike North America and Europe, where Turner syndrome is the most commonly reported chromosomal abnormality in increased NT cases (26.5%), no cases were reported in our review. This discrepancy likely reflects the low karyotyping and molecular testing rates in Latin America, thereby leading to potential underdiagnosis [7–9].

4.2 Comparison With International Data

The absence of CMA data in this review highlights the significant gap between Latin America and developed countries. While the ACOG and SOGC recommend CMA as the first-line diagnostic tool for fetuses with increased NT due to its ability to detect submicroscopic chromosomal imbalances [7], none of the included Latin American studies reported CMA use, which suggests limited accessibility.

Table 2. Characteristics of the included studies on NT screening.

Study	Year	Study period	Design	Setting	Screening criteria	GA at inclusion (weeks)	N	NT cutoff	Karyotype method	Chromosomal defects n, % (types)
Brizot, *et al*. [17]	2001	1999–2001	Prospective cohort	University Hospital Sao Paulo, Brazil	FMF Software, NT and Maternal age, Risk >1/300	10–14	173	>P95	Amniocentesis/CVS	22, 12.7% (7 T21, 9 other)
Saldanha, *et al*. [18]	2009	2008–2009	Prospective cohort	Hospital das Clinicas, Sao Paulo, Brazil	NT >P95 (Pandya *et al*. [27] curve)	11–13.6	246	>P95	Amniocentesis/CVS	35, 14.2% (NA)
Llanusa Ruiz, *et al*. [11]	2009	2006–2007	Retrospective cohort	Hospital Dr. Ramón González Coro, Cuba	NT >P95 (Nicolaides curves)	10–13.6	43	>P95	Amniocentesis/ cordocentesis	9, 20.9% (NA)
Alcedo Ramírez, *et al*. [26]	2009	2005–2007	Retrospective	Genetic private lab, Bogotá, Colombia	Invasive testing (maternal age, sonographic markers, biomarkers)	-	26 (6.9%)	Enlarged NT	Amniocentesis	7, 26.9% (5 T21 and 2 structural alterations)
Mendoza-Caamal, *et al*. [20]	2010	-	Case series	Instituto Nacional de Perinatologia, Mexico	NT >P95, FMF guidelines	11–14	48	>P95	CVS/Amniocentesis	9, 18.9% (3 T21, 3 XO, 2 T 18, 1 47, XYY)
González Herrera, *et al*. [21]	2014	2006–2010	Retrospective	National Prenatal Program, Cuba	NT >3 mm, Maternal age >37 years	11–13.6	71 (0.24%)	≥3 mm	CVS/Amniocentesis	40, 56.3%, (7 aneuploidies)
Vieira, *et al*. [19]	2013	2005–2011	Prospective	Hospital Francisco Morato de Oliveira, Sao Paulo, Brazil	NT >P95 (Wright curves), Or, Risk >1/100	10–14	116 (3.8%)	>P95	CVS/Amniocentesis	36, 31.0% (14 T21, 9 T18, 3 T13, 2 XO, 2 47XXY, 6 other)
Huamán, *et al*. [22]	2013	2007–2012	Prospective	Instituto Latinoamericano de Salud Reproductiva, Perú	NT >P95, Risk >1/200	11–13.6	30	>P95	CVS/Amniocentesis	12, 40.0% (8 T21, 4 T18)
Sepulveda, *et al*. [24]	2009	2003–2007	Retrospective	Ultrasound clinic, IVF Clinic (40% Twin pregnancies), Chile	NT and nasal bone	11–14	16 (3.6%)	>P95	CVS	5, 31.2% (3 T21, 1 T 18 and 1 X0)
Diez Chang and Bazán Lossio de Diez, [23]	2019	2012–2019	Retrospective	Clinica Santa Isabel, Lima, Perú	FMF software NT >5.5 mm	11–13	NR	>5.5 mm	Amniocentesis	17, 62.0% (7 T 21, 4 T 18, 5 XO and 1 T 22)
Vázquez Martinez, *et al*. [25]	2019	2006–2008	Retrospective	National Prenatal Diagnosis Program, Hospital Gineco, Cuba	Increased NT	10–13.6	73	>P95	Amniocentesis/ cordocentesis	4, 5.5% (4 T21)

GA, gestational age.

Table 3. Methodological quality assessment and risk of bias (JBI checklist).

Study	Sample frame appropriate?	Sampling method	Adequate sample size?	Subjects & setting described?	Valid condition identification?	Condition measured reliably?	Statistical analysis appropriate?	Response rate addressed?	Total score (0–8)	Risk of bias
Alcedo Ramírez, *et al.* [26]	No	No	No	No	Yes	Yes	Yes	No	3	High
Brizot, *et al.* [17]	Yes	Yes	Unclear	Yes	Unclear	Yes	No	No	4	High
Diez Chang and Bazán Lossio de Diez, [23]	Yes	No	No	No	Yes	Yes	No	No	3	High
Huamán, *et al.* [22]	Unclear	Yes	No	No	Yes	Yes	No	No	3	High
Llanusa Ruiz, *et al.* [11]	Yes	No	Yes	No	Yes	Unclear	No	No	3	High
Saldanha, *et al.* [18]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	Low
Sepulveda, *et al.* [24]	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	7	Low
González Herrera, *et al.* [21]	Yes	Yes	Unclear	No	Yes	Yes	No	No	4	High
Mendoza-Caamal, *et al.* [20]	No	No	No	No	Yes	Yes	No	No	2	High
Vázquez Martinez, *et al.* [25]	Yes	Yes	Yes	No	Yes	Yes	Yes	No	6	Moderate
Vieira, *et al.* [19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8	Low

Table 4. Comparison of NT findings, structural abnormalities, and genetic testing trends across regions.

Variable	Panama	Latin America (SR)	North America (Canada, USA)	Europe (Mastromoro *et al*. 2023 [28])	Asia (Hong Kong, Turkey)	Most Frequent Fetal Abnormalities
Total Cases Analyzed	1236 fetuses	Varies (16–246 per study)	226 cases (NT ≥3.5 mm) USA: Large datasets	Meta-analysis: 59 studies, thousands of cases	Hong Kong: 300 cases (NT ≥3.5 mm), Turkey: 158 cases (NT >99th percentile)	Congenital heart defects, cystic hygroma, abnormal nasal bone
NT ≥95th Percentile	77 fetuses (6.23%)	Ranges: 3.6–62% per study	226 cases (all NT ≥3.5 mm)	NT ≥3.5 mm associated with 34% aneuploidy	Higher NT linked to genetic conditions	Cystic hygroma, structural heart defects, skeletal dysplasias
Chromosomal Abnormalities	11/19 MCs had aneuploidy (57.9%)	Varies: 10.5–62% per study	Canada: 51.3% aneuploidy	34.35% aneuploidy for NT ≥3.5 mm, with CMA adding 3.89% more diagnoses	Turkey: 44.6% normal karyotype in NT >4.5 mm	Trisomy 21, Trisomy 18, Trisomy 13, Turner syndrome
Cystic Hygroma Prevalence	9/19 MCs (47.4%)	Frequently observed, not always quantified	Canada: 47.8% had cystic hygroma	1:285 pregnancies, strongly linked to aneuploidy and CHD	Turkey: Highly correlated with miscarriage and anomalies	Cystic hygroma associated with chromosomal and heart defects
Live Births with No Anomalies	58/77 (75.3%) in NT ≥P95	Varies from 40–70%	Canada: 36.7% live births	30–50% depending on NT severity	Turkey: Only 10.7% of NT >4.5 mm had normal postnatal outcomes	Higher NT associated with congenital anomalies, but some cases remain normal
Pregnancy Loss (MC, Stillbirths, TOPs)	25/77 (32.5%) in NT ≥P95	Varies (17.5–56%)	Canada: 46.9% terminated pregnancies, 6.6% intrauterine deaths	30–50% pregnancy loss in NT ≥3.5 mm cases	Turkey: Higher loss rates in NT >4.5 mm (66.1%)	MC often associated with cystic hygroma and chromosomal abnormalities
Invasive Testing Rate (CVS/Amnio)	20/77 (26.0%)	Varies (6.9–56%)	Canada: 100% underwent invasive testing	50–70% invasive testing for NT ≥3.5 mm	Turkey: All patients with NT >99th percentile were offered testing	Most cases with NT >3.5 mm recommended for invasive testing
TOP	4/77 cases (5.2%)	Ranges: 10–40%	Canada: 46.9% termination rate	30–50% TOP rate in NT ≥3.5 mm	Turkey: 66.1% of NT >4.5 mm cases terminated	TOP more common in cases with major structural anomalies and aneuploidy

SR, systematic review.

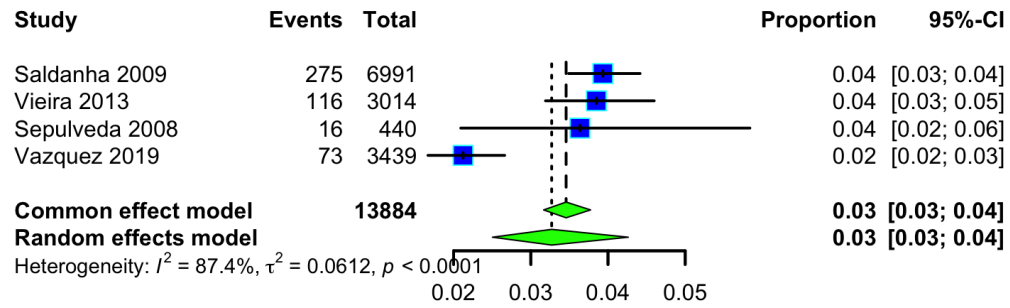

Fig. 3. Pooled proportion of fetuses with increased NT.

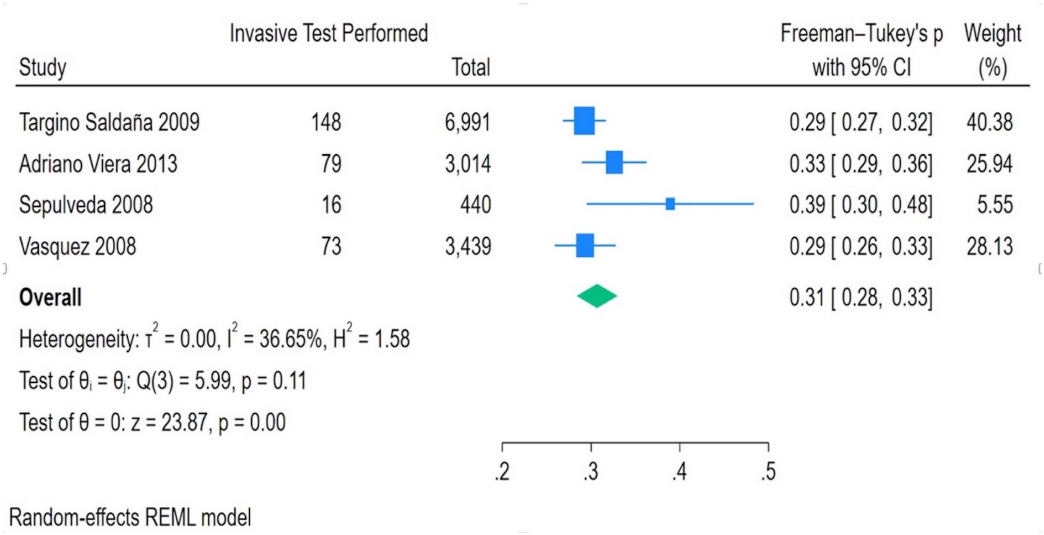

Fig. 4. Invasive test performed in fetuses with increased NT.

Besides, invasive testing rates also vary widely. While Latin America reports a 31% invasive testing rate, nearly 100% of patients with NT >3.5 mm undergo invasive procedures in Canada and Europe, reflecting differences in healthcare policies, patient preferences, and access to genetic services [3,9,10]. Pregnancy termination rates also differ, with Latin America reporting it at a rate of 7.1–7.8%, compared to 47.8% in Canada. This is likely influenced by legal and cultural factors [29–33].

4.3 Clinical Implications

Our findings emphasize the urgent need for expanded access to genetic testing and counseling in Latin America [34–38]. Although cfDNA testing is a viable noninvasive alternative, it fails to detect 2–10% of chromosomal aberrations, making it inadequate as a standalone test for high-risk cases [39–41]. Additionally, the absence of molecular testing in Latin America limits the identification of RASopathies and other monogenic disorders, which are increasingly recognized as contributors to increased NT in fetuses with normal karyotypes [42–45]. Exome sequencing is increasingly recommended for cases when both CMA and karyotype are normal because identifies pathogenic variants in up to 10% of these cases [46]. Exome sequencing remains largely inaccessible in Latin America.

4.4 Strengths and Limitations

This study has several strengths. For instance, we conducted a systematic review of Latin American studies, incorporating data from multiple national and regional databases to ensure a comprehensive representation of prenatal diagnostic trends in the region. Additionally, our Panamanian cohort provides direct insights into local screening practices and their alignment with global recommendations.

However, the limitations of this study must also be acknowledged. First, the lack of large, multicenter, or population-based studies in Latin America restricts the generalizability of our findings. Second, no CMA or molecular testing data were available for either the Panamanian cohort or the systematic review, limiting the ability to detect submicroscopic chromosomal imbalances and monogenic disorders. Finally, differences in healthcare infrastructure, socioeconomic factors, and legal frameworks across Latin American countries may contribute to variability in prenatal diagnostic practices, requiring further investigation.

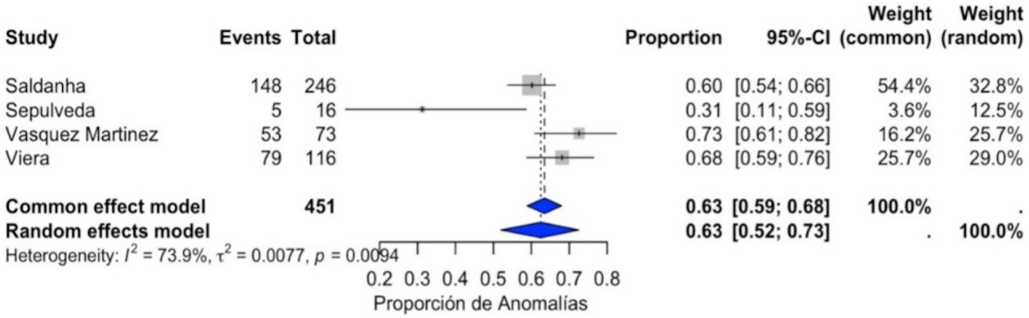

Fig. 5. Prevalence of fetal anomalies in fetuses with increased NT.

5. Conclusions

This study highlights the disparities in prenatal genetic testing for increased NT in Latin America, where only 31% of high-risk pregnancies undergo invasive testing, and no reported cases include CMA analysis. These findings contrast sharply with those of developed regions, where universal access to invasive and molecular genetic testing is standard practice. Therefore, efforts to improve genetic counseling, expand CMA availability, and standardize prenatal screening guidelines are urgently required to ensure that patients receive equitable access to prenatal diagnostics. Hence, addressing barriers such as the lack of genetic specialists, limited reimbursement, and legal restrictions on pregnancy termination will be essential to align Latin American prenatal care practices with international standards. Future research should focus on evaluating patient and provider perspectives regarding genetic testing uptake, assessing healthcare disparities, and conducting cost-effectiveness studies to support the implementation of CMA and expanded genetic testing programs in Latin America.

Abbreviations

SOGC, Canadian Society of Obstetrics and Gynecology; CMA, chromosomal microarray analysis; NT, nuchal translucency; cfDNA, cell-free DNA; ACOG, American College of Obstetricians and Gynecologists; MC, miscarriages; TOP, termination of pregnancy; FMF, fetal medicine foundation; REML, restricted maximum likelihood; CVS, chorionic villous sampling; CHD, congenital heart defect; BMI, body mass index.

Availability of Data and Materials

The datasets used and analyzed during the current study are available upon reasonable request.

Author Contributions

TTH, AHV and AG conceived the study. TTH and AHN developed and conducted the search strategy. YCR, AHN and JMR assisted with clinical data aquisitation and verification.TTH, ICB, and AG jointly screened the titles and abstracts, performed the full-text screening, and conducted data extraction and bias evaluation. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study followed the ethical guidelines and the country-specific regulatory guidelines (RESEGIS 2397). This study was exempt from the Institutional Review Board of Hospital Punta Pacifica (CBI-21-104). This study was conducted in accordance with the principles of the Declaration of Helsinki. It was part of the standard of care in the first-trimester screening program. Written informed consent was obtained from all patients. The collected data were anonymously transferred to a central database, and coding and data analyses were performed by non-clinicians.

Acknowledgment

We thank all peer reviewers for their opinions and suggestions.

Funding

This work was funded with the support of the Secretaría Nacional de Ciencia, Tecnología e Innovación, and Sistema Nacional de Investigación Grant No.136-2022.

Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors use ChatGPT-4o to improve readability and language. After using this tool, we reviewed and edited content as needed and took full responsibility for the final publication.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG39182.

References

[1] Baer RJ, Norton ME, Shaw GM, Flessel MC, Goldman S, Currier RJ, *et al*. Risk of selected structural abnormalities in infants after increased nuchal translucency measurement. American Journal of Obstetrics and Gynecology. 2014; 211: 675.e1–675.e19. https://doi.org/10.1016/j.ajog.2014.06.025.

[2] Xue S, Yan H, Chen J, Li N, Wang J, Liu Y, *et al*. Genetic Examination for Fetuses with Increased Fetal Nuchal Translucency by Genomic Technology. Cytogenetic and Genome Research. 2020; 160: 57–62. https://doi.org/10.1159/000506095.

[3] Sinajon P, Chitayat D, Roifman M, Wasim S, Carmona S, Ryan G, *et al*. Microarray and RASopathy-disorder testing in fetuses with increased nuchal translucency. Ultrasound in Obstetrics & Gynecology. 2020; 55: 383–390. https://doi.org/10.1002/uog.20352.

[4] Bakker M, Pajkrt E, Bilardo CM. Increased nuchal translucency with normal karyotype and anomaly scan: what next? Best Practice & Research. Clinical Obstetrics & Gynaecology. 2014; 28: 355–366. https://doi.org/10.1016/j.bpobgyn.2013.10.004.

[5] Bilardo CM, Timmerman E, Pajkrt E, van Maarle M. Increased nuchal translucency in euploid fetuses–what should we be telling the parents? Prenatal Diagnosis. 2010; 30: 93–102. https://doi.org/10.1002/pd.2396.

[6] Audibert F, De Bie I, Johnson JA, Okun N, Wilson RD, Armour C, *et al*. No. 348-Joint SOGC-CCMG Guideline: Update on Prenatal Screening for Fetal Aneuploidy, Fetal Anomalies, and Adverse Pregnancy Outcomes. Journal of Obstetrics and Gynaecology Canada. 2017; 39: 805–817. https://doi.org/10.1016/j.jogc.2017.01.032.

[7] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics, Committee on Genetics, Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Obstetrics and Gynecology. 2020; 136: e48–e69. https://doi.org/10.1097/AOG.0000000000004084.

[8] Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org, Norton ME, Biggio JR, Kuller JA, Blackwell SC. The role of ultrasound in women who undergo cell-free DNA screening. American Journal of Obstetrics and Gynecology. 2017; 216: B2–B7. https://doi.org/10.1016/j.ajog.2017.01.005.

[9] Hui L, Pynaker C, Bonacquisto L, Lindquist A, Poulton A, Kluckow E, *et al*. Reexamining the optimal nuchal translucency cutoff for diagnostic testing in the cell-free DNA and microarray era: results from the Victorian Perinatal Record Linkage study. American Journal of Obstetrics and Gynecology. 2021; 225: 527.e1–527.e12. https://doi.org/10.1016/j.ajog.2021.03.050.

[10] Crombag NMTH, Vellinga YE, Kluijfhout SA, Bryant LD, Ward PA, Iedema-Kuiper R, *et al*. Explaining variation in Down's syndrome screening uptake: comparing the Netherlands with England and Denmark using documentary analysis and expert stakeholder interviews. BMC Health Services Research. 2014; 14: 437. https://doi.org/10.1186/1472-6963-14-437.

[11] Llanusa Ruiz C, Nodarse Rodríguez A, Vázquez YE, Carrillo Bermúdez L, Sánchez Lombana R. Valor de los marcadores epidemiológicos y sonográficos del primer trimestre como indicadores de riesgo de cromosomopatías. Revista Cubana de Obstetricia y Ginecología. 2009; 35: 75–84. (In Spanish)

[12] Méndez-Rosado LA, Hechavarría-Estenoz D, de la Torre ME, Pimentel-Benitez H, Hernández-Gil J, Perez B, *et al*. Current status of prenatal diagnosis in Cuba: causes of low prevalence of Down syndrome: Causes of low Down syndrome prevalence in Cuba. Prenatal Diagnosis. 2014; 34: 1049–1054. https://doi.org/10.1002/pd.4421.

[13] Herrera TT, Cubilla-Batista I, Britton CB, Goodridge A. Valores de referencia de la translucencia nucal en Panamá y su comparación con diferentes regiones del mundo. Clínica e Investigación en Ginecología y Obstetricia. 2021; 48: 100651. https://doi.org/10.1016/j.gine.2020.11.002. (In Spanish)

[14] Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ (Clinical Research Ed.). 2021; 372: n160. https://doi.org/10.1136/bmj.n160.

[15] Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. International Journal of Evidence-based Healthcare. 2015; 13: 147–153. https://doi.org/10.1097/XEB.0000000000000054.

[16] Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E, *et al*. Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. BMC Medical Research Methodology. 2021; 21: 189. https://doi.org/10.1186/s12874-021-01381-z.

[17] Brizot ML, Carvalho MH, Liao AW, Reis NS, Armbruster-Moraes E, Zugaib M. First-trimester screening for chromosomal abnormalities by fetal nuchal translucency in a Brazilian population: nuchal translucency in Brazil. Ultrasound in Obstetrics & Gynecology. 2001; 18: 652–655. https://doi.org/10.1046/j.0960-7692.2001.00588.x.

[18] Saldanha FAT, Brizot MDL, Moraes EAD, Lopes LM, Zugaib M. Increased fetal nuchal translucency thickness and normal karyotype: prenatal and postnatal follow-up. Revista Da Associacao Medica Brasileira (1992). 2009; 55: 575–580. https://doi.org/10.1590/s0104-42302009000500022. (In Portuguese)

[19] Vieira LA, Silva SVL, de Faria RB, Lippi UG, Lopes RGC. Perinatal and pediatric follow up of children with increased nuchal translucency and normal karyotype. Revista Brasileira De Ginecologia E Obstetricia. 2013; 35: 274–280. https://doi.org/10.1590/s0100-72032013000600007. (In Portuguese)

[20] Mendoza-Caamal EC, Grether-González P, Hernández-Gómez M, Guzmán-Huerta M, Aguinaga-Ríos M. Birth defects associated with increased nuchal translucency. Ginecologia Y Obstetricia De Mexico. 2010; 78: 533–539.

[21] González Herrera L, Rodríguez Royero L, García Rodríguez N, Valero Abreu M, Herrera Martínez M, Jure Rodríguez V. Efectividad de la translucencia nucal aumentada en la detección de embarazos con riesgo de cromosomopatías. Medisur. 2014; 12: 63–76. (In Spanish)

[22] Huamán M, Sosa A, Campanero M. Higroma quístico y translucencia nucal aumentada como marcadores de anomalías cromosómicas. Revista peruana de Ginecología y Obstetricia. 2013; 58: 267–271. (In Spanish)

[23] Diez Chang G, Bazán Lossio de Diez MG. Pronóstico de la translucencia nucal fetal $\geq$ 5,5 mm en Lima, Perú. Revista Peruana de Ginecología y Obstetricia. 2019; 65: 455–459. (In Spanish)

[24] Sepulveda W, Wong AE, Casasbuenas A. Nuchal translucency and nasal bone in first-trimester ultrasound screening for aneuploidy in multiple pregnancies. Ultrasound in Obstetrics & Gynecology. 2009; 33: 152–156. https://doi.org/10.1002/uog.6222.

[25] Vázquez Martinez YE, Carrillo Bermúdez LM, Lemus Valdés MT. Síndrome de Down y su pesquisa durante el primer trimestre de la gestación. Revista Cubana de Obstetricia y Ginecología.

2019; 45: e440. (In Spanish)
[26] Alcedo Ramírez D, Serrano CS, Rojas JL, Giraldo SM, Osorio EA, Franco A, *et al*. Indicaciones de estudio genético invasivo en una población seleccionada: agosto de 2005 a diciembre del 2007. Revista Repertorio de Medicina y Cirugía. 2009; 18: 97–105. https://doi.org/10.31260/RepertMedCir.v18.n2.2009.538. (In Spanish)
[27] Pandya PP, Kondylios A, Hilbert L, Snijders RJ, Nicolaides KH. Chromosomal defects and outcome in 1015 fetuses with increased nuchal translucency. Ultrasound in Obstetrics & Gynecology: the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology. 1995; 5: 15–19. https://doi.org/10.1046/j.1469-0705.1995.05010015.x.
[28] Mastromoro G, Guadagnolo D, Khaleghi Hashemian N, Bernardini L, Giancotti A, Piacentini G, *et al*. A Pain in the Neck: Lessons Learnt from Genetic Testing in Fetuses Detected with Nuchal Fluid Collections, Increased Nuchal Translucency versus Cystic Hygroma-Systematic Review of the Literature, Meta-Analysis and Case Series. Diagnostics (Basel, Switzerland). 2022; 13: 48. https://doi.org/10.3390/diagnostics13010048.
[29] Kenkhuis MJA, Bakker M, Bardi F, Fontanella F, Bakker MK, Fleurke-Rozema JH, *et al*. Effectiveness of 12-13-week scan for early diagnosis of fetal congenital anomalies in the cell-free DNA era. Ultrasound in Obstetrics & Gynecology. 2018; 51: 463–469. https://doi.org/10.1002/uog.17487.
[30] Herrera TT, Sinisterra S, Solis A, Britton GB. First trimester screening using ultrasound and serum markers in Panamanians: Factors associated with adverse pregnancy outcomes. Journal of Research in Medical Sciences. 2014; 19: 451–456.
[31] Oviedo-Cruz H, Hernández-Paredez J, Ruíz-Ramírez AV. Prenatal screening for anueploidies in the first trimester: Audit to a Fetal Medicine Centre with specialized Laboratory in Mexico. Ginecologia Y Obstetricia De Mexico. 2015; 83: 259–276. (In Spanish)
[32] Ekelund CK, Petersen OB, Jørgensen FS, Kjaergaard S, Larsen T, Olesen AW, *et al*. The Danish Fetal Medicine Database: establishment, organization and quality assessment of the first trimester screening program for trisomy 21 in Denmark 2008-2012. Acta Obstetricia et Gynecologica Scandinavica. 2015; 94: 577–583. https://doi.org/10.1111/aogs.12581.
[33] Méndez-Rosado LA, Quiñones-Masa O, Vaglio A, Quadrelli R, Sanchez-Peñarate D, Soriano-Torres M, *et al*. Antenatal Diagnosis of De Novo Balanced Structural Chromosome Aberrations in Latin America. MEDICC Review. 2018; 20: 27–34. https://doi.org/10.37757/MR2018.V20.N4.7.
[34] Pinzón-Espinosa J, van der Horst M, Zinkstok J, Austin J, Aalfs C, Batalla A, *et al*. Barriers to genetic testing in clinical psychiatry and ways to overcome them: from clinicians' attitudes to sociocultural differences between patients across the globe. Translational Psychiatry. 2022; 12: 442. https://doi.org/10.1038/s41398-022-02203-6.
[35] Penchaszadeh VB. Ethical issues in genetics and public health in Latin America with a focus on Argentina. Journal of Community Genetics. 2015; 6: 223–230. https://doi.org/10.1007/s12687-015-0217-5.
[36] Bidondo MP, Groisman B, Duarte S, Tardivo A, Liascovich R, Barbero P. Prenatal detection of congenital anomalies and related factors in Argentina. Journal of Community Genetics. 2020; 11: 313–320. https://doi.org/10.1007/s12687-019-00451-6.
[37] Méndez-Ríos JD. Guía de Procedimientos Operacionales y Recomendaciones en la Implementación de Secuenciación de Nueva Generación para Diagnóstico Clínico. Revista Médica de Panamá. 2019; 39. (In Spanish)
[38] Alvarez-Gomez RM, De la Fuente-Hernandez MA, Herrera-Montalvo L, Hidalgo-Miranda A. Challenges of diagnostic genomics in Latin America. Current Opinion in Genetics & Development. 2021; 66: 101–109. https://doi.org/10.1016/j.gde.2020.12.010.
[39] Srebniak MI, de Wit MC, Diderich KEM, Govaerts LCP, Joosten M, Knapen MFCM, *et al*. Enlarged NT (≥3.5 mm) in the first trimester - not all chromosome aberrations can be detected by NIPT. Molecular Cytogenetics. 2016; 9: 69. https://doi.org/10.1186/s13039-016-0279-z.
[40] Mula R, Goncé A, Bennásar M, Arigita M, Meler E, Nadal A, *et al*. Increased nuchal translucency and normal karyotype: perinatal and pediatric outcomes at 2 years of age. Ultrasound in Obstetrics & Gynecology. 2012; 39: 34–41. https://doi.org/10.1002/uog.10059.
[41] Shakoor S, Dileep D, Tirmizi S, Rashid S, Amin Y, Munim S. Increased nuchal translucency and adverse pregnancy outcomes. The Journal of Maternal-Fetal & Neonatal Medicine. 2017; 30: 1760–1763. https://doi.org/10.1080/14767058.2016.1224836.
[42] Schreurs L, Lannoo L, De Catte L, Van Schoubroeck D, Devriendt K, Richter J. First trimester cystic hygroma colli: Retrospective analysis in a tertiary center. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2018; 231: 60–64. https://doi.org/10.1016/j.ejogrb.2018.10.019.
[43] Ali MM, Chasen ST, Gardner V, Pena S, Norton ME. Testing for Noonan syndrome after increased nuchal translucency. American Journal of Obstetrics and Gynecology. 2016; 214: S183–S184.
[44] Ali MM, Chasen ST, Norton ME. Testing for Noonan syndrome after increased nuchal translucency. Prenatal Diagnosis. 2017; 37: 750–753. https://doi.org/10.1002/pd.5076.
[45] Stuurman KE, Joosten M, van der Burgt I, Elting M, Yntema HG, Meijers-Heijboer H, *et al*. Prenatal ultrasound findings of rasopathies in a cohort of 424 fetuses: update on genetic testing in the NGS era. Journal of Medical Genetics. 2019; 56: 654–661. https://doi.org/10.1136/jmedgenet-2018-105746.
[46] Cao C, Liu F, Yang Y, Zhang Q, Huang J, Liu X. Prenatal whole-exome sequencing in fetuses with increased nuchal translucency. Molecular Genetics & Genomic Medicine. 2023; 11: e2246. https://doi.org/10.1002/mgg3.2246.