VELOCIDAD DE FLUJO DE LA VENA UMBILICAL ENTRE LA SEMANA 36 A 40 Y SU ASOCIACIÓN CON EL RESULTADO PERINATAL ADVERSO

YUDIS MORENO RICO
EILEN MILENA OSPINA BARRIOS

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Tutores:

MIGUEL PARRA SAAVEDRA
ANA MARIA RIVERA CASAS
HENRY JOSETH GONZÁLEZ TORRES

RESUMEN

El flujo venoso umbilical se ha convertido en un indicador potencialmente clave para la evaluación prenatal de la salud fetal. Por lo tanto, la necesidad de comprender el papel del flujo sanguíneo del cordón umbilical como predictor de complicaciones obstétricas y neonatales es fundamental.

Objetivo: Evaluar el volumen de flujo de la vena umbilical entre la semana 36 a 40 como predictor de complicaciones maternas y desenlaces perinatales adversos.

Metodología: Se llevó a cabo un estudio de cohorte con componente analítico en una clínica en Atlántico, Colombia. Se analizaron los datos utilizando estadísticas descriptivas y pruebas de comparación adecuadas para cada tipo de variable (Cuantitativas: Kruskall Wallis o ANOVA y cualitiativas: Chi-cuadrado o Fisher). Se aplicó una regresión logística multivariada ajustada para identificar factores asociados a complicaciones materno-perinatales. Se utilizó la curva ROC para determinar el punto óptimo de corte y evaluar el rendimiento del modelo. Se consideró un valor $p < 0.05$ como significativo, y se empleó el software estadístico R-CRAN versión 4.3.0.

Resultados: En un estudio en una clínica de BAQ, se analizaron 585 gestantes con edad promedio de 30 años y gestación de 37.6 semanas. La hipertensión crónica fue la comorbilidad más común (8.4%). Las complicaciones maternas predominantes fueron hipertensión gestacional (12.3%), preeclampsia (11%), y diabetes gestacional (6.8%). Se observaron diferencias significativas en parámetros fetales, uterinos y vasculares. El flujo venoso umbilical (VFU) se destacó como predictor de complicaciones maternas, con 98.5 ml/min como punto de corte óptimo para preeclampsia (sensibilidad 70.6%, especificidad 78.5%). VFU y UAPI fueron identificados como factores predictores relevantes. VFU también fue útil para predecir bajo peso al nacer, con 93 ml/min como mejor punto de corte (sensibilidad 79.1%, especificidad 78.9%, AUC 85%).

Conclusión: El VFU se puede constituir como un indicador aceptable para la prediccion de complicaciones materno-perinatales, teniendo los mejores puntajes en la Preeclampsia, y para los RN se encontró un buen rendimiento en la discriminación entre RN con bajo peso y sin bajo peso al nacer.

Palabras clave: Evaluación prenatal; Complicaciones obstétricas; Desenlaces perinatales adversos; Hipertensión crónica; Hipertensión gestacional

ABSTRACT

Umbilical venous flow has emerged as a potentially key indicator for prenatal assessment of fetal health. Therefore, understanding the role of umbilical cord blood flow as a predictor of obstetric and neonatal complications is crucial.

Objective: To assess umbilical vein flow volume between weeks 36 to 40 as a predictor of maternal complications and adverse perinatal outcomes.

Methodology: An analytical study was conducted in a clinic in Atlántico, Colombia. Data were analyzed using descriptive statistics and appropriate comparison tests for each type of variable (Quantitative: Kruskall Wallis or ANOVA, and qualitative: Chi-square or Fisher). Adjusted multivariate logistic regression was applied to identify factors associated with maternal-infant complications. The ROC curve was used to determine the optimal cutoff point and evaluate the model's performance. A p-value <0.05 was considered significant, and R-CRAN statistical software version 4.3.0 was used.

Results: In a study at a clinic in BAQ, 585 pregnant women were analyzed with an average age of 30 years and gestation of 37.6 weeks. Chronic hypertension was the most common comorbidity (8.4%). The predominant maternal complications were gestational hypertension (12.3%), preeclampsia (11%), and gestational diabetes (6.8%). Significant differences were observed in fetal, uterine, and vascular parameters. Umbilical venous flow (UVF) stood out as a predictor of maternal complications, with 98.5 ml/min as the optimal cutoff point for preeclampsia (sensitivity 70.6%, specificity 78.5%). UVF and UAPI were identified as relevant predictor factors. UVF was also useful in predicting low birth weight, with 93 ml/min as the best cutoff point (sensitivity 79.1%, specificity 78.9%, AUC 85%).

Conclusion: The VFU can be constituted as an acceptable indicator for the prediction of maternal-perinatal complications, having the best scores in Preeclampsia, and for NBs, good performance was found in discriminating between NBs with low birth weight and without low birth weight.

Keywords: Prenatal assessment; Obstetric complications; Adverse perinatal outcomes; Chronic hypertension; Gestational hypertension.

REFERENCIAS BIBLIOGRÁFICAS

1. Zavala Coca C, Pacheco Romero J. Flujo Venoso Fetal E Índice Cerebro Placentario Como Indicadores De Hipoxia Fetal En Gestantes Preeclámpticas Severas. Rev Peru Ginecol y Obstet. 2015;57(3):175–80.
2. Méndez L Y, Estévez R E, Álvarez De La Rosa R M, Coloma E M, Padilla P AI, Troyano L JM. Resultados perinatales en fetos con flujo umbilical diastólico ausente. Rev Chil Obstet Ginecol [Internet]. 2014 Oct;79(5):384–9. Available from: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0717-75262014000500005&lng=en&nrm=iso&tlng=en
3. Yin Q, Zhang Y, Ma Q, Gao L, Li P, Chen X. The clinical value of blood flow parameters of the umbilical artery and middle cerebral artery for assessing fetal distress. Am J Transl Res [Internet]. 2021;13(5):5280–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/34150119
4. Baschat AA, Gembruch U, Reiss I, Gortner L, Weiner CP, Harman CR. Relationship between arterial and venous Doppler and perinatal outcome in fetal growth restriction. Ultrasound Obstet Gynecol [Internet]. 2000 Oct;16(5):407–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11169323
5. Otero-Rosales MC, Olarte-Marín CD, Padilla-Serpa JD, Morales-Duarte PA, Quintero-Roa EM. Utilidad de la evaluación USG Doppler de las arterias uterinas entre las semanas 11 y 13+6 y su aplicación en las calculadoras de riesgo para predecir preeclampsia. MedUNAB [Internet]. 2022 Jan 5;24(3):375–83. Available from: https://revistas.unab.edu.co/index.php/medunab/article/view/3953
6. Reyes LM, García RG, Ruiz SL, Camacho PA, Ospina MB, Aroca G, et al. Risk factors for preeclampsia in women from Colombia: A case-control study. PLoS One. 2012;7(7).
7. Sandoval I, Véliz R, Sepúlveda Á, Candia AA, Herrera EA. Utilidad de la ecografía Doppler en el diagnóstico, el pronóstico y el manejo de la restricción del crecimiento fetal: situación en Chile. Rev Chil Obstet Ginecol [Internet]. 2022 Jul 12;87(3). Available from: https://www.rechog.com/frame_esp.php?id=85
8. Kauffmann T, Silberman M. Fetal Monitoring [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28157275
9. AGOSTINI M De, MORAN R, CORDANO C, GARAT F. Utilidad de la ecografía y del eco-doppler color en pacientes de alto riesgo obstétrico. Rev uruguaya Med interna [Internet]. 2021 Jul 17;06(02):67–71. Available from: https://revistamedicinainterna.uy/index.php/smiu/article/view/147/125
10. Yu X, Yao Y, Wang D, Tang J, Lu J. Prediction of Fetal Growth Restriction for Fetal Umbilical Arterial/Venous Blood Flow Index Evaluated by Ultrasonic Doppler under Intelligent Algorithm. Comput Math Methods Med [Internet]. 2022;2022:7451185. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35633923
11. Ozawa K, Kanazawa S, Mikami M, Muromoto J, Sugibayashi R, Wada S, et

al. Ultrasound measurement of umbilical venous flow volume at the intra-abdominal portion in normal fetuses. J Med Ultrason (2001) [Internet]. 2023 Jul;50(3):427–32. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37171782

12. Gill RW, Kossoff G, Warren PS, Garrett WJ. Umbilical venous flow in normal and complicated pregnancy. Ultrasound Med Biol [Internet]. 1984;10(3):349–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6464221
13. Laurin J, Lingman G, Marsál K, Persson PH. Fetal blood flow in pregnancies complicated by intrauterine growth retardation. Obstet Gynecol [Internet]. 1987 Jun;69(6):895–902. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3554065
14. Jouppila P, Kirkinen P. Umbilical vein blood flow as an indicator of fetal hypoxia. Br J Obstet Gynaecol [Internet]. 1984 Feb;91(2):107–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6696854
15. Kassaw A, Debie A, Geberu DM. Quality of Prenatal Care and Associated Factors among Pregnant Women at Public Health Facilities of Wogera District, Northwest Ethiopia. J Pregnancy [Internet]. 2020;2020:9592124. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32411469
16. Mendes RB, Santos JM de J, Prado DS, Gurgel RQ, Bezerra FD, Gurgel RQ. Avaliação da qualidade do pré-natal a partir das recomendações do Programa de Humanização no Pré-natal e Nascimento. Cien Saude Colet [Internet]. 2020 Mar;25(3):793–804. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232020000300793&tlng=pt
17. López CL, Wilson MD, Hou MY, Chen MJ. Racial and Ethnic Diversity Among Obstetrics and Gynecology, Surgical, and Nonsurgical Residents in the US From 2014 to 2019. JAMA Netw open [Internet]. 2021 May 3;4(5):e219219. Available from: http://www.ncbi.nlm.nih.gov/pubmed/34009352
18. Relph S, Vieira MC, Copas A, Coxon K, Alagna A, Briley A, et al. Improving antenatal detection of small-for-gestational-age fetus: economic evaluation of Growth Assessment Protocol. Ultrasound Obstet Gynecol [Internet]. 2022 Nov;60(5):620–31. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35797108
19. Center for Disease Control and Prevention (CDC). Pregnancy Mortality Surveillance System. 2019. p. 8 Pregnancy Mortality Surveillance System.
20. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-Related Mortality in the United States, 2011–2013. Obstet Gynecol. 2017 Aug;130(2):366–73.
21. Spurway J, Logan P, Pak S. The development, structure and blood flow within the umbilical cord with particular reference to the venous system. Australas J ultrasound Med [Internet]. 2012 Aug;15(3):97–102. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28191152
22. Basta M, Lipsett BJ. Anatomy, Abdomen and Pelvis: Umbilical Cord [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28884482

23. Marty M, Kerndt CC, Lui F. Embryology, Fetal Circulation. StatPearls. 2023.
24. Casanello P, Sobrevia L. Intrauterine growth retardation is associated with reduced activity and expression of the cationic amino acid transport systems y+/hCAT-1 and y+/hCAT-2B and lower activity of nitric oxide synthase in human umbilical vein endothelial cells. Circ Res [Internet]. 2002 Jul 26;91(2):127–34. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12142345
25. Barbera A, Galan HL, Ferrazzi E, Rigano S, Józwik M, Battaglia FC, et al. Relationship of umbilical vein blood flow to growth parameters in the human fetus. Am J Obstet Gynecol. 1999 Jul;181(1):174–9.
26. Heil JR, Bordoni B. Embryology, Umbilical Cord. StatPearls. 2023.
27. Moorthy RS. DOPPLER ULTRASOUND. Med journal, Armed Forces India [Internet]. 2002 Jan;58(1):1–2. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27365648
28. Shah A, Irshad A. Sonography Doppler Flow Imaging Instrumentation [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35145104
29. Kiserud T, Haugen G. Umbilical Circulation. In: Fetal and Neonatal Physiology. Elsevier; 2017. p. 599-611.e2.
30. Pinter SZ, Rubin JM, Kripfgans OD, Treadwell MC, Romero VC, Richards MS, et al. Three-dimensional sonographic measurement of blood volume flow in the umbilical cord. J Ultrasound Med [Internet]. 2012 Dec;31(12):1927–34. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23197545
31. Tchirikov M, Schröder HJ, Hecher K. Ductus venosus shunting in the fetal venous circulation: regulatory mechanisms, diagnostic methods and medical importance. Ultrasound Obstet Gynecol [Internet]. 2006 Apr;27(4):452–61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16565980
32. Gürses C, Karadağ B, İsenlik BST. Normal variants of ductus venosus spectral Doppler flow patterns in normal pregnancies. J Matern Fetal Neonatal Med. 2020 Apr;33(8):1288–94.
33. Society for Maternal-Fetal Medicine Publications Committee, Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction. Am J Obstet Gynecol [Internet]. 2012 Apr;206(4):300–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22464066
34. Alfirevic Z, Stampalija T, Dowswell T. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. Cochrane database Syst Rev [Internet]. 2017 Jun 13;6(6):CD007529. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28613398
35. Mari G, Deter RL, Carpenter RL, Rahman F, Zimmerman R, Moise KJ, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses. N Engl J Med [Internet]. 2000 Jan 6;342(1):9–14. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10620643

36. Strijowa NW. [Continuous monitoring of the fetus using an ultrasonic-Doppler-device during delivery]. Zentralbl Gynakol [Internet]. 1978;100(16):1053–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/726724
37. Alfirevic Z, Stampalija T, Medley N. Fetal and umbilical Doppler ultrasound in normal pregnancy. Cochrane database Syst Rev [Internet]. 2015 Apr 15;2015(4):CD001450. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25874722
38. Kamath SA. Hypertension in pregnancy. Vol. 54, Journal of Association of Physicians of India. Elsevier; 2006. 269–270 p.
39. Quintanilla Rodriguez BS, Mahdy H. Gestational Diabetes [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23536513
40. Kim J, Ayabe A. Obesity in Pregnancy [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19136980
41. Iftikhar SF, Biswas M. Cardiac Disease in Pregnancy [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28840470
42. Kataoka MC, Carvalheira APP, Ferrari AP, Malta MB, de Barros Leite Carvalhaes MA, de Lima Parada CMG. Smoking during pregnancy and harm reduction in birth weight: a cross-sectional study. BMC Pregnancy Childbirth [Internet]. 2018 Mar 12;18(1):67. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29530015
43. Nicoll R. Environmental Contaminants and Congenital Heart Defects: A Re-Evaluation of the Evidence. Int J Environ Res Public Health [Internet]. 2018 Sep 25;15(10). Available from: http://www.ncbi.nlm.nih.gov/pubmed/30257432
44. Prince MK, Daley SF, Ayers D. Substance Use in Pregnancy [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28938182
45. Mehari MA, Maeruf H, Robles CC, Woldemariam S, Adhena T, Mulugeta M, et al. Advanced maternal age pregnancy and its adverse obstetrical and perinatal outcomes in Ayder comprehensive specialized hospital, Northern Ethiopia, 2017: a comparative cross-sectional study. BMC Pregnancy Childbirth [Internet]. 2020 Jan 30;20(1):60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32000714
46. Chew LC, Verma RP. Fetal Growth Restriction [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19404231
47. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. Clin Med Insights Pediatr [Internet]. 2016;10:67–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27441006
48. Sun HY. Prenatal diagnosis of congenital heart defects: echocardiography. Transl Pediatr [Internet]. 2021 Aug;10(8):2210–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/34584892
49. Hammad IA, Blue NR, Allshouse AA, Silver RM, Gibbins KJ, Page JM, et al. Umbilical Cord Abnormalities and Stillbirth. Obstet Gynecol [Internet]. 2020 Mar;135(3):644–52. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/32028503
50. Moldenhauer JS. MANUAL MDS. 2021. POSICIÓN Y PRESENTACIÓN ANÓMALAS DEL FETO.
51. Silvestro S, Calcaterra V, Pelizzo G, Bramanti P, Mazzon E. Prenatal Hypoxia and Placental Oxidative Stress: Insights from Animal Models to Clinical Evidences. Antioxidants (Basel, Switzerland) [Internet]. 2020 May 12;9(5). Available from: http://www.ncbi.nlm.nih.gov/pubmed/32408702
52. Akpan US, Pillarisetty LS. Congenital Cytomegalovirus Infection [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21631642
53. Mawson AR, Croft AM. Rubella Virus Infection, the Congenital Rubella Syndrome, and the Link to Autism. Int J Environ Res Public Health [Internet]. 2019 Sep 22;16(19). Available from: http://www.ncbi.nlm.nih.gov/pubmed/31546693
54. Prefumo F, Fichera A, Fratelli N, Sartori E. Fetal anemia: Diagnosis and management. Best Pract Res Clin Obstet Gynaecol [Internet]. 2019 Jul;58:2–14. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30718211
55. Wei J, Wu QJ, Zhang TN, Shen ZQ, Liu H, Zheng DM, et al. Complications in multiple gestation pregnancy: A cross-sectional study of ten maternal-fetal medicine centers in China. Oncotarget [Internet]. 2016 May 24;7(21):30797–803. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27127170
56. Dudenhausen JW, Maier RF. Perinatal problems in multiple births. Dtsch Arztebl Int [Internet]. 2010 Sep;107(38):663–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20953254
57. Wang KG, Chen CY, Chen YY. The Effects of Absent or Reversed End-diastolic Umbilical Artery Doppler Flow Velocity. Taiwan J Obstet Gynecol [Internet]. 2009 Sep;48(3):225–31. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1028455909602941
58. Battaglia C, Artini PG, Galli PA, D'Ambrogio G, Droghini F, Genazzani AR. Absent or reversed end-diastolic flow in umbilical artery and severe intrauterine growth retardation. An ominous association. Acta Obstet Gynecol Scand [Internet]. 1993 Apr;72(3):167–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8385850
59. Manoli M JC, Carvajal C J. SIGNIFICADO DE FLUJO DIASTÓLICO AUSENTE O REVERSO EN EL DOPPLER DE ARTERIA UMBILICAL COMO ÚNICA ALTERACIÓN EN LA EVALUACIÓN DE BIENESTAR FETAL EN FETOS CON TRISOMÍA 21. Rev Chil Obstet Ginecol [Internet]. 2010;75(3). Available from: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0717-75262010000300008&lng=en&nrm=iso&tlng=en
60. Hutter D, Kingdom J, Jaeggi E. Causes and mechanisms of intrauterine hypoxia and its impact on the fetal cardiovascular system: a review. Int J Pediatr [Internet]. 2010;2010:401323. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20981293
61. Romero Salinas G, Viveros Alcaraz M, Gutiérrez Cárdenas ME, Torres Cosme M, Bobadilla Lugo RA, Gil Yoguez J, et al. La frecuencia cardiaca en

fetos con circular de cordón. Clin Invest Ginecol Obstet [Internet]. 2013 Sep;40(5):207–12. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0210573X12001128

62. Sohaey R. Amniotic fluid and the umbilical cord: The fetal milieu and lifeline. Semin Ultrasound, CT MRI [Internet]. 1998 Aug;19(4):355–69. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0887217198900932
63. Chang KJ, Seow KM, Chen KH. Preeclampsia: Recent Advances in Predicting, Preventing, and Managing the Maternal and Fetal Life-Threatening Condition. Int J Environ Res Public Health [Internet]. 2023 Feb 8;20(4):2994. Available from: https://www.mdpi.com/1660-4601/20/4/2994
64. Karrar SA, Hong PL. Preeclampsia [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32443079
65. Li H, Qufeng W, Wei W, Lin X, Zhang X. Umbilical artery thrombosis: Two case reports. Medicine (Baltimore) [Internet]. 2019 Nov;98(48):e18170. Available from: http://www.ncbi.nlm.nih.gov/pubmed/31770267
66. Dussaux C, Picone O, Chambon G, Tassin M, Martinovic J, Benachi A, et al. Umbilical vein thrombosis: to deliver or not to deliver at the time of diagnosis? Clin case reports [Internet]. 2014 Dec;2(6):271–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25548629
67. Pass RF, Arav-Boger R. Maternal and fetal cytomegalovirus infection: diagnosis, management, and prevention. F1000Research [Internet]. 2018;7:255. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29560263
68. Klaritsch P, Haeusler M, Karpf E, Schlembach D, Lang U. Spontaneous intrauterine umbilical artery thrombosis leading to severe fetal growth restriction. Placenta [Internet]. 2008 Apr;29(4):374–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18289672
69. Frey HA, Klebanoff MA. The epidemiology, etiology, and costs of preterm birth. Semin Fetal Neonatal Med [Internet]. 2016 Apr;21(2):68–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26794420
70. Tsai MH, Hsu JF, Chu SM, Lien R, Huang HR, Chiang MC, et al. Incidence, clinical characteristics and risk factors for adverse outcome in neonates with late-onset sepsis. Pediatr Infect Dis J [Internet]. 2014 Jan;33(1):e7–13. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23899966
71. Marcelino Díaz Macaya C, Rodríguez González A, Amores LLanes I, Magdalena Sáez Martínez D, Daisy Dueñas Díaz D, Adnery Luaces Casas L. Aspectos relevantes de la restricción del crecimiento intrauterino Highlights on Intrauterine Growth Restriction. Rev Cuba Obstet y Ginecol [Internet]. 2012;38(3):322–32. Available from: http://scielo.sld.cu
72. Pereira S, Chandraharan E. Recognition of chronic hypoxia and pre-existing foetal injury on the cardiotocograph (CTG): Urgent need to think beyond the guidelines. Porto Biomed J [Internet]. 2017 Jul;2(4):124–9. Available from: https://journals.lww.com/02054639-201707000-00007
73. Danieli-Gruber S, Shalev-Rosenthal Y, Matot R, Brzezinski-Sinai N, Zeevi G, Pardo A, et al. Risks of urgent cesarean delivery preceding the planned schedule: A retrospective cohort study. PLoS One [Internet]. 2023;18(8):e0289655. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/37549150
74. Odigboegwu O, Pan LJ, Chatterjee P. Use of Antihypertensive Drugs During Preeclampsia. Front Cardiovasc Med [Internet]. 2018 May 29;5. Available from: https://www.frontiersin.org/article/10.3389/fcvm.2018.00050/full
75. Magley M, Hinson MR. Eclampsia [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30940374
76. Batres E, Contreras F, Pinel S, Ardón E, Nazar S, Silva K, et al. Manejo de las Complicaciones Obstetricas. 2016;3:1–267. Available from: https://n9.cl/6vnpg
77. Domínguez-Mejías M, Culsán-Fernández R, Ortigosa-Arrabal A. Uso de oxigenoterapia materna para aumentar el bienestar fetal en la sala de paritorios. Rev científico-sanitaria SANUM [Internet]. 2022;6(1):94–101. Available from: https://www.revistacientificasanum.com/pdf/sanum_v6_n1_a9.pdf
78. Valdés R E. ROL DE LA MONITORIZACION ELECTRONICA FETAL INTRAPARTO EN EL DIAGNOSTICO DE SUFRIMIENTO FETAL AGUDO. Rev Chil Obstet Ginecol [Internet]. 2003;68(5). Available from: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0717-75262003000500010&lng=en&nrm=iso&tlng=en
79. Parra-Saavedra M, Crovetto F, Triunfo S, Savchev S, Parra G, Sanz M, et al. Added value of umbilical vein flow as a predictor of perinatal outcome in term small-for-gestational-age fetuses. Ultrasound Obstet Gynecol [Internet]. 2013 Aug;42(2):189–95. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23288780
80. Cruz-Martinez R, Savchev S, Cruz-Lemini M, Mendez A, Gratacos E, Figueras F. Clinical utility of third-trimester uterine artery Doppler in the prediction of brain hemodynamic deterioration and adverse perinatal outcome in small-for-gestational-age fetuses. Ultrasound Obstet Gynecol [Internet]. 2015 Mar;45(3):273–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25346413
81. Ozyüncü O, Saygan-Karamürsel B, Armangil D, Onderoğlu LS, Yiğit S, Velipaşaoğlu M, et al. Fetal arterial and venous Doppler in growth restricted fetuses for the prediction of perinatal complications. Turk J Pediatr [Internet]. 2010;52(4):384–92. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21043384
82. Hübner G ME, Juárez H ME. Test de Apgar: Después de medio siglo ¿sigue vigente? Rev Med Chil [Internet]. 2002 Aug;130(8). Available from: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0034-98872002000800014&lng=en&nrm=iso&tlng=en
83. Jansen PW, Tiemeier H, Verhulst FC, Burdorf A, Jaddoe VW V, Hofman A, et al. Employment status and the risk of pregnancy complications: the Generation R Study. Occup Environ Med [Internet]. 2010 Jun;67(6):387–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19955575
84. Kim MK, Lee SM, Bae SH, Kim HJ, Lim NG, Yoon SJ, et al. Socioeconomic status can affect pregnancy outcomes and complications, even with a universal healthcare system. Int J Equity Health [Internet]. 2018 Dec

5;17(1):2. Available from: https://equityhealthj.biomedcentral.com/articles/10.1186/s12939-017-0715-7

85. Tirosh D, Benshalom-Tirosh N, Novack L, Press F, Beer-Weisel R, Wiznitzer A, et al. Hypothyroidism and diabetes mellitus - a risky dual gestational endocrinopathy. PeerJ [Internet]. 2013;1:e52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23638390
86. Lykke JA, Langhoff-Roos J, Sibai BM, Funai EF, Triche EW, Paidas MJ. Hypertensive Pregnancy Disorders and Subsequent Cardiovascular Morbidity and Type 2 Diabetes Mellitus in the Mother. Hypertension [Internet]. 2009 Jun;53(6):944–51. Available from: https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.109.130765
87. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. Ann Nutr Metab [Internet]. 2015;66 Suppl 2:14–20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26045324
88. Luger RK, Kight BP. Hypertension In Pregnancy [Internet]. StatPearls. 2023. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30260586
89. van Asselt K, Gudmundsson S, Lindqvist P, Marsal K. Uterine and umbilical artery velocimetry in pre-eclampsia. Acta Obstet Gynecol Scand [Internet]. 1998 Jul;77(6):614–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9688238
90. Wang L, Zhou D, Long B, Wang J, Li L, Peng Y, et al. The abnormal umbilical venous-arterial index in the second half of pregnancy is associated with fetal outcome: A retrospective cross-sectional study. Front Pediatr [Internet]. 2023;11:1036359. Available from: http://www.ncbi.nlm.nih.gov/pubmed/36969267
91. Nakimuli A, Starling JE, Nakubulwa S, Namagembe I, Sekikubo M, Nakabembe E, et al. Relative impact of pre-eclampsia on birth weight in a low resource setting: A prospective cohort study. Pregnancy Hypertens [Internet]. 2020 Jul;21:1–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32330863