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Full length article

Utility of cervical pessary in the prevention of preterm birth in triplet pregnancies: A single-center observational retrospective study of 165 triplet pregnancies

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ABSTRACT

Objective: Premature births are a health problem arising in triplet pregnancies, resulting in high levels of morbidity and mortality. The objective of this study is to evaluate the utility of cervical pessaries in reducing prematurity (<34 weeks) in triplet pregnancies.
Methods: This is a single-center, retrospective case-control study regarding triplet pregnancies with follow-up at the La Paz University Hospital between 2000 and 2023. Maternal characteristics, obstetric and perinatal outcomes, and the use of cervical pessaries were examined.
Results: 165 triplet pregnancies were analyzed: 87 (52.7 %) in the case group (premature triplet pregnancies) and 78 in the control group (non-premature triplet pregnancies). A cervical pessary was inserted in 15 (17.2 %) triplet pregnancies in the case group and in 12 (16.7 %) triplet pregnancies in the control group ($p = 0.92$; OR = 1.04 (0.46–2.35)). A pessary was later inserted in the non-premature group ($p = 0.01$). The risk of preterm labor and the use of tocolytics ± glucocorticoids were found to be significantly more frequent in the premature group, with $p = 0.01$; OR = 2.30 (1.21–4.36) and $p < 0.01$; OR = 2.36 (1.23–4.44), respectively. Protocol-based cesarean sections were more frequent in the non-premature group ($p < 0.01$), while cesarean sections due to maternal complications ($p < 0.01$) and premature membrane rupture ($p < 0.01$) were more frequent in the premature group.
Conclusion: The cervical pessary is not useful in preventing preterm births (< 34 weeks) in triplet pregnancies. It is likely that being pregnant with triplets is a powerful independent factor associated with prematurity, despite other pregnancy conditions. Women who are pregnant with triplets and at risk of preterm labor and those taking tocolytics ± glucocorticoids may benefit from pessary insertion.

Introduction

Triplet pregnancies have increased over recent decades due to the rise in assisted reproductive techniques (ART) [1]. In Madrid (Spain) 0.15 % of all pregnancies are triplets [2]. Premature births (birth before 37 weeks of gestation [3]) are a health problem having high associated morbidity and mortality [4]. Prematurity is especially frequent in multiple gestations [5]. Other maternal and obstetric factors such as parity, previous preterm delivery, monochorionic pregnancy, short cervix (< 25 mm), obesity, and tobacco use have also been related to prematurity [5–9].

Interventions carried out to reduce preterm birth in multiple gestations based on vaginal progesterone, 17α-hydroxyprogesterone caproate, or cervical cerclage have not proven successful [10–12]. Studies have shown that the use of pessaries does not prevent preterm birth in asymptomatic women having multiple pregnancies and having a short cervix [13,14]. However, some studies have shown that pessaries may prevent preterm birth in twin pregnancies [15–18]. To the best of our knowledge, studies have yet to examine the use of pessaries exclusively in triplet pregnancies. Our aim is to analyze the usefulness of cervical

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pessaries to prevent preterm birth in triplet pregnancies. We hypothesize that the cervical pessary will be useful in reducing prematurity (<34 weeks) in triplet pregnancies since uterine overdistension in triplet pregnancies reduces cervical length earlier as compared to singleton or twin pregnancies.

Materials and Methods

The La Paz University Hospital is a tertiary hospital having 1200 beds, at which 1100 doctors and 2000 nurses serve 1.5 million patients. It is a referral hospital for multiple pregnancies in Spain. Approximately 200 multiple births, mostly twins, deliver annually.

Study design and eligibility criteria

This is a retrospective case-control study in which cases were the premature triplet pregnancies (delivery < 34 weeks) and the matched controls were the non-premature triplet pregnancies (delivery ≥ 34 weeks), from January 2000 to April 2023. Clinical information from medical records of triplet pregnancies followed at the Maternal-Fetal Medicine Unit at the La Paz University Hospital was retrieved after the Research Ethics Committee of the La Paz University Hospital approval. The diagnosis of the triplet pregnancies, amnionicity and chorionicity, and gestational age was made by sonographic obstetrician experts in the first and second trimesters in our center. Chorionicity was confirmed after birth by pathological examination of the placenta. Cervical length was measured in the routine ultrasonography evaluation at 18–22 gestational weeks by transvaginal ultrasonographic. Since no well-defined recommendations for cervical pessary placement in triplet pregnancies exist, it has been being placed in some cases where the cervical length was less than 25 mm and with threatened preterm labour and/or tocolytics ± glucocorticoids (Betamethasone (12 mg/24 h x2 doses) for lung maturation) use, based on experienced obstetricians' opinion. The inclusion criteria were patients with triplet pregnancies since the beginning of the pregnancy, who had been diagnosed in our center or in other centers with posterior confirmation of triplet pregnancy in our center, and that were monitored and delivered the three babies at our hospital. The exclusion criteria were patients that did not deliver in our hospital, gestations with stillbirth of at least one of the three fetuses, and patients that were lost in the follow-up during pregnancy.

Study variables

The following data were collected: maternal age, pre-pregnancy maternal body mass index (BMI), maternal tobacco use, parity, conception type (spontaneous or ART), chorionicity, cervical length (short cervix was considered when it measured < 25 mm), pessary use, gestational age of pessary placement, prematurity antecedents, threatened preterm labor, tocolytics ± glucocorticoids use, cesarean section indication, birth weight and Apgar test scores at 5-minutes.

Statistical analysis

Quantitative variables were expressed as means of standard deviations in normally distributed variables or medians and interquartile ranges in non-normally distributed variables. Qualitative variables were expressed as frequencies and percentages. A Kolmogorov-Smirnov (K-S) and Shapiro-Wilk (S-W) tests were used to find whether the quantitative variables were normally distributed. An analysis of the qualitative variables was carried out using a chi2 or Fisher's exact test, a Student's *t*-test for parametric quantitative variables, and a Mann Whitney-*U* test for non-parametric quantitative variables. The selected association measure for qualitative variables was the Odds Ratio (OR) with a 95 % confidence interval (CI). No multivariate analysis was performed in base of the univariate analysis results. All performed tests were bilateral and a statistically significant difference was considered when p was less than 0.05. A statistical analysis of the data was performed using the Statistical Package for Social Science (SPSS) software version 25 (SPSS Inc., Chicago, IL).

Results

216 triplet pregnancy women were recruited at the beginning of the study. In 21 cases at least one of the three fetuses died intrauterus. 5 patients were lost during follow-up (one moved to another country and four cases did not deliver in our hospital). Not enough data information was available on medical records in 25 triplet pregnancies. Finally, 165 triplet pregnancy women were analyzed the study, 87 in the case group and 78 in the control group. The results are summarized in Table 1 (Table 1).

Maternal age did not follow a normal distribution (K-S test $p < 0.01$). The global median age was 35 years (P25 = 33, P75 = 37). There were no differences between the groups (Mann Whitney-*U* test $p = 0.94$). Pre-pregnancy maternal BMI did follow a normal distribution (K-S test $p = 0.06$). Global median BMI was 25.53 ± 5.56 kg/m^2. There were no differences between groups (T-student test $p = 0.14$). According to smoking, 13 (7,3 %) women smoked during pregnancy, 6 (6.9 %) in the premature triplet pregnancies and 7 (9.0 %) in the non-premature cases ($p = 0.62$).

Regarding the type of conceptions, 43 (26.1 %) were spontaneous (22 in the non-premature group vs 21 in the premature group) and 122 (73.9 %) were conceived by ART (65 vs 57), $p = 0.81$. Monochorionic triamniotic pregnancies were seen in 5 triplet pregnancies (6.9 %), 3 in the premature group and 2 in the non-premature group, with $p = 0.74$. In relation to parity, 97 (58,8 %) pregnant women were primiparous and 68 (41.2 %) multiparous (39 in the case group and 29 in the control group). There were not statistically differences regarding the parity ($p = 0.32$). There were no cases with more than one triplet pregnancy.

Cervical pessary was placed in 28 cases (17 %), 15 (17,2 %) in the premature triplet pregnancies group and 12 (16,7 %) in the non-premature triplet pregnancies group, being this difference not statistically significant ($p = 0.92$; OR = 1.04 (0.46–2.35)). A secondary analysis revealed 44 % of the pregnant woman with pessary placement presented preterm delivery and 55 % of the pregnant woman with pessary placement did not present preterm delivery, being this difference not statistically significant ($p = 0,74$; OR = 1.14 (0.50–2.62)). It was placed at a mean gestational age of 25.13 ± 3.52 weeks (S-W test $p = 0.07$). Within the premature group cases the mean gestational age was 23.27 ± 3.10 weeks and within the non-premature group it was 26.83 ± 3.07 weeks (T-student test $p = 0.01$). The mean gestational time the patients carried the cervical pessary was 7.52 ± 3.00 weeks (S-W test $p = 0.06$), 7.45 ± 2.88 weeks in the case group and 7.58 ± 3.23 weeks in the control group (T-student test $p = 0.92$). Cervical length was measured in 64 patients. In 18 cases (28.1 %) it measured < 25 mm, 10 (26.3 %) in the premature cases and 8 (30.8 %) in the non-premature cases ($p = 0.70$).

Whitin all pregnancy women, 6 cases had prematurity antecedents, 5 (5.7 %) in the premature group and 1 (1.3 %) in the non-premature group, being this difference not statistically significant ($p = 0.21$). 68 cases (42.1 %) presented threatened preterm labor, 44 (50.6 %) in the premature group and 24 (30.8 %) in the non-premature group, being this difference statistically significant ($p = 0.01$; OR = 2.30 (1.22–4.36)). A secondary analysis revealed threatened preterm labor was present in 44 cases (32.1 %) in the women with no pessary use while it was present in 24 (85.5 %) cases in the patients that used pessary, with a statistically significant difference ($p < 0.01$; OR = 12.68 (4.14–38.77)). Tocolytics ± glucocorticoids treatment was administered in 100 triplet pregnancies (60.6 %), 61 (70.1 %) in the case group and 39 (50 %) in the control group ($p < 0.01$; OR = 2.35 (1.24–4.44)). A secondary analysis showed tocolytics ± glucocorticoids were administered in all cases where pessary was used while they were used in the 52.6 % of the cases where pessary was not placed, being this difference statistically

Table 1
Maternal, obstetric and neonatal characteristics.

Variable	Total, n = 165	Premature triplets, n = 87	Non-premature triplets, n = 78	Significance (p)	Odds Ratio (OR)	CI 95 %
Maternal characteristics						
Maternal age (years)	35 (P25 = 32, P75 = 37)	35 (P25 = 32, P75 = 37)	35 (P25 = 32, P75 = 37)	0.94	–	–
Prepregnancy body mass index (kg/m^2)	25.53 ± 5.56	24.54 ± 6.11	26.71 ± 4.66	0.14	_	_
Tobacco use	13 (7.9)	7 (9.0)	6 (6.9)	0.62	0.75	0.24–2.34
Multiparous women	68 (41.2)	39 (44.8)	29 (37.2)	0.32	1.37	0.74–2.56
Prematurity antecedents	6 (3.6)	5 (5.7)	1 (1.3)	0.21	4.70	0.54–41.10
Short uterine cervix (<25 mm)	18 (28.1)	10 (26.3)	8 (30.8)	0.70	0.80	0.27–2.42
Pregnancy characteristics						
Conceived by ART	122 (73.9)	65 (74.4)	57 (73.1)	0.83	1.09	0.54–2.18
Monochorionic triamniotic placenta	5 (3.0)	3 (1.8)	2 (1.2)	0.74	1.35	0.22–8.34
Obstetrics characteristics						
Threatened preterm labor	68 (41.2)	44 (50.6)	24 (30.8)	**0.01**	2.30	1.22–4.36
Tocolytics ± glucocorticoids use	100 (60.6)	61 (70.1)	39 (50.0)	**< 0.01**	2.35	1.24–4.44
Cervical pessary						
Use	27 (17.0)	15 (17.2)	12 (16.7)	0.92	1.04	0.46–2.35
Insertion gestational weeks	25.13 ± 3.52	23.27 ± 3.10	26.83 ± 3.07	**0.01**	–	–
Insertion time length	7.52 ± 3.00	7.45 ± 2.88	7.58 ± 3.23	0.92	–	–
Cesarean section type						
- Programmed	84 (51.5)	20 (23.0)	64 (84.2)	**< 0.01**	0.07	0.03–0.14
- PROM	31 (19.0)	29 (33.3)	2 (2.6)	**< 0.01**	19.00	4.36–82.89
- Uterine dynamic	27 (16.6)	19 (21.8)	8 (10.5)	0.05	2.45	1.00–5.96
- Maternal Pathology	14 (8.6)	13 (14.9)	1 (1.3)	**< 0.01**	13.53	1.73–106.101
- Fetal well-being loss risk	7 (4.3)	6 (6.9)	1 (1.3)	0.50	0.52	0.45–0.60
Perinatal results						
Neonatal death	1 (0.6)	1 (1.1)	0 (0)	1.00	0.52	0.45–0.60
Birth weight (g)						
- < 1500 g	23 (13.3)	15 (17.2)	8 (10.5)	0.11	2.20	0.86–5.62
- > 2500 g	12 (7.6)	6 (6.9)	6 (6.5)	1.00	1.03	0.31–3.38
Apgar score ≤ 5 at 5 min	6 (4.4)	5 (5.7)	1 (1.3)	0.21	4.92	0.56–4.30

significant ($p < 0.01$; OR = 1.38 (1.22–1.56)).

Regarding the delivery, a cesarean section was performed in all cases according to our protocol. In 84 cases (20 in the non-premature group vs 64 in the premature group; $p < 0.01$, OR = 0.07 (0.03–0.14)) there was a programmed cesarian section; in 31 cases (29 vs 2; $p < 0.01$, OR = 19.00 (4.36–82.89)) there was a premature rupture of membranes (PROM); in 27 (19 vs 8, $p = 0.05$) it was due to uterine contractions; in 14 (13 vs 1; $p < 0.01$, OR = 13.53 (1.73–106.01)) it was related to maternal pathology; and in 7 cases (6 vs 1, $p = 0.50$) it was because of fetal well-being loss risk.

Only one neonatal death case at 5 hours-old after the delivery was registered, in the premature group. No differences were found in birth weight < 1500 g (15 vs 8, $p = 0.11$) or > 2500 g (6 vs 6, $p = 1$). Apgar test score ≤ 5 at 5 min was observed in 6 cases (5 vs 1, $p = 0.21$). No differences in neonatal results were found between cases where pessary was not used and where it was placed (neonatal death 1 vs 0; $p = 0.65$, Apgar test score ≤ 5 at 5 min 5 vs 1, $p = 0.98$; birth weight < 1500 g 18 vs 5, $p = 0.51$; and > 2500 g 10 vs 2; $p = 0.97$). Based on these results, no multivariate analysis was performed.

Discussion

A significant percentage (47.3 %) of triplet gestations in our study were not premature (< 34 weeks). Our work reveals that the placement of cervical pessaries in triplet pregnancies is not useful in preventing preterm birth. Based on these results, it may be concluded that prematurity in triplet gestations is not necessarily due to marked uterine overdistension but may also be caused by uterine contractions.

The use of the cervical pessary in triplet pregnancies was initiated in our center in 2012. The pessary was inserted significantly earlier in the premature group, given the short uterine cervix and the likely occurrence of uterine contractions at the time of the pessary insertion. This may be related to the fact that these patients also had other risk factors for preterm birth, such as multiparity, a background of prematurity, or high risk for preterm labor.

Eighteen triplet pregnancies were included in the ProTWIN study [15], seven cases in the cohort study performed by Monfrance et al. [16] and three cases in the KarisAllen et al. [19] Canadian population study. However, no specific conclusions were mentioned with regard to these pregnancies. In the studies conducted by Tajik et al. [9], considering 18 triplet pregnancies, they concluded that women with triplet pregnancies in which pessaries were inserted had a higher risk of adverse perinatal outcomes (more prematurity, lower birth weight). They also found triplet pregnancy to be a predictive factor of possible harm from pessary use. This is the first study to focus exclusively on triplet pregnancies.

Results on twin pregnancies in these studies have been contradictory. Two studies found that pessary use did not prevent preterm birth in asymptomatic women having a short cervix (< 38 cm) [13,14]. However, the same researchers (ProTWIN study) found that the cervical pessary reduced the risk of preterm birth and poor perinatal outcome in women with a short cervix (< 38 cm) [15] and leads to the significant reduction of very preterm birth rates (< 28 weeks of gestation) [16]. Another group of researchers (PECEP-Twins) also found results similar to those of Leim et al. [17,18]. A study on twin pregnancies suggested that the use of cervical pessaries may extend gestation in women with an extremely short cervix, but only until viable gestational age [20].

Short cervix was present in 28.1 % of our pregnant women. This was not associated with prematurity in our study since the percentage of pregnant women with a short cervix was lower in premature pregnancies. This may be because these patients had other risk factors for preterm birth, such as multiparity, premature membrane rupture, or threat of preterm labor. Routinary cervicometry was incorporated in our population in 2011 and this data was only available for 64 pregnant women. Transvaginal sonographic cervical length has become the method of choice for screening asymptomatic pregnant women at risk for preterm birth (< 24 weeks) in twin pregnancies [21]. Another study [22] found cervical length decreases with gestational age in triplet pregnancies and showed that the measurement of second-trimester

cervical length to screen asymptomatic pregnant women at risk for preterm birth (< 28 and 32 weeks) is poor.

Differences in maternal characteristics associated with prematurity (age, pre-pregnancy BMI, tobacco use, prematurity antecedents, conception mode, and parity) were not statistically significant between groups, although multiparous women and prematurity antecedents were found to be more frequent in the premature triplet group. Based on our results, the ongoing practice of monthly cervicometry should be considered for symptomatic women pregnant who are pregnant with triplets or in cases in which there are antecedents of prematurity or multiparity are present. In other cases, optional measurement is recommended.

Monochorionic triamniotic placentas were only found in 3 % of all triplet births, with no differences being found between groups. It is likely to have a lower magnitude related to prematurity than to the triplet pregnancy itself.

Risk for preterm labor was found to be significantly more frequent in the premature cases and a secondary analysis revealed that pessary use was also significantly more frequent in patients at elevated risk for preterm labor. Tocolytics ± glucocorticoids were more frequently administered in the premature triplet pregnancies and in those in which pessaries were inserted. Pregnant women at risk of preterm labor and taking tocolytics ± glucocorticoids may benefit from pessary insertion to extend the weeks of gestation until reaching their planned cesarean section date.

The most frequent cesarean section indication in the non-premature group was programmed surgery at 34–35 weeks, in accordance with our hospital protocol. PROM, uterine dynamic, and maternal pathology were most frequent in the premature group. PROM and tocolysis protocols have varied over the years at our center and these pregnancies could have extended until 34–35 weeks with the current antibiotic therapy administration, use of Atosiban, and maintenance tocolysis.

Regarding perinatal results, no differences were found in neonatal death rate, birth weight, or Apgar test score at 5 min between the premature and non-premature groups or between cases where a pessary was or was not inserted. No other studies have reported differences in neonatal outcomes based on pessary use [13,15–17].

No statistically significant association exists between cervical pessary placement and preterm delivery in our pregnant women; therefore, its insertion does not result in a decreased prematurity rate in triplets. Cervical pessary placement is not effective in preventing prematurity in non-complicated and non-symptomatic triplet pregnancies women. Women who are pregnant with triplet pregnancies who are at risk of preterm labor or who are taking tocolytics ± glucocorticoids may benefit from pessary insertion to prolong their pregnancies. We suggest continuing to conduct monthly cervicometry in symptomatic women pregnant with triplets or in cases where there are antecedents of prematurity or multiparity are present.

Some of the strengths of our study include a very large cohort and extensive data collection. One of the main study biases relates to its retrospective nature, with the resulting limitations, as well as the distinct protocols used over the years. Some data were unavailable in medical reports. Another relevant limitation of our work relates to the fact that medical care of pregnancies has improved considerably over the past twenty years and our work includes cases from all of these years.

Conclusion

The use of cervical pessaries has not been found to be useful in preventing preterm birth (< 34 weeks) in triplet pregnancies. Being pregnant with triplets is likely to be a powerful independent factor associated with prematurity, given the resulting marked uterine overdistention, despite other pregnancy conditions. Women who are pregnant with triplets and those at risk of preterm labor who are taking tocolytics ± glucocorticoids may benefit from pessary insertion to prolong their pregnancies. Multicentric randomized studies with a larger patient sample are necessary to clarify these results and detect women who are pregnant with triplets who may benefit from pessary insertion.

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CRediT authorship contribution statement

E.M. Pena-Burgos: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. **M. Sintes Álvarez-Arenas:** Conceptualization, Data curation, Methodology, Writing – original draft. **V. Quirós-González:** Methodology, Writing – review & editing. **J.L. Bartha:** Writing – review & editing. **M. De La Calle:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Murray SR, Norman JE. Multiple pregnancies following assisted reproductive technologies – A happy consequence or double trouble? *Semin* Fetal Neonatal Med 2014;19(4):222–7. https://doi.org/10.1016/j.siny.2014.03.001.
[2] Duyos Mateo I, de la Calle M, Revello R, Salas P, Zapardiel I, González A. Fetal complications and early neonatal outcomes on 147 triplets. Ginecol Obstet Mex 2013;81(2):86–91.
[3] Silver RM, Branch DW. Cervical Pessary to Prevent Preterm Birth. JAMA 2017;318 (23):2299. https://doi.org/10.1001/jama.2017.18955.
[4] Jin Z, Chen L, Qiao D, et al. Cervical pessary for preventing preterm birth: a meta-analysis. J Matern Fetal Neonatal Med 2019;32(7):1148–54. https://doi.org/10.1080/14767058.2017.1401998.
[5] Wetta LA, Biggio JR. Cervical Pessary Use and Preterm Birth. Clin Obstet Gynecol 2014;57(3):607–15. https://doi.org/10.1097/GRF.0000000000000036.
[6] To MS, Fonseca EB, Molina FS, Cacho AM, Nicolaides KH. Maternal characteristics and cervical length in the prediction of spontaneous early preterm delivery in twins. Am J Obstet Gynecol 2006;194(5):1360–5. https://doi.org/10.1016/j.ajog.2005.11.001.
[7] Cobo T, Kacerovsky M, Jacobsson B. Risk factors for spontaneous preterm delivery. Int J Gynaecol Obstet 2020;150(1):17–23. https://doi.org/10.1002/ijgo.13184.
[8] van Zijl MD, Koullali B, Mol BW, Pajkrt E, Oudijk MA. Prevention of preterm delivery: current challenges and future prospects. Int J Womens Health 2016;8: 633–45. https://doi.org/10.2147/IJWH.S89317.
[9] Tajik P, Monfrance M, van 't Hooft J, et al. A multivariable model to guide the decision for pessary placement to prevent preterm birth in women with a multiple pregnancy: a secondary analysis of the ProTWIN trial: Pessary in multiple pregnancy. Ultrasound Obstet Gynecol 2016;48(1):48–55. https://doi.org/10.1002/uog.15855.
[10] Roman AS, Rebarber A, Pereira L, Sfakianaki AK, Mulholland J, Berghella V. The efficacy of sonographically indicated cerclage in multiple gestations. J Ultrasound Med 2005:24(6):763-768; quiz 770-771. 10.7863/jum.2005.24.6.763.
[11] Lim AC, Schuit E, Bloemenkamp K, et al. 17α-Hydroxyprogesterone Caproate for the Prevention of Adverse Neonatal Outcome in Multiple Pregnancies: A Randomized Controlled Trial. Obstet Gynecol 2011;118(3):513–20. https://doi.org/10.1097/AOG.0b013e31822ad6aa.
[12] Norman JE, Mackenzie F, Owen P, et al. Progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT): a randomised, double-blind, placebo-controlled study and meta-analysis. Lancet 2009;373(9680):2034–40. https://doi.org/10.1016/S0140-6736(09)60947-8.
[13] Nicolaides KH, Syngelaki A, Poon LC, et al. Cervical pessary placement for prevention of preterm birth in unselected twin pregnancies: a randomized controlled trial. Am J Obstet Gynecol 2016;214(1):3.e1–9. https://doi.org/10.1016/j.ajog.2015.08.051.
[14] Monfrance MJM, Schuit E, Groenwold RH, et al. Pessary placement in the prevention of preterm birth in multiple pregnancies: a propensity score analysis. Eur J Obstet Gynecol Reprod Biol 2016;197:72–7. https://doi.org/10.1016/j.ejogrb.2015.11.001.
[15] Liem S, Schuit E, Hegeman M, et al. Cervical pessaries for prevention of preterm birth in women with a multiple pregnancy (ProTWIN): a multicentre, open-label randomised controlled trial. Lancet 2013;382(9901):1341–9. https://doi.org/10.1016/S0140-6736(13)61408-7.
[16] Liem SMS, Schuit E, van Pampus MG, et al. Cervical pessaries to prevent preterm birth in women with a multiple pregnancy: a per-protocol analysis of a randomized

clinical trial. Acta Obstet Gynecol Scand 2016;95(4):444–51. https://doi.org/10.1111/aogs.12849.

[17] Goya M, de la Calle M, Pratcorona L, et al. Cervical pessary to prevent preterm birth in women with twin gestation and sonographic short cervix: a multicenter randomized controlled trial (PECEP-Twins). Am J Obstet Gynecol 2016;214(2):145–52. https://doi.org/10.1016/j.ajog.2015.11.012.

[18] Goya M, Pratcorona L, Merced C, et al. Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial. Lancet 2012;379(9828):1800–6. https://doi.org/10.1016/S0140-6736(12)60030-0.

[19] KarisAllen L, Schulz J, Flood C, Ross S, Naud K. Retrospective Cohort Study of Cervical Pessary Use in Women with Short Cervix at Risk of Preterm Delivery. J Obstet Gynaecol Can 2017;39(12):1137–42. https://doi.org/10.1016/j.jogc.2017.05.017.

[20] Jung DU, Choi MJ, Jung SY, Kim SY. Cervical pessary for preterm twin pregnancy in women with a short cervix. Obstet Gynecol Sci 2020;63(3):231–8. https://doi.org/10.5468/ogs.2020.63.3.231.

[21] Conde-Agudelo A, Romero R, Hassan SS, Yeo L. Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: a systematic review and metaanalysis. Am J Obstet Gynecol 2010;203(2):128.e1–128.e12. https://doi.org/10.1016/j.ajog.2010.02.064.

[22] Rodo C, de la Calle M, Maroto A, et al. Gestational age-based reference ranges for cervical length and preterm birth prediction in triplet pregnancies: an observational retrospective study. BMC Pregnancy Childbirth 2022;22(1):669. https://doi.org/10.1186/s12884-022-04997-1.