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Investigating the predictive role of uterocervical angle in predicting preterm labor ın singleton pregnancies: a meta-analysis

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ABSTRACT

Objectives: In this meta-analysis, we aimedto demonstrate the relationship between uterocervical angle and preterm labor in singleton pregnancies more clearly and reliablywith this meta-analysis.

Material and metods: In this study, we use keywords such as "uterocervical angle," "cervical angle," "angle," "cervix," "cervical," "preterm," and "preterm labour." We searched various databases, including PubMed, MEDLINE, ClinicalKey, Scopus, ScienceDirect, Web of Science, and Google Scholar. The search encompassed the period from January 1, 2010, to December 27, 2020. As a result of the literature review, a total of 585 articles were identified. After the screening and selection process, six studies met the inclusion criteria and were included in the analysis. These six studies were deemed relevant and provided valuable information on the research topic.

Results: When the Egger test (p = 0.020) and Begg test (p = 0.188) were performed, no significant publication bias was found in the studies examined. These statistical tests assess publication bias, and the resulting p-values indicate a low probability of bias in the included studies. Cochran's Q test revealed the presence of heterogeneity among the included studies. Heterogeneity indicates variability in the results beyond what would be expected by chance alone. This finding suggests that the studies may differ in methodologies, populations, or other factors, which could impact the overall results and require further investigation. There was a significant difference between the patient and control groups (p < 0.001). This result provides strong evidence to support the importance of the difference between the two groups compared.

Conclusions: Based on the findings of this study, a wider uterocervical angle appeared to be significantly associated with an increased risk of preterm delivery in overall effect. It concluded that a wide uterocervical angle may be a potential risk factor for preterm delivery. Moreover, the study revealed a significant association between wider uterocervical angles and an elevated risk of preterm labour in singleton pregnancies. In this study, the definition of preterm birth accepts as birth before 37 weeks of gestation. These results highlight the potential significance of evaluating the uterocervical angle as a meaningful predictor for identifying the propensity of preterm labour in singleton pregnancies.

Keywords: meta-analysis; preterm labor; singleton pregnancy; uterocervical angle

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INTRODUCTION

Preterm birth (PB) is defined as birth between 20 0/7 and 36 6/7 weeks of gestation [1]. Despite advancements in technology and medical care, preterm labour remains a significant cause of neonatal morbidity and mortality. Premature birth is associated with several complications, such as cerebral palsy, bronchopulmonary dysplasia, retinopathy of prematurity, and several other health issues problems common in premature infants. These morbidities highlight the importance of addressing preterm labour and implementing effective interventions to improve the outcomes for preterm infants [1, 2]. This situation, which is seen in 5–18% of pregnancies and is an important reason for hospitalizations, creates a serious charge on the economies of the countries [3]. Less than 10% of patients with preterm labor who are hospitalized give birth within

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7 days. Therefore, it is essential to develop strategies that will prevent unnecessary hospitalizations and identify at-risk pregnant women and thus indirectly improvethe country's economies.

In recent years, different measurements and tests have been developed for the prediction of preterm labor [2]. The leading ones include cervical length measurement, fetal fibronectin testing, and biochemical markers obtained from maternal serum and amnion [4]. Maternal blood and amniotic fluid inflammatory markers may cause anxiety in pregnant women due to the interventional nature of the procedures. The cervical length measured in the second trimester is a more commonly used measurement for preterm labor [5]. According to previous reports, the 10th percentile threshold for cervical length at 24 weeks of gestation was defined as 25 mm, indicating the risk of preterm birth (PB) [6]. Sensitivity at this threshold was reported to be about 37.3%, meaning that 37.3% of pregnancies at risk of preterm labour were correctly identified. The specificity, on the other hand, was reported to be around 92.2%, indicating that 92.2% of pregnancies not at risk for preterm birth were correctly identified as such. The most effective threshold for predicting true preterm labour was found to be a cervical length of 15 mm or less, yielding a specificity of 81% and a positive predictive value of 83% [2].

Newer tools, such as uterocervical angle (UCA),have beendeveloped to predict PB. With the widespread use of UCA in studies in the last decade, UCA has become more prominent. However, most studies have a small sample size. The subject of UCA is relatively new, and there is limited availability of systematic reviews on this topic. These reviews indicate the necessity for more robust scientific evidence to establish the success of UCA in predicting preterm birth (PB). In such cases, conducting a meta-analysis can be an appropriate approach to enhance the sample size and consolidate findings from similar studies. Therefore, our objective is to use this meta-analysis to provide a clearer and more reliable understanding of the relationship between UCA and preterm labour in singleton pregnancies. By synthesizing the available data, we aim to contribute valuable insights and strengthen the existing evidence on this topic.

MATERIAL AND METHODS

Search strategy

For our research, we implemented a systematic electronic search strategy to explore published literature. We conducted searches across multiple databases, namely PubMed Medline, ClinicalKey, ScienceDirect, Web of Science, and Google Scholar. Our search encompassed the period from January 1, 2010, to December 27, 2020. We employed a combination of the following keywords: uterocervical angle, cervical angle, angle, cervix cervical, preterm, and preterm labour. The appropriate database-specific suffixes were employed in the search to optimize results. We focused exclusively on studies conducted on humans and published in the English language. The search process and results are presented in a structured flow diagram, as depicted in Figure 1 of our thesis.

Study selection

All included studies in our meta-analysis were prospective observational studies that examined the relationship between preterm labour and the anterior uterine cervix. While these studies varied in terms of diagnosing preterm labour, parity, gravidity, presence of previous preterm births, and prior cervical or uterine surgeries, they were all considered for inclusion in the meta-analysis. In addition, studies that defined preterm labor as delivery before 37 weeks were subgrouped and evaluatedseparately. However, our study excluded studies that involved patients with preterm premature rupture of membranes, polyhydramnios, multiple gestations, and cerclage. Additionally, conference abstracts were also excluded. Furthermore, trials were excluded if they reported results in a manner that hindered pooling for meta-analysis, such as failure to provide mean and standard deviation values.

All the studies included in our analysis provided a clear definition of the method used for ascertaining the uterine cervical angle. Most of the studies utilized similar measurements, concerning Dziedz et al. [7], to ensure uniformity in the assessment of the uterine cervical angle. The UCA was defined as the value obtained by measuring the triangle formed between the lower uterine segment and the cervical canal using transvaginal ultrasound. During the measurement process, the first line of callipers was placed at the junction where the anterior and posterior walls of the cervix meet, including the internal and external os along the endocervical canal. If the cervix appeared curved, the measurement was taken vertically from the internal os to the external os. The second line was drawn by averaging a 3 cm line from the internal os of the cervix to the upper uterine segment. The angle formed between these two lines was recorded. It is worth noting that all participants in the trials had an empty bladder during the ultrasound scan.

Quality and risk of bias assessment

Before conducting the meta-analysis, the publication bias of the included studies was assessed using Begg's and Egger's tests.

Data extraction

The studies were selected in three consecutive stages. Following deduplication, the titles and abstracts of all electronic articles were screened by N.N.Y. to assess their

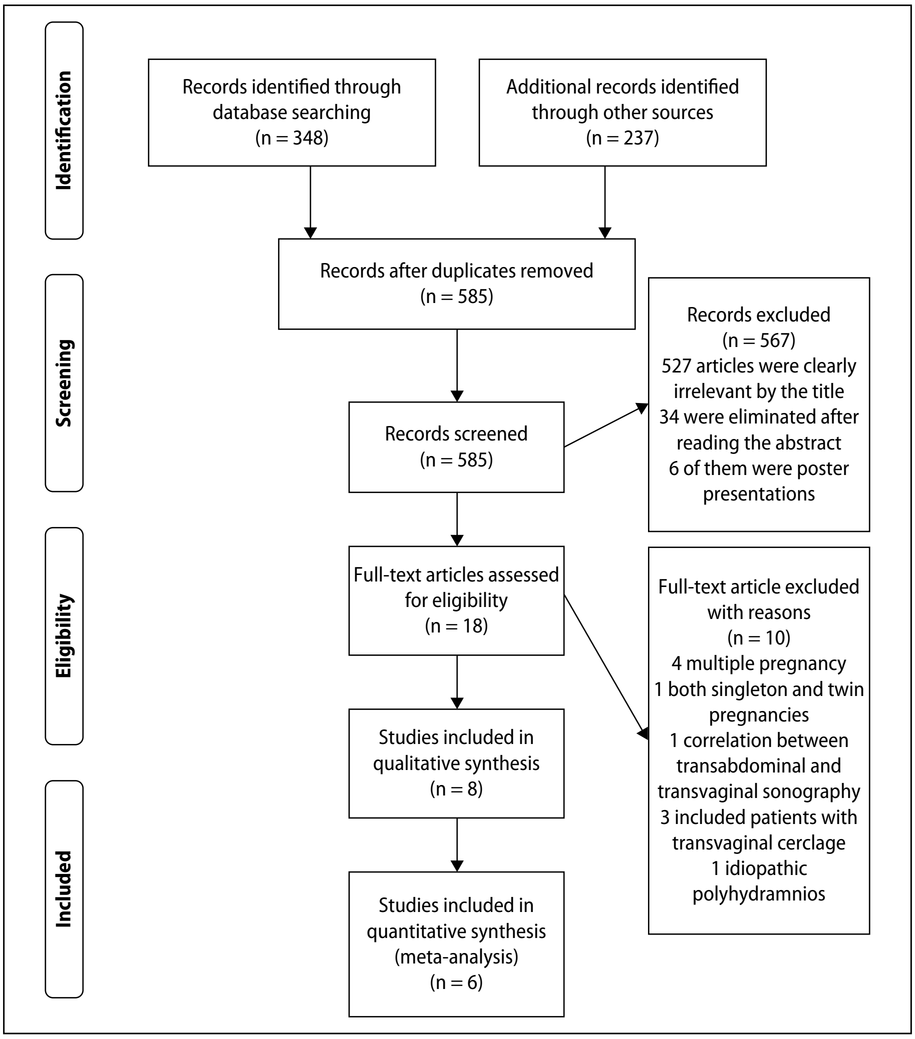

Figure 1. Flow diagram

eligibility. The decision to include studies in the present meta-analysis was made after retrieving and reviewing the full text of articles that were held potentially eligible. Potential discrepancies in this latter stage were resolved by the consensus of all the authors.

Summary measures

The main outcome measure chosen for the present meta-analysis was the success of the UCA in preterm labor prediction. Subgroup analyses were done for studies that described preterm labor as before 37 weeks.

Quantitative data synthesis

The heterogeneity of the studies was evaluated according to Cochran's Q test, while to determine the degree of statistic was employed. In the meta-analyses, the lowest number of studies taken for analysis was three. In the studies, the value of α was taken as 0.10 for the homogeneity and publication bias tests.

In cases where heterogeneity was determined in the publications following Cochran's Q test, the DerSimonian-Laird method was carried out using the random-effects model. In the statistical analyses, MedCalc version 20.009 program was used.

RESULTS

Literature search and study characteristics

The literature search uncovered 585 articles (Fig. 1). Among these, 527 articles were considered unrelated due to their titles, 34 articles were excluded after reviewing the abstracts, six articles were in the format of poster presentations [8–13], and 18 articles were thoroughly examined in their entirety.

Of the 18 full-text articles evaluated, four were excluded because patients with multiple pregnancies were includedin the studies [14–17], 1 because patients with both singleton and twin pregnancies were included [18], and 1 because it was difficult to determine the correlation between transabdominal

Table 1. Study characteristics

Source	Studydesign	No. of patients	Including criterias	Week of UCA measurement	UCA value (mean ± SD)
Martinez et al. [20]	Retrospective	318	Singleton pregnancies with history of preterm labor	20–24 week	106.1 ± 26.4 (preterm) 99.5 ± 26.4 (term)
Dziadosz et al. [1]	Retrospective	972	Singleton pregnancies with history of abnormal smear, cervical surgery and preterm labor	16–24 week	120 ± 27 (preterm) 93 ± 26 (term)
Sur et al. [21]	Prospective	100	Singleton pregnancies with history of preterm labor	Second trimester	127.66 ± 6.61 (preterm) 103.65 ± 14 (term)
Llobet et al. [22]	Prospective	275	Singleton pregnancies with history of preterm labor	18–24 week	105.2 ± 21.6 (preterm) 94.5 ± 22.7 (term)
Sawaddisan et al. [23]	Prospective	356	Singleton pregnancies with a history of cesarean or D/C	16–24 week	111.8 ± 25.4 (preterm) 104.8 ± 26.7 (term)
Borna et al [24]	Prospective	100	Singleton pregnancies that had bleeding during pregnancy	18–24 week	102.12 ± 7.13 (preterm) 86.15 ± 5.78 (term)

UCA — uterocervical angle; SD — standard deviation

and transvaginal sonography UCA measurement [19]. Two additional articles were excluded because they compared the UCA as predictors of preterm delivery in patients with transvaginal cerclage [20, 21], and one other because they included the patients who underwent cerclage in the study groups [22]. One article was excluded because it specifically included pregnant women diagnosed with idiopathic polyhydramnios [23]. Of the eight articles remaining for a more thorough evaluation, one was excluded from the quantitative meta-analysis, as it hadan uninterpretable or incomplete data set [24], andanother one because it presented the data as median, not mean values [25]. Thus, six articles remained to be included in the meta-analysis [7, 26-30]. Relevant characteristics of the trials included in this review are given in Table 1.

This meta-analysis includes 6 articles with a sample size between 100 and 972 published in 2016 and 2020. The studies determined that UCA values were assessed using transvaginal ultrasound during the second trimester. In the articles, alterations were observed in the weeks of the second trimester when the measurements were conducted: four of them were taken between 17/18 weeks and 24 weeks [7, 28–30], one between 20–24 weeks [26], and one during the second trimester [27].

Qualitative analysis

All studies reported that UCA is a good predictive tool for preterm labor that was measured at the begining of the second trimester. Only Borna et al.'s [30] reported that UCA could be a good predictive tool for preterm labor in patients with vaginal bleeding complaints. In all thestudies included, birth weeks were correlated with the UCA measurement performed at different time intervals at the beginning of the second trimester. Only Sawaddisan et al. [24] evaluated the UCA prediction success according to the weeks in which UCA measurement was performed. In this study, while comparing UCA values with term and spontaneous preterm deliveries, the patients were divided into two groups: gestational age $16^{0/7}$-$24^{0/7}$ weeks (n = 356) and gestational age above 19.5 weeks (n = 141). There was a statistically significant difference in value between the groups when the UCA measurement was made only over 19.5 weeks (p = 0.017).

There were some differences in terms of the definition of preterm labor in the studies. Martinez et al. [26] defined preterm labor as less than 34 weeks. On the other hand, Llobet et al. [28] divided the patients into those who gave birth after 37 weeks and those who gave birth after 34 weeks. Dziadosz et al. [7] Llobet et al. [28] and Borna et al. [30] defined preterm labor as births less than 37 weeks. In Sur et al.'s [27] study, we did not find a specific week definitionfor preterm labor. All casesdefined as preterm labor independent of the week were included in this meta-analysis. In addition, subgroup analysis was performed in three studies in which preterm labor was defined as less than 37 weeks [7, 28, 30].

Quantitative analysis

As a result of Egger's test (p = 0.220) and Begg's test (p = 0.188), it was determined that there was no publication bias. Cochran's Q test revealed that there was heterogeneity (p < 0.001 = 94.49%). There was a significant difference between the patient and control groups(p < 0.001) (Tab. 2).

In the subgroup consisting of studies in which preterm labor wasdefined as before 37 weeks, through Egger's test (p = 0.704) and Begg's test (p = 0.601), it was determined that there was no publication bias. Cochran's Q test revealed that there was heterogeneity (p < 0.001 = 95.11%). There was a significant difference between the patient and control groups (p = 0.012) (Tab. 3). The results of the meta-analysis were shown in Figures 2 and 3.

Table 2. Meta-analysis of all studies

Study	Preterm (n1)	Term (n2)	Total	SMD	SE	95% CI	t	p	Weight [%]	
									Fixed	Random
Martinez	93	225	318	0.249	0.123	0.006–0.492			29.46	17.54
Dziadosz	84	888	972	1.034	0.116	0.806–1.263			33.08	17.60
Sur	37	63	100	2.013	0.250	1.517–2.509			7.18	16.08
FarrasLlobet	34	241	275	0.473	0.184	0.111–0.835			13.28	16.93
Sawaddisan	31	325	356	0.263	0.188	–0.107 to 0.632			12.71	16.89
Borna	17	83	100	2.632	0.323	1.991–3.273			4.30	14.97
Total (random effects)	296	1825	2121	1.068	0.302	0.476–1.660	3.537	< 0.001	100.00	100.00

SMD — Standart mean difference; SE — standart error; CI — confidence interval

Table 3. Meta-analysis of the subgroup with diagnosis preterm labor before 37 weeks

Study	Preterm (n1)	Term (n2)	Total	SMD	SE	95% CI	t	p	Weight [%]	
									Fixed	Random
Dziadosz	84	888	972	1.034	0.116	0.806–1.263			66.04	34.98
Sawaddisan	31	325	356	0.263	0.188	–0.107 to 0.632			25.38	33.96
Borna	17	83	100	2.632	0.323	1.991–3.273			8.58	31.07
Total (random effects)	132	1296	1428	1.269	0.503	0.283–2.254	2.524	0.012	100.00	100.00

SMD — Standart mean difference; SE — standart error; CI — confidence interval

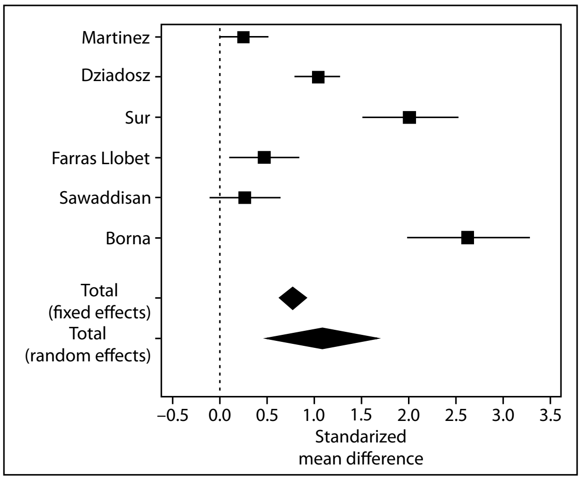

Figure 2. Forest graph in evaluating the success of anterior uterocervical angle in predicting preterm labor

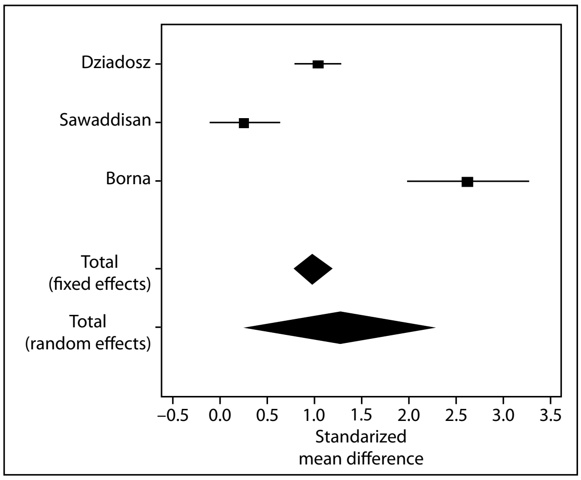

Figure 3. Forest graph in evaluating the success of anterior uterocervical angle in predicting preterm labor before 37 weeks

DISCUSSION

Principal findings

The meta-analysis, results indicated that a wider UCA was associated with a higher risk of preterm labour in the overall effect. A significant correlation was also observed between UCA and preterm labour occurring before 37 weeks.

Results in the context of what is known

Uterocervical angle, in the prediction of preterm labor, is an important tool that has been emphasized in recent years [7]. Studies have continued to assessseveral areas, such as preterm labor, termination time, and latent phase periods of labor. A recent indirect comparison between collagen fiber orientation and dispersion in the upper cervix of pregnant and nonpregnant women suggested that collagen fiber dispersion and direction may influence cervical remodeling during pregnancy [31]. In this sense, a predictive tool originating from the upper cervix and uterus may be more meaningful than biochemical markers. Since 2016, many studies have been conducted showing the success of UCA in preterm labor prediction. However, there is no meta-analysis to increase the level of evidence, except for the systematic review in 2018 [32]. Outcomes of the present study can provide clinical applicability for UCA.

Two of the studies [7, 26], UCA measured depends on previously measured and archived cervical length images. Hovever, both studies were written prospectively and the journals in which they were published accepted these publications as prospective. For this reason, we accepted these two articles as prospective in accordance with the literature. Our most important inclusion criteria were singleton pregnancies. However, the preterm labor risk status of the patients included in the analysis was not similar. For example, we could not exclude studies that included patients with a history of preterm labor or previous cervical surgery because we have reached only a few studies in the literature on low-risk pregnant women in terms of singleton and preterm labor.

Clinical implications

The study's analysis was not the standardized diagnosis of preterm labour diagnosis. All patients are defined as preterm regardless of week. Even in this way, we tried to create a more specific and near-standard subgroup to increase the power of our analysis, which turned out to be meaningful. We performed a subgroup analysis of studies defining preterm labor as less than 37 weeksand found a significant difference from the control group [7, 29, 30]. Moreover, UCA measurement weeks were not standard. This prevented us from drawing attention to a cut-off value obtained by measuring in a certain week.

Research implications

Studies show that UCA measurement can be a good tool for predicting preterm labor. But none of these studies were randomized. Ensuring randomization in future studies will also be important for publications to be included in future meta-analyses.

Strengths and limitations

One of the strengths of the present study is thatwe discussed a subject that becamepopular recently, but little is known about it. To the best of our knowledge, this is limited data evaluating the role of UCA in prediction of preterm labor in singleton pregnancies. In addition, we analyzed preterm labor independent of the week and preterm labor defined as before 37 weeks; therefore, rendering our results more reliable.

One of the limitations of this meta-analysis is that we retained broad criteria for the inclusion of studies. For example, patients with a history of preterm labor were not further subgrouped or mechanical reasons that could affect UCA measurements such as conization and previous cesarean history could not be excluded from all the studies included in the meta-analysis. In other words, patients could not be analyzed according to risk groups for preterm labor. The primary factor that limited us is the fact that UCA is a new subject, and there were only a few studies with similar patient groups. Second, the literature search strategy was limited to the published papers that were used, which were in English, whilestudies published in other languageswere excluded.

CONCLUSIONS

This meta-analysis found that preterm births both before 34 weeks and up to 37 weeks could be predicted by UCA measurement in the second trimester. To improve the diagnostic value of the uterine cervical angle in predicting preterm birth, further studies should establish more specific patient groups and standardise the cut-off value. In addition, further larger studies should be performed to confirm these findings.

Article information and declarations

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Conflict of interest

The authors reports no conflict of interest.

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