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Dr. Hemant Deshpande
Professor and HOD, Department
of Obstetrics and Gynaecology,
DY Patil Vidyapeeth, Pimpri,
Pune 18 Maharashtra, India

Dr. Madhukar Shinde
Associate professor, Department of
Obstetrics and Gynaecology, DY
Patil Vidyapeeth, Pimpri, Pune 18,
Maharashtra, India

Dr. Chirag Wagh
Department of Obstetrics and
Gynaecology, DY Patil
Vidyapeeth, Pimpri, Pune 18,
Maharashtra, India

Dr. CS Madkar
Professor, Department of
Obstetrics and Gynaecology, DY
Patil Vidyapeeth, Pimpri, Pune 18,
Maharashtra, India

Dr. Vilisha Kothari
Department of Obstetrics and
Gynaecology, DY Patil
Vidyapeeth, Pimpri, Pune 18,
Maharashtra, India

Correspondence

Dr. Madhukar Shinde
Associate Professor, Department of
Obstetrics and Gynaecology,
DY Patil Vidyapeeth, Pimpri,
Pune 18, Maharashtra, India

To assess the significance of cervical length in determination of preterm labour in primigravida

**Dr. Hemant Deshpande, Dr. Madhukar Shinde, Dr. Chirag Wagh, Dr. CS
Madkar and Dr. Vilisha Kothari**

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Abstract

Preterm labour is defined as commencement of labour pains starting at any time before 37 completed weeks of gestation and is associated with many complications. Thus its early detection and prevention is of paramount importance to the obstetrician. This study highlights the importance of cervical length measurement by ultrasound as a predictor of preterm labour and importance of its serial estimation in both 1st and 2nd trimester.

Materials and Methods: This study was a Prospective Observational type of a study done in Dr. D.Y. Patil Medical College, Pune including all the pregnant women attending the OPD in the study period. Total 304 cases studied during the observation period.

Results: The detection of short cervix is having a statistically significant predictive value for pre-term labour. When we combine 1st and 2nd trimester cervical length's relation with term and pre term delivery we can say that short cervix (1st & 2nd) trimester has a significant percentage of predictive value for preterm delivery.

Conclusion: Our study showed the importance of cervical length estimation as a predictor of preterm labour and its assessment for risk stratification in patients to reduce morbidity.

Keywords: Preterm labour; cervical length; Primigravida; Prematurity

Introduction

Preterm delivery is defined as delivery after 24 but before 37 weeks of gestation or before completion of period of viability which is variable in different countries (20 weeks in developed countries where NICU facilities are able to salvage the newborn and 28 weeks period of viability in developing countries).

Preterm birth is the leading cause of perinatal death, complicating more than 10% of births internationally [1].

Preterm birth (<37 weeks' gestation) is the most significant clinical problem facing contemporary obstetrics in the developed world. Preterm birth occurs in 5–18 percent of all deliveries worldwide with most developed countries reporting an increased incidence over the last 3 decades [25]. It is estimated that 15 million preterm births occur each year with 1.1 million infants dying from preterm birth complications. Fifteen populous countries (including the USA) account for 75 percent of these deaths [26]. The significance of premature birth cannot be underestimated. Being born too early is the major cause of perinatal morbidity and mortality accounting for 85 percent of all early infant deaths, not secondary to congenital abnormality [27]. Advances in perinatology and neonatology in the past decade have resulted in increased survival rates, particularly for the extremely premature baby (born between 24 and 27 weeks' gestation) but unfortunately the associated morbidity for these survivors remains significant where one-fifth to one-quarter will suffer at least one major disability including chronic lung disease, impaired mental development, cerebral palsy, deafness, or blindness [29, 30]. Even late preterm infants (born between 32 and 36 weeks' gestation) have a greater risk of respiratory distress syndrome, feeding difficulties, temperature instability, jaundice, and delayed brain development [28]. Predicting preterm delivery is a matter of considerable importance in Obstetrics as its prevention helps improve perinatal outcomes and reduce neonatal morbidity and mortality [2].

Risk factors for preterm birth include a prior history of preterm birth, cervical incompetence (which can be assessed by cervical length estimation), infections of the genital tract, multifetal gestation and polyhydramnios [3].

Preterm babies are prone to serious illness or death during the neonatal period. Complications of prematurity are the single largest cause of neonatal death and the second leading cause of deaths among children under the age of 5 years. Infant death and morbidity following preterm birth can be reduced through interventions provided to the mother before or during pregnancy, and to the preterm infant after birth. Infant mortality and morbidity from preterm birth can be reduced through interventions delivered to the mother before or during pregnancy, and to the preterm infant after birth.^[4] Babies born preterm – that is, before 37⁺0 weeks of pregnancy – have high rates of early, late and postneonatal mortality, with the risk of mortality being inversely proportional to gestational age at birth. The major long-term consequence of prematurity is neurodevelopmental disability. (This can range from severe motor abnormalities, such as cerebral palsy, through to less severe cognitive abnormalities). In the majority of women with preterm labour, a ‘cause’ is not found, although it is known that a significant proportion of preterm labours are associated with infection. Preterm labour may or may not be preceded by preterm prelabour membrane rupture (P-PROM)^[5].

It has been shown that a shortened cervix is a powerful indicator of preterm births in women with singleton and twin gestations – the shorter the cervical length, the higher the risk of spontaneous preterm birth. Ultrasound measurements of the cervix are a more accurate way of determining cervical length (CL) than using a digital method. here are three approaches that may be used to perform ultrasound measurements of the cervix; these are the transabdominal (TA), transperineal (TP) and the transvaginal (TV) approach. The TV approach is considered to be the gold standard^[6].

Cervical insufficiency has no consistent definition, but is usually characterized by dilatation and shortening of the cervix before the 37th week of gestation in the absence of preterm labour, and is most classically associated with painless, progressive dilatation of the uterine cervix in the second or early third trimester resulting in membrane prolapse, premature rupture of the membranes, mid-trimester pregnancy loss, or preterm birth^[15, 16].

Assessment of the cervix typically reports the cervical length and identifies any evidence of cervical funnelling. Although funnelling is typically reported when the cervix is assessed, it should be noted that data do not support the placement of a cerclage on the basis of funnelling, but rather on residual cervical length.^[17] Relying solely on cervical length is not sufficient and shape of internal os and cervical funnelling on transvaginal ultrasound also must be considered by T-Y-V-U method. Transfundal pressure created by applying fundal pressure in the direction of the uterine axis for 15 seconds is more effective than coughing or standing in eliciting cervical changes and signs of progressive second trimester cervical shortening during active assessment of the cervix^[18, 19, 20].

A number of risk factors are involved in the development of spontaneous PTB,⁶ which are detailed as follows:

- Reproductive history of previous spontaneous preterm birth and use of assisted reproductive technology.
- Antepartum bleeding, rupture of membranes, cervical insufficiency, uterine anomalies, fibroids and excisional cervical treatment for cervical intraepithelial neoplasia.
- Fetal/uterine factors of multifetal gestation, fetal anomaly and polyhydramnios.
- Infection due to chorioamnionitis, bacteriuria, periodontal disease, current bacterial vaginosis.
- Demographic factors of low socioeconomic status, single

marital status, low level of education, First Nations ethnicity, or maternal age < 15 years or > 35 years.

- Lifestyle issues including cigarette smoking, illicit drug use, stress and physical abuse.
- Inadequate prenatal care, low pre-pregnancy weight and poor weight gain in pregnancy.

However, many women who deliver preterm do not have any known risk factors.⁶ The risk factor with the best correlation to preterm birth is a history of prior preterm birth(s). These women have a 2.5- fold increase in risk of PTB. However this risk factor is not useful in the nulliparous patients who make up nearly one half of all patients experiencing PTB^[7].

Cervical length is one of the major determinants of preterm delivery. The risk of preterm birth varies inversely with cervical length measured by transvaginal/ transabdominal scan 20-22 weeks.^[8] In some women, a shortened cervical length can be due to natural biological variation. In other cases early cervical shortening or effacement may be due to haemorrhage or infection leading to inflammation, or due to biophysical effects of uterine overdistension (e.g., multifetal gestation) or subclinical contractions. Using transvaginal ultrasound, a cervical length below the 10th centile for gestational age increased by 6-fold the risk of delivery prior to 35 weeks' gestation^[21]. A review of 35 studies using sonographically assessed cervical length to predict preterm delivery in asymptomatic women and found sensitivities ranging from 68% to 100% and specificities from 44% to 79% with wide variations in their predictive values^[22]. A more recent meta-analysis of 28 studies assessing cervical length (<15 mm) in symptomatic women with threatened preterm labour found sensitivities ranging from 53% to 67% and specificities ranging from 89% to 92% for delivery within one week^[23]. Due to limitations in ultrasound availability and operator expertise, cervical length alone cannot be reliably utilised to predict preterm labour or used as a routine screening tool^[24].

A cut-off value of cervical length of 2.5mm has been used by clinicians and researchers to screen for women at the highest risk of spontaneous preterm birth^[9].

Previous researchers have evaluated the use of serial transvaginal ultrasound assessments in predicting preterm birth^[10, 11]. Many of these studies, however, evaluated low-risk women or those with symptoms of preterm labor^[11].

Transvaginal ultrasonography (TVU) CL assessment is the gold standard and preferred screening test for a short cervix. TVU is more sensitive than transabdominal ultrasound. Transabdominal measurements overestimate CL by 8 mm among women with a short cervix, and have resulted in underdiagnosis of 57% of cases^[12].

Many studies have found that cervical length at 20-22 weeks is a reliable predictor of preterm delivery^[13].

There are various markers which can determine preterm labour apart from cervical length like cytokinins, fetal fibronectin, activin a.

Many studies have been put fourth comparing cervical length with other factors determining preterm birth.

However all the studies include only those subjects which are at high risks of preterm birth?

This study aims to include all pregnant women irrespective of risks factors for preterm birth.

This study aims at assessing and comparing the predictive value of cervical length at 11-14 weeks and 18-22 weeks in prediction of preterm labour.

Aims and Objectives

Assessment of cervical length significance in prediction of preterm labour. To compare the measurement of cervical length at 11-14 weeks and 20-22 weeks of gestation and to correlate measurements with gestational age at delivery. To compare the predictive value for the same for Preterm delivery. To study other factors contributing towards preterm labour.

Materials and methods

This study was done in Dr. D.Y. Patil Medical College & Hospital, Pune from August 2017– March 2019. This study included all the pregnant women attending the OPD at Dr. D.Y. Patil medical College & Hospital Pune during this period.

Observations

Total 304 cases studied during the study. This is a Prospective Observational type of a study. The inclusion criteria of this study:

- Primigravida
- Singleton pregnancy
- Women undergoing obstetric scan at gestational age 11-14 weeks and 18-22 weeks.
- The exclusion criteria of this study:
- Women with uterine anomalies.
- Iatrogenic prematurity for maternal or fetal causes.

The statistical analysis of this study is done using chi-square tests and regression analysis. Other high risk factors like PIH, GDM, are excluded.

Table 1: Prevalence of preterm labour in relation to 1st trimester cervical length screening

| 1ST trimester Scan Cervical length | Term | Early Preterm | Late Preterm |
|------------------------------------|-----------|---------------|--------------|
| Normal 293 (96.4%) | 252 (86%) | 7 (2.3%) | 34(11.6%) |
| Short 11 (3.6%) | 4(36.6%) | 3 (27.2%) | 4 (36.3%) |

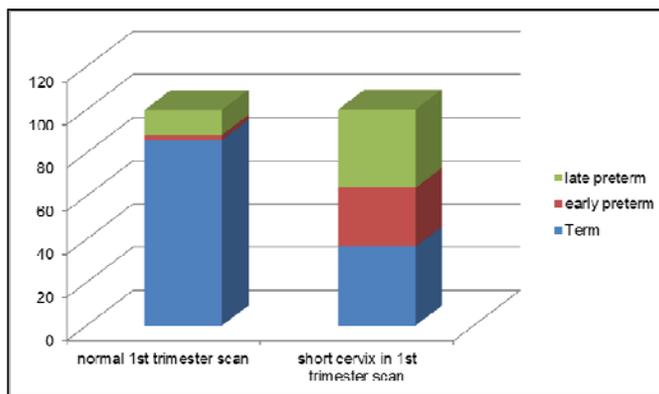


Fig 1: Prevalence of preterm labour in relation to 1st trimester cervical length screening

Table 2: According to one study. Cervical length classification was given based on the gestational age.^[14]

| Gestational age (weeks) | Cervical length (mm) | Gestational age (weeks) | Cervical length (mm) | Gestational age (weeks) | Cervical length (mm) |
|-------------------------|----------------------|-------------------------|----------------------|-------------------------|----------------------|
| 8 | 40.97±4.31 | 19 | 37.70±4.94 | 30 | 37.53±4.98 |
| 9 | 39.53±3.84 | 20 | 38.30±7.28 | 31 | 37.03±4.70 |
| 10 | 38.33±3.73 | 21 | 38.93±5.43 | 32 | 37.06±3.48 |
| 11 | 38.40±3.97 | 22 | 37.33±5.45 | 33 | 37.21±3.29 |
| 12 | 39.01±3.98 | 23 | 37.53±4.93 | 34 | 37.11±4.13 |
| 13 | 38.43±5.66 | 24 | 38.03±5.61 | 35 | 36.80±4.98 |
| 14 | 38.97±3.99 | 25 | 37.63±5.55 | 36 | 36.36±5.68 |
| 15 | 39.01±4.90 | 26 | 37.63±4.93 | 37 | 33.40±2.47 |
| 16 | 39.20±4.78 | 27 | 36.50±4.12 | 38 | 33.00±2.75 |
| 17 | 38.73±4.37 | 28 | 37.03±4.82 | | |
| 18 | 38.03±4.98 | 29 | 37.01±5.55 | | |

Data were expressed as mean±SD

Table 3: (n=293) 2nd Trimester cervical length’s relation with term and pre term delivery.

| 2 nd Trimester scan cervical length | Term | Early Preterm | Late Preterm |
|--|------------|---------------|--------------|
| Normal 248 (84.7%) | 220(88.7%) | 5 (2%) | 23 (9.8%) |
| Short 45 (15.3%) | 28 (62.2%) | 3 (6%) | 14 (31.1%) |

Table 4: Bacteriuria in relation with pre-term delivery

| Bacteriuria in relation with preterm delivery | No. of patients | Preterm delivery percentage |
|---|-----------------|-----------------------------|
| Bacteriuria alone | 24 | 62.5% |
| Bacteriuria with short cervix | 5 | 60% |

Table 5: Anaemia in pregnancy in relation with pre-term delivery

| Anaemia in pregnancy in relation with pre-term delivery | No. of patients | Preterm delivery percentage |
|---|-----------------|-----------------------------|
| Anaemia | 67 | 20.8% |
| Anaemia with short cervix | 15 | 53.3% |

Table 6: cervix treatment and preterm delivery

| Short cervix | Term | Preterm |
|-----------------------------------|------------|------------|
| Treated 38 (77.5%) | 26 (68.4%) | 12 (31.5%) |
| 1 st trimester treated | 2 | 5 |
| 2 nd trimester treated | 24 | 7 |
| Defaulter 11 (22.5%) | 4 (36.5%) | 7 (63.7%) |

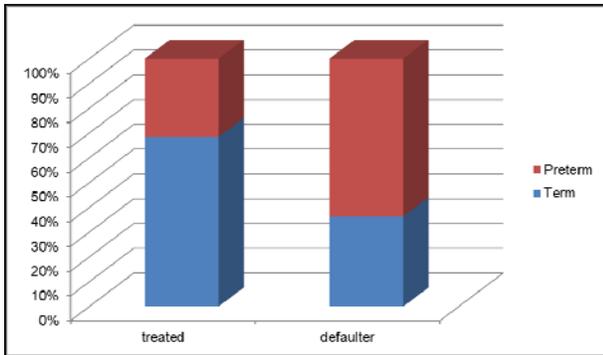


Fig 2: Decreased incidence of preterm labour after appropriate treatment of short cervix

Table 7: Combined 1st and 2nd Trimester cervical length's relation with term and pre term delivery.

| 1 st Scan 2 nd Scan | TERM | PRE TERM |
|---|-------------|------------|
| Normal & Normal (248) | 220 (88.7%) | 28 (11.3%) |
| Normal & Short (38) | 26 (68.4%) | 12 (31.6%) |
| Short & Short (7) | 2 (28.5%) | 5 (71.4%) |

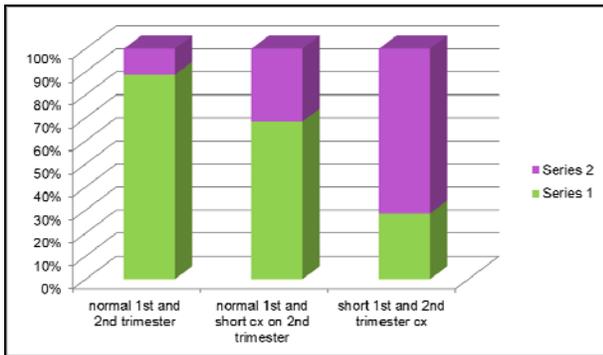


Fig 3: Combined 1st and 2nd Trimester cervical length's relation with term and pre term delivery.

Results

Preterm delivery percentage as a result of short cervix in the 1st trimester scan was 63.6%.

According to table 1 correlation of 1st Trimester cervical length's relation with term and pre term delivery. (n=304)

Table no. 1 shows that patients found to have a short cervix in first trimester scan were 3.6% but the percentage of pre-term deliveries amongst them was 63.6%. Table no. 2 shows that patients having short cervix in second trimester is 15.3% and preterm birth amongst them was 37.7% done at 18-20 weeks.

Here we can see as compared to previous table that percentage of short cervix has increased because of the progressive change

in the cervical length as observed in table 2. Even though cervical length done around 24 weeks of gestation is a better predictor of preterm labour it causes additional cost to the patient for doing an additional scan for cervical length after having done a routine anomaly scan.

Table 2 shows 2nd Trimester cervical length's relation with term and pre term delivery.

Pre-term delivery percentage as a result of short cervix in the 2nd trimester scan was 37.7%.

Table 3 compares Bacteriuria in relation with pre-term delivery n=24. Bacteriuria alone is found to be a significant risk factor for predicting pre-term labor.

Table 4 shows Anaemia in pregnancy in relation with pre-term delivery n= 67

Anaemia alone is not a good predictor but significant difference is observed when short cervix is considered.

Table 5: Short cervix treatment and preterm delivery n=49

Treatment improves the outcome. Medically progesterone support was given and surgically cervical encirclage was done before 24 weeks of gestation.

Table 6: Combined 1st and 2nd Trimester cervical length's relation with term and pre term delivery. p value for normal and short = 0.012 p value for short and short = 0.007

Short cervix (1st & 2nd) trimester has a significant 71.4% of pre-term delivery.

Discussion

In the present study cervical length in 304 primigravida was studied in first and second trimesters. Other risk factors for preterm labor were also noted.

Interaction of risk factors and their effect on preterm labor were studied.

Percentage of preterm labour in our study is 15.7%. The statistical analysis in our study was done using chi - square test and regression analysis.

The results obtained were short cervix, fetal fibronectin, low body mass index & bacterial vaginosis are significant predictors of preterm birth. Table no. 6 states that patients having short cervical length in 1st as well as 2nd trimester scan s has a significant high rate of preterm deliveries(71.4%). 31.6% of preterm deliveries were patients having a normal first trimester cervical length and a short cervix in the second trimester, stating the importance of second trimester scan for cervical length.

This means that if the cervical length is normal in both the scans, the percentage of pre-term labour is 11.3%, comparable with the overall incidence in the literature.

But, if we pay attention to cervical length in the first trimester, we can find out high risk group for preterm labour. This can very well be done along when patient comes for NT scan.

Further, when patient comes for anomaly scan, we can re-assess the cervical length and find out further addition to high risk group.

Summary

In the present study cervical length in 304 primigravida was

studied. Percentage of pre-term labour in our study is 15.7%.

It was seen that out of 304 patients, 49 had short cervix, which is about 16.1% of the total patients.

11 patients had a short cervix in the first trimester scan and number of patients having a short cervical length in the second trimester scan were 38. The percentage of patients landing in preterm labour due to a short cervix in the first trimester scan was 63.6% which is significantly high compared to 37.7% as a result of short cervical length in second trimester scan.

When we combine 1st and 2nd trimester cervical length's relation with term and pre term delivery we can say that short cervix (1st & 2nd) trimester has a significant percentage of preterm delivery. Thus, stating the importance of a first trimester scan in predicting a high risk group for preterm labour. There is a significant difference seen in the percentage of term and preterm deliveries when a short cervix is subjected to treatment. 63.7% landed in preterm labour in patients who lost follow up and hence did not receive treatment, thus stating the importance of treating a short cervix.

Conclusion

- The detection of short cervix is having a statistically significant predictive value for pre-term labour.
- Even though short cervix in the first trimester is a better predictor, specificity increases due to a short cervix scan in the first trimester but sensitivity increases when we add a second trimester scan to it.
- Bacteriuria is another significant factor for preterm labour.
- Other risk factors are not significant, but if we consider short cervix with the other risk factors, then the predictability of other risk factors also increases.
- Proper diagnosis of short cervix is important in early trimester, so that definite measures to prevent preterm labour like 2nd trimester cervical encirclage can be considered.

References

1. Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, *et al.* Preventing preterm births: Analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet.* 2013; 381:223-243.
2. Kinney MV, Lawn JE, Howson CP, Belizan J. 15 Million preterm births annually: what has changed this year? *Reprod Health.* 2012; 9:28.
3. Jolley JA, Wing DA. Pregnancy management after cervical surgery. *Curr Opin Obstet Gynecol.* 2008; 20: 528–533.
4. Green Ink, United Kingdom. WHO recommendations on interventions to improve preterm birth outcomes, World Health Organization. 2015,(1)
5. NICE Guideline, No. 25, National Collaborating Centre for Women's and Children's Health (UK)., London: National Institute for Health and Care Excellence (UK); 2015 Nov.
6. Lim K, Butt K, Crane JM. SOGC Clinical Practice Guideline. Ultrasonographic cervical length assessment in predicting preterm birth in singleton pregnancies. *J Obstet Gynaecol Can.* 2011; 33(5):486–99.
7. Sandra O'Hara, Marilyn Zelesco, *et al.* Cervical length for predicting preterm birth and a comparison of ultrasonic measurement techniques; *Australas J Ultrasound Med.* 2013; 16(3):124–134.
8. Iams JD, Goldenberg RL, Meis PJ. The length of the cervix and the risk of spontaneous premature delivery. National Institute of Child Health and Human Development Maternal Fetal Medicine Unit Network. *N Engl J Med.* 1996;334:567-72
9. Conde-Agudelo A, Romero R, Nicolaides K, Chaiworapongsa T, O'Brien JM, Cetingoz E, da Fonseca E, Creasy G, Soma-Pillay P, Fusey S, Cam C, Alfirevic Z, Hassan SS. Vaginal progesterone vs. cervical encirclage for the prevention of preterm birth in women with a sonographic short cervix, previous preterm birth, and singleton gestation: a systematic review and indirect comparison metaanalysis. *Am J Obstet Gynecol* 2013;208:42.e1-42.e18.
10. Yoshizato T, Obama H, Nojiri T, Miyake Y, Miyamoto S, Kawarabayashi T. Clinical significance of cervical length shortening before 31 weeks' gestation assessed by longitudinal observation using transvaginal ultrasonography. *J Obstet Gynaecol Res.* 2008; 34:805-811.
11. Sotiriadis A, Kavvadias A, Papatheodorou S, Paraskevaidis E, Makrydimas G. The value of serial cervical length measurements for the prediction of threatened preterm labour. *Eur J Obstet Gynecol Reprod Biol.* 2009; 148:17-20.
12. Hernandez-Andrade E, Romero R, Ahn H, *et al.* Transabdominal evaluation of uterine cervical length during pregnancy fails to identify a substantial number of women with a short cervix. *J. Matern. Fetal Neonatal Med.* 2012; 25(9):1682-1689.
13. Kagan KO, To M, Tsoi E, Nicolaides KH. Preterm birth: the value of sonographic cervical length measurement. *BJOG.* 2006; 113:52-6.
14. Hoesli I, Tercanli S, Holzgreve W. Cervical length assessment by ultrasound as a predictor of preterm labour—is there a role for routine screening? *Bjog.* 2003; 110(Suppl 20):61-5.
15. McDonald, I.A. Incompetence of the cervix. *Aust N Z J Obstet Gynaecol.* 1978; 18:34-37.
16. Shennan, A. and Jones, B. The cervix and prematurity: aetiology, prediction and prevention. *Semin Fetal Neonatal Med.* 2004; 9:471-479.
17. To MS, Skentou C, Liao AW, Cacho A, Nicolaides KH. Cervical length and funneling at 23 weeks of gestation in the prediction of spontaneous early preterm delivery. *Ultrasound Obstet Gynecol.* 2001; 18:200-203.
18. Guzman ER, Pisatowski DM, Vintzileos AM, Benito CW, Hanley ML, Ananth CVA. comparison of ultrasonographically detected cervical changes in response to transfundal pressure, coughing, and standing in predicting cervical incompetence. *Am J Obstet Gynecol.* 1997; 177:660-665.
19. Guzman ER, Vintzileos AM, McLean DA, Martins ME, Benito CW, Hanley ML. The natural history of a positive response to transfundal pressure in women at risk for cervical incompetence. *Am J Obstet Gynecol.* 1997; 176:634-638.
20. Guzman E, Rosenberg J, Houlihan C, Ivan J, Waldron R, Knuppel R. A new method using vaginal ultrasound and transfundal pressure to evaluate the asymptomatic incompetent cervix. *Obstet Gynecol.* 1994; 83:248-252
21. Norwitz ER, Robinson JN. A systematic approach to the management of preterm labor, *Seminars in Perinatology.* 2001; 25(4):223-235.
22. Watson WJ, Stevens D, Welter S, Day D. Observations on the sonographic measurement of cervical length and the risk of premature birth, *Journal of Maternal-Fetal Medicine.* 1999; 8(1):17-19.
23. Sotiriadis A, Papatheodorou S, Kavvadias A, Makrydimas

- G. Transvaginal cervical length measurement for prediction of preterm birth in women with threatened preterm labor: a meta-analysis,” *Ultrasound in Obstetrics and Gynecology* 2010; 35(1):54-64.
24. Berghella V, Baxter JK, Hendrix NW. Cervical assessment by ultrasound for preventing preterm delivery, *Cochrane Database of Systematic Reviews*, vol. 1, Article ID CD007235, 2013.
 25. March of Dimes Foundation, March of Dimes White Paper on Preterm Births: The Global and Regional Toll, March of Dimes Foundation, White Plains, NY, USA, 2009.
 26. March of Dimes, PMNCH, Save the Children, and WHO, *Born Too Soon: The Global Action Report on Preterm Birth*, edited by: C. P. Howson, M. V. Kinney, J. E. Lawn, WHO, Geneva, Switzerland, 2012.
 27. Norwitz ER, Robinson JN. A systematic approach to the management of preterm labor, *Seminars in Perinatology*. 2001; 25(4):223-235.
 28. Kugelman A, Colin AA. Late preterm infants: near term but still in a critical developmental time period, *Pediatrics*, vol. 2013; 132(4):741-751.
 29. Chandiramani M, Tribe RM, Shennan AH. Preterm labour and prematurity, *Obstetrics, Gynaecology and Reproductive Medicine*. 2007; 17(8):232-237.
 30. Johnson S, Fawke J, Hennessy E, *et al.* Neurodevelopmental disability through 11 years of age in children born before 26 weeks of gestation, *Pediatrics*. 2009; 124(2):e249–e257.