

Transvaginal nUltrasound Measurement of Lower Uterine Segment Myometrial Thickness for the Prediction of Preterm Labor in Twins Gestations. Observational Study

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ABSTRACT

Background: Transvaginal ultrasound evaluation of cervical length considered a good predictor of PTL and recently lower uterine segment myometrial thickness had been used for this purpose.

Objectives: Evaluating the efficacy and validity of transvaginal ultrasound measurement of lower uterine segment myometrial thickness (LUS-MT) in prediction of preterm delivery (PTL) in twins pregnancies.

Patients and Methods: This is an observational prospective cohort study where ninety six (96) twins pregnant women were enrolled. *LUS-MT* and CL were measured by transvaginal ultrasound between 16-24 gestational weeks. All patients were scheduled for routine antenatal care till delivery and divided in two groups: preterm group and full-term group.

Results: 58 patients delivered at full term and 38 patients had preterm delivery. Among patients who had preterm delivery, 25 patients (56.8%) had LUS-MT <4.26 and 2 patients (3.8%) only had LUS-MT \geq 4. among patients who delivered at full term, 50 patients (96.2%) had LUS-MT \geq 4.26 and 19 patients (43.2%) had LUS-MT <4.26. The best cutoff value for LUS was 4.26 mm with area under the ROC curve (AUC) 0.917, sensitivity 92.1 %, specificity 86.2%, PPV 81.3%, NPV 94.3% and Accuracy 92.1 %.

Conclusion: Transvaginal ultrasound measurement of LUS-MT is an effective, precise, applicable and safe procedure in predicting the preterm labor in twins gestation with high validity than cervical length. Use of lower uterine wall as a substitution of CL measurement in order to predict population at risk of preterm labor needs to be investigated.

Keywords: Cervical length, Lower Uterine Segment Myometrial Thickness, Preterm Labor, Transvaginal Ultrasound.

INTRODUCTION

Twins pregnancy constitutes 2-4% of all births, and the rate of twinning has increased by 76 % between 1980 and 2009. Preterm birth is the most common complication of twins pregnancy affecting 40-60% of such gestations ⁽¹⁾. There is a substantial long-term health impact from preterm birth due to increased risk of death and of developing a wide range of chronic physical and neurological disabilities compared to full term births ⁽²⁾.

In twins pregnancy, etiological factors for preterm birth include uterine over distention ⁽³⁾. Myometrial distention increases myometrial contractility, releases prostaglandins, and up regulates oxytocin receptors, all of which are implicated in the cascade of events that occur in early labor ⁽⁴⁾.

Obstetrical history, demographic factors and symptoms were traditionally used for prediction of PTL ⁽⁵⁾. Also, numbers of biologic markers in serum, amniotic fluid, and cervical secretions were evaluated for this purpose like cervicovaginal fetal fibronectin (fFN) and serum Ferritin ^(6,7).

Now it is established that cervical length measurement using transvaginal ultrasound is the best method for prediction of preterm birth in twin pregnancies and was demonstrated as sensitive in

twins as in singletons ⁽⁸⁾. Most published studies agreed on cervical length measurement between 16-24 weeks ⁽⁹⁾.

Lower uterine wall lies closely to the cervix so the changes that originated in the cervix could possibly involve the adjacent lower uterine wall as well ⁽¹⁰⁾. There is inverse association between the thickness of the lower uterine segment and cervical length and advancing gestational age as the lower segment becomes thinner ⁽¹¹⁾.

So, we conducted this study to evaluate the efficacy and validity of transvaginal ultrasound measurement of lower uterine segment myometrial thickness (LUS-MT) and its correlation with cervical length in prediction of preterm delivery in twin pregnancies.

PATIENTS AND METHODS

This is an observational prospective cohort study carried out in the department of Obstetrics and Gynecology at Menoufia University Hospital, Menoufia governorate, Egypt.

Ninety six (96) twins pregnant women their gestational age ranged from 16-24 weeks were enrolled in the period from December 2016 to October 2018.



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Ethical approval:

- **The study protocol was approved by the local Ethics and Research Committees at Menoufia University Hospital.**
- Written consent was been obtained from all patients before getting them involved in the study.
- The steps of the study; the aims, the benefits and disadvantages have been discussed with the patients.
- The patients have been informed about any abnormal results of the procedures and were instructed and were treated accordingly.
- The patients were having the right to refuse participation.
- All data and test results of the study population have been preserved.

Exclusions criteria: women with late established preterm labor pain (cervix \geq 3cm), preterm premature rupture of membranes (PPROM), known cervical or uterine abnormalities and fibroid uterus, placenta previa, and severe preeclampsia.

Inclusions criteria: In our study we included pregnant women with twins pregnancy at 16-25 weeks of gestation, intact membranes, primigravida or multigravida, reassuring fetal heart rate and without vaginal bleeding.

All patients were subjected to complete history taking, complete general, abdominal and local examination with emphasis on uterine contractions and cervical changes, abdominal ultrasound for number of fetuses, fetal biometry, congenital anomalies, amniotic fluid index and Placental site and grade.

Procedure:

Patients were placed in dorsal position with hips and knees flexed, the probe covered with a non-latex sheath or condom that was removed after use. Ultrasonographic examination was carried out transvaginally with the bladder partially filled to allow good imaging of the lower uterine segment. The probe was placed against the anterior lip of the cervix moving beyond the posterior limit of bladder to bring the lower uterine segment and cervix into the field. This transducer probe had a frequency of 7.5MHz (Mindray DP-30 portable ultrasound machine, China).

Lower uterine segment myometrial thickness (LUS-MT) measured by TVUS where the first caliper arranged at the interface between the amniotic fluid and the decidua and the second caliper between the myometrium and the bladder serosa at a level 2 cm above the internal os ⁽¹²⁾ (Fig. 1).

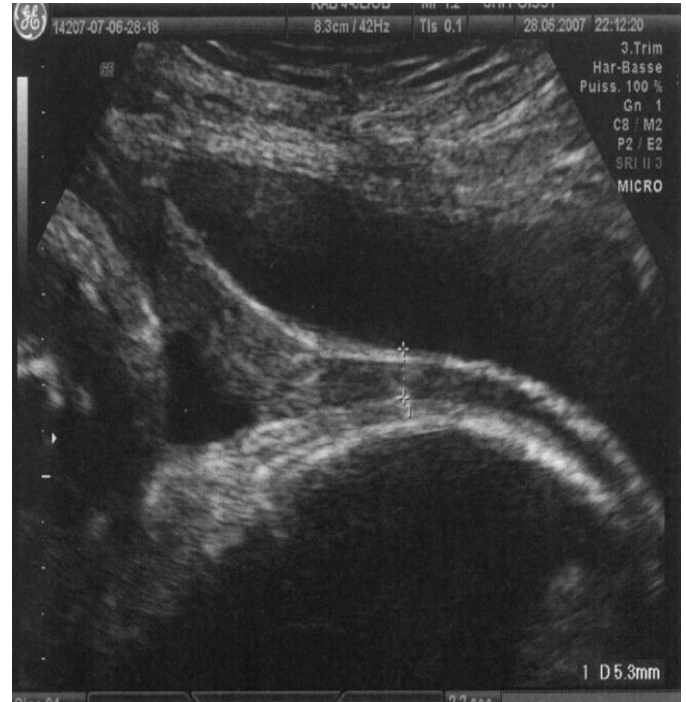


Figure (1): Ultrasonographic measuring of the lower uterine segment thickness (U =uterus, B = urinary bladder).

Cervical length measured by TVUS (TVUS-CL) as the length between the external os and the functional internal os of the uterine cervix according to the ISUOG 2015 recommendations ⁽¹³⁾ (Fig. 2). All examinations were performed by the same examiner.

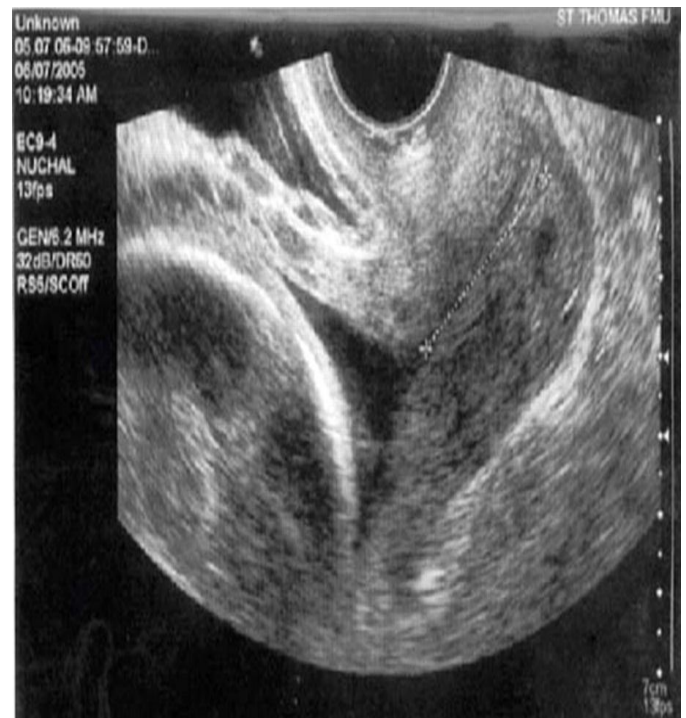


Figure (2): Transvaginal ultrasonographic measurement of cervical length (U =uterus, B = urinary bladder).

Follow up of the cases:

All patients were scheduled for routine antenatal care till delivery, with assessment of fetal well-being, fetal measurements, fetal growth, amniotic fluid and Doppler ultrasound of the umbilical artery at every visit, and all data registered in antenatal care records.

We gave patients some advices as mild exercises, sleep, rest, and no coitus. We supplied all patients with minerals, vitamins, iron, and calcium. all patients were followed up to exclude symptoms and signs of preterm labor and any patients presented with symptoms and signs of preterm labor (include at least two regular, painful uterine contractions within 10 min accompanying with cervical changes less than 3 and effacement of less than 80%) were managed with our department standard protocol for acute tocolysis as 10 mg oral nifedipine (Epilate caps 10 mg) which was repeated every 15 min till contraction stopped or 4 capsules administered provided that ABP more than 90/60 and pulse less than 110 b/min before each capsule, then nifedipine 20 mg tab for 48 h (Epilate Retard®, EIPICO, Egypt) (14, 15).

Dexamethasone was used for accelerating fetal lung maturation. Magnesium sulfate was used for fetal neuroprotection if the gestational age was ≤ 32 weeks).

Data on pregnancy outcome were obtained from the filing system in the delivery ward, and for

those that delivered at home or in other hospitals from the women themselves through phone contact.

Statistical Analysis

Data collected were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative were represented as number and percentage, quantitative continues group were represented by mean ± SD. P value was set at <0.05 for significant results and <0.001 for high significant result.

ROC curve was for detection of validity and cutoff point in comparison to sure diagnostic test. Calculation of Spearman correlation coefficient was also used.

RESULTS

During the study period out of 250 pregnant women's, 143 women excluded because 100 women had singleton pregnancy and 43 women refused to participate. 107 twins pregnant women were included with 11 cases excluded (6 abortion, 3 uterine anomaly, 2 uterine fibroid). 96 women were enrolled and statistically analyzed. 69 (71.9%) women were primigravida and 27 (28.1%) were multigravida. 38 women had preterm delivery and 58 women delivered at term (Fig 3).

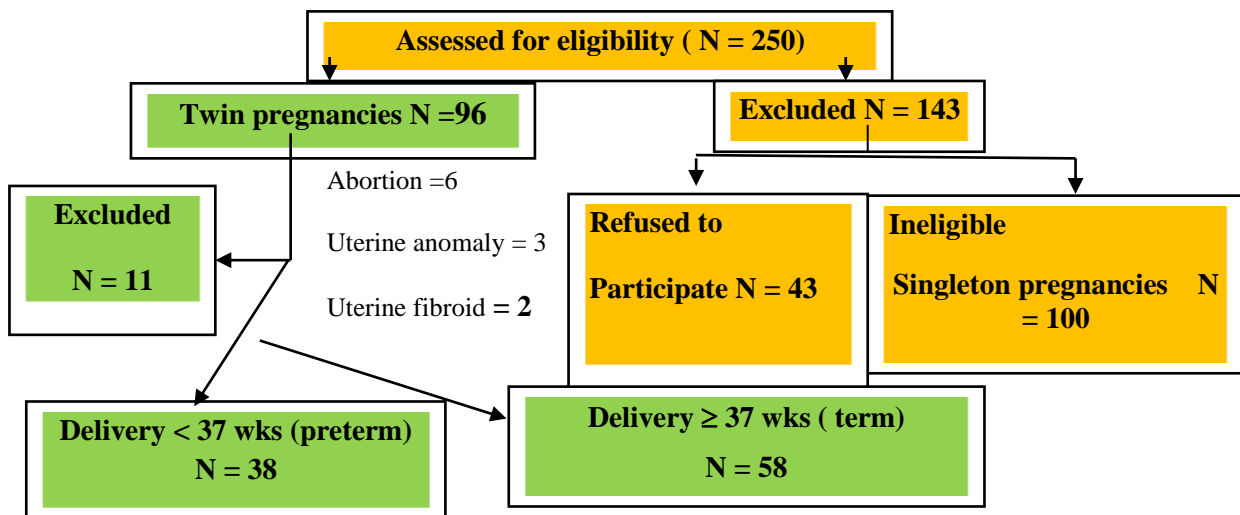


Figure (3): flow chart.

Mean age of the study populations with preterm labor was 30.3±6.05 with gestational age ranged from 25-35 week and Mean ± SD 32.6 ± 2.74 and mean age of patients who delivered at full term was 26.4±5.23 with gestational age ranged from 37-39 Mean ± SD ranged from 38.06 ± 0.74. Mean BMI of the participants with preterm labor was 29.1±5.48 (ranged from 19 -37) and for those who delivered at full term was 26.3±5.32 (ranged from 20-37).

Table 1: represent a highly significant statistical difference with TVUS-CL measurement and TVUS-MT measurement in prediction of preterm labor in twins pregnancy (p value <0.001).

Table (1): The relation between CL and LUS-MT with preterm delivery.

Variable	Maturity	No	Mean ± SD	T	P value
Cervical length (CL)	Preterm	38	27.17 ± 9.31	4.041	< 0.001
	Full term	58	35.3 ± 9.83		
Lower uterine segment myometrial thickness (LUS-MT)	Preterm	38	3.41 ± 0.522	0.936	< 0.001
	Full term	58	5.78 ± 1.26		

Table 2: when using the cutoff point, there was a highly significant difference between preterm and full term labor as regard CL and LUS- MT.

Table (2): Relation between TVUS measurement of CL and LUS –MT in prediction of preterm labor.

Variable	Cutoff	Maturity	N	%	X2	P value
Cervical length (CL)	<25 mm	Preterm	16	66.7%	23.51	<0.001
		Full term	8	33.3%		
	≥25 mm	Preterm	11	15.3%		
		Full term	61	84.7%		
Lower uterine segment myometrial thickness (LUS-MT)	<4.26	Preterm	25	56.8%	33.08	<0.001
		Full term	19	43.2%		
	≥4.26	Preterm	2	3.8%		
		Full term	50	96.2%		

Table 3 and figure 4: showed that the best cutoff value for LUS was 4.26 mm with area under the ROC curve 0.917, sensitivity 92.1 %, specificity 86.2%. Positive predictive value (PPV) 81.3%, Negative predictive value (NPV) 94.3% and Accuracy 92.1 %. The best cutoff value for CL was 25mm mm with the AUC 0.873, sensitivity 84.2 %, specificity 81 %%, PPV 74.4%, NPV 88.6 %and Accuracy 84.2 %.

Table (3): Receiver–operating characteristic (ROC) for various cutoff points for the (LUS-MT) between 16 – 25 gestational weeks.

Variables	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
CL	25 mm	0.873	84.2 %	81 %	74.4%	88.6%	84.2 %
LUS-MT	4.26 mm	0.917	92.1 %	86.2 %	81.3%	94.3%	92.1 %

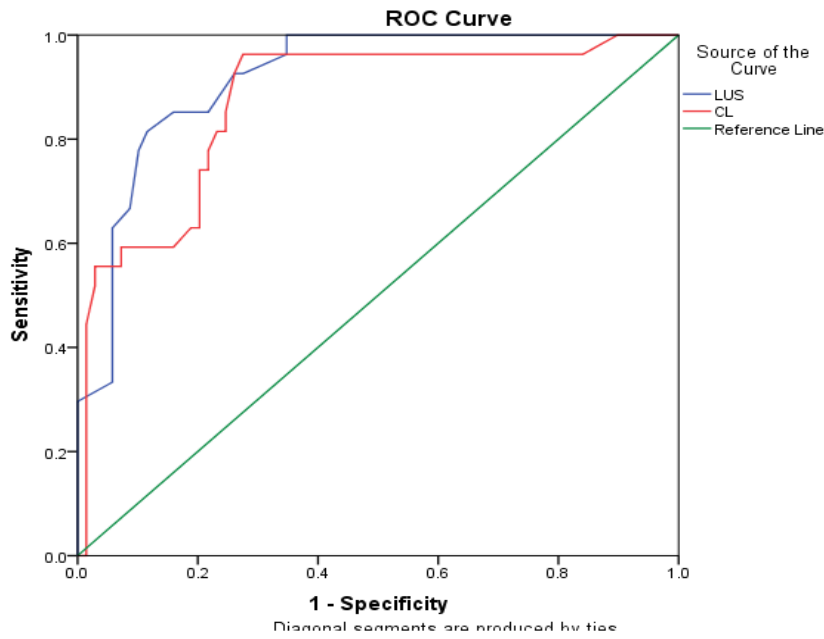


Figure (4): Receiver–operating characteristic (ROC) for various cutoff points for the (LUS-MT) between 16 – 25 gestational weeks.

Table (4): Represent the (ROC) curve using the lower uterine segment thickness and cervical length to determine the sensitivity and specificity with a range of cutoffs. Although LUS apparently better than CL but by comparing the two areas under the curve we found that the two variables were excellent in detecting the preterm status and statistically were not different from each other (p value 0.376).

Table 4: Area under the Curve cutoffs between LUS and CL.

Test Result Variable(s)	Area	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
LUS	0.917	0.028	<0.001	0.863	0.972
CL	0.873	0.041	<0.001	0.792	0.953

Table (5): Show that there is a significant positive correlation between cervical length (CL) and lower uterine segment (LUS) measured trans vaginally in prediction of preterm labor in twins pregnancy (**Figure 5**).

Table (5): Correlation coefficient between LUS and CL.

	LUS	
	r*	P value
	0.304	0.003*

*Pearson correlation coefficient

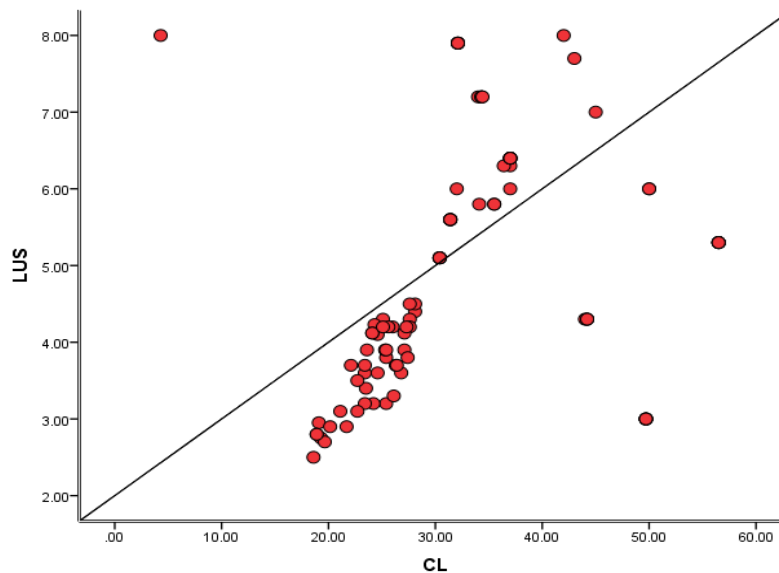


Figure (5): Correlation coefficient between CL and LUS

DISCUSSION

Multiple pregnancies increase the risk of PTL, which is considered the major cause of neonatal morbidity and mortality. Prediction and prevention of PTL is a primary goal for obstetricians all over the world⁽¹⁴⁾.

One of the greatest aims of this study was not only to demonstrate a strong positive correlation between lower uterine segment thicknesses measured by TVUS between 16 -24 gestational weeks and prediction of preterm labor; but also to determine a cutoff value for LUS thickness that can be used with safety. This cutoff value must yield the best sensitivity and specificity for this purpose. So, a receiver-operating characteristic (ROC) curve was constructed using the lower uterine segment thickness between 16 -24 gestational weeks and then determining the sensitivity and specificity with a range of cutoffs.

From this study, 38 patients who delivered prematurely, 35 patients had LUS-MT thickness less than 4.26 mm and 3 patients had LUS-MT thickness more than 4.26 mm. Among the 58 patients who delivered maturely, 50 patients had LUS-MT thickness more than 4.26 mm and 8 patients had LUS-MT thickness less than 4.26 mm.

Erzincan et al.⁽¹²⁾ analyzed the combined use of myometrial thickness (MT) measured trans abdominally from the fundal, mid-anterior walls and the lower uterine segment (LUS) and CL measurements as a ratio to differentiate and identify the women truly at risk for preterm birth after an

episode of threatened preterm labor in 46 singleton pregnancies.

They concluded that the optimal cutoff values for CL, fundal MT-to-CL and mid-anterior MT-to-CL ratios in predicting PTB were calculated as 31.1 mm, 0.19 and 0.20, respectively. Fundal MT-to-CL ratio predicted preterm delivery with 71% sensitivity, 72% specificity, 68% positive and 75% negative predictive values. For mid-anterior MT-to-CL ratio, respective values were 76, 76, 73 and 79%. They found that fundal MT-to-CL and mid-anterior MT-to-CL ratios can predict preterm birth. They suggested that in addition to CL measurement, a woman after an episode of PTL, with a fundal MT-to-CL ratio < 0.19 or mid-anterior MT-to-CL ratio < 0.20 can be followed as an outpatient setting. This supports our result in prediction of PTL by TVUS measurement of MT⁽¹⁶⁾.

Our study showed that there was a significant positive correlation between cervical length (CL) and lower uterine segment (LUS) measured trans vaginally in prediction of preterm labor in twins pregnancy when the cutoff value for LUS was 4.26 mm. This is in consistence with **Woraboot et al.**⁽¹⁰⁾, where transabdominal ultrasonography (TAUS) was performed to measure the lower uterine wall thickness (LUS) and TVUS was performed to measure the cervical length in 166 singleton pregnant women and found a highly positive correlation between (LUS) when cutoff value for LUS was 4.4 mm, and CL at 16-32 weeks of gestation ($r_s \frac{1}{4}0.767$, $n \frac{1}{4}166$, $p < 0.001$). For those who had short cervical length

(defined as less than 30 mm) at GA 16-24 weeks ($n=10$). So they believe that it's reasonable to imply that when the cervix is long the lower uterine wall would be thick, and when the cervix gets shorter the lower uterine wall would change in the same direction i.e. thinner.

From our point of view the drawback of the previous two studies was the use of transabdominal route for measurement of MT, which may be imprecise in obese patients and other abdominal wall abnormalities but in our study TVUS was used to overcome these obstacles as it has high accuracy and better resolution.

Our study is consistent with the study conducted by **Goldstein et al.** ⁽¹⁷⁾, to establish normal values for the lower uterine segment (LUS) thickness during gestation in twin pregnancies and concluded that LUS-MT thickness during 2nd trimester greater than 4.45 mm was found to be protective against preterm labor while LUS-MT thickness less than 2.3 mm was associated with a higher risk of preterm labor.

Sfakianaki et al. ⁽¹⁸⁾ assessed myometrial thickness serially during gestation in 92 twin pregnant female to determine pregnancy outcome using TAUS at which patients with LUS-MT thickness in 2nd trimester measured (4.5 mm – 6.0 mm) delivered at full term after 35 week' gestation, while patients with LUS-MT thickness (3.5 mm-5.6 mm) had preterm delivery before 35 week' gestation. This little difference between this study and our study may be due to use of TAUS instead of TVUS in our study.

To the best of our knowledge, our study is preliminary study about the measurement of LUS-MT with TVUS, which is easily, available and applicable toll for early prediction of PTL in twins gestations and its correlation with CL; accordingly such high risk pregnant women will be closely monitored for PTL so we could advise life style modification and tocolytics drugs.

We believed that the effective prevention of preterm birth is a very hard work and requires collaborations from every level of maternal health care providers, so further studies on this field are needed to validate our results. We hoop that the data obtained from this study may be used as a baseline data for further studies using TVS measurement of myometrial thickness in prediction of preterm deliveries in twins gestation.

CONCLUSIONS

Transvaginal ultrasound measurement of lower uterine segment thickness is an effective, precise, applicable and safe procedure in predicting the preterm labor in twins gestation with high validity than cervical length. We recommend that high-risk pregnancies for PTL might especially benefit from TVS measurement of LUS-MT. However, whether the lower uterine wall thickness could be used as a substitution of CL measurement in order to predict population at risk of preterm labor needs to be investigated.

Strength of the study:

Our study is preliminary study about the measurement of LUS-MT with TVUS. Another strength point is screening in twins pregnant patients who are increasing and more liable for preterm birth. Our study followed a well-defined methodology for measuring the LUS thickness and all examinations were performed by the same examiner thereby eliminating the inter observer bias. We believed that the measurement technique used in this study was easy to follow, required minimal training and was feasible in almost all obstetric settings.

Limitations of the study:

Inability to recruit a large cohort and to design a multicenter trial was unintended limitation of current study. Also, the mean gestational age at assessment was 32.6 ± 2.74 weeks; meaning that mostly late preterm patients were included and those actually troubled < 28 weeks were not.

We used single TVUS measurement in contrary with other study that used serial measures.

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