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The Value of Serum Calponin 1 in Maternal Blood as Marker for Prediction of Short Preterm Labour with Intact Membrane

Dalal I. Hussein [(1)]; **Alaa O. Mohammad** [(2)]

[(1)] [(2)] **M.B.Ch.B., D.O.G; Specialist in Obstetrics & Gynecology**

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ABSTRACT

Background: Preterm birth is a worldwide epidemic with a global incidence of (5%- 15%). It is important risk factor for perinatal morbidity and mortality.
Calponin 1 is a basic smooth muscle protein that had biological process as actinomycin structure organization and regulation of contractile function. The uterus containing the largest volume of smooth muscle, myometrial destruction occurs when uterine contractions start leading to increased maternal serum calponin 1 levels.

Aim of study: To investigate the level of serum calponin 1 in maternal blood as marker for prediction of short onset preterm labor with intact membrane within one week.

Methods: A prospective observational study that collected in obstetrical department of the al-yarmouk hospital in cooperation with the laboratory department of hospital through the period from Feb till Dec 2019. It included 88 pregnant women between 28 – 36+6 gestational weeks admitted to the hospital diagnosed as threatened preterm labor. Follow up done with each participant admitted in hospital until the time of delivery to determine the gestational age at delivery and record the birth interval from blood sampling till delivery, Serum Calponin 1 level positive and negative predictive values were compared for the prediction of short onset preterm birth within seven days or more

Results: In this study, 73.9% of the study patients were delivered within one week after presentation. Mean of calponin 1 was significantly higher in study groups who delivered within one week than those who delivered after one week. Serum calponin 1 > 0.6 ng/ml is predictive for short onset preterm birth

Conclusion: Serum calponin 1 may play an important role at pregnancy as non-invasive predictor for short onset preterm labour in cases diagnosed as threatened preterm labour

Recommendation Further larger prospective studies are needed larger sample size and longer duration to: confirm the standard diagnostic level of calponin 1 to diagnosis short onset preterm labour, perform antenatal checkup and testing by other modalities, take in consideration researches on the genetics or environmental factors (smoking) and their role in the development of preterm labour.

Corresponding author E mail: ah77.mohamd@tu.edu.iq

Introduction:

Preterm birth means early delivery of baby before 37 completed weeks of pregnancy. It is a commonest cause of perinatal morbidity and mortality. (1).Preterm birth is a worldwide epidemic with a global incidence of (5% - 15%) (2) . A round 45-50% are idiopathic preterm birth , 30% are preterm rupture of membranes, 15-20% are medically indicated or elective preterm deliveries, Severals mechanisms of preterm birth are proposed: Degradation of prostaglandins leads to initiations of contractions (3),maternal physical and psychological stress, genital infections ,and vaginal bleeding. all stimulate myometrial contractions (4).

Diagnostic assessment of women with premature labor ; cardiotocography, vaginal examination (Cervical smear for microbiology, measurement of vaginal PH, amniotic fluid testing, fibronectin test, palpation for cervical assessment) , transvaginal ultrasound for measurement of cervix length, abdominal and doppler ultrasound of the uteroplacental and fetoplacental vessels (5).

Calponin1 is an actin filament protein a molecular weight 34–37 kDa (consist of 292–330 amino acids), Calponin1 is a basic smooth muscle protein that have biological activities as organize actinomycin structure, organize contraction of smooth muscle, and negative effect of cell proliferation in vascular smooth muscle (6).Calponin1 may serve as a marker for prediction of short onset preterm birth. This play role in the following facts;

i. Calponin H1 (basic) isoform is smooth muscle specific protein (7).

ii. The uterus had mainly smooth muscle in second and third trimesters of pregnancy: (8).

iii. Myometrial destruction occurs when uterine contractions start leading to increase maternal serum calponin 1 levels (9).

Aim of study

To investigate the level of serum calponin 1 in maternal blood as marker for prediction of short onset preterm labor with intact membrane within one week.

Patient and method

This is a prospective observational study that collected the patients who admitted to obstetrical department of the al-yarmouk hospital from Feb till Dec 2019.In this study used marker Human Calponin1 ELISA, number of kit 96 . Initially included 96 pregnant women between 28 – 36+6 gestational weeks who admitted to the hospital diagnosed as preterm labor. Six participants showed invalid or missing Calponin 1 serum level, and two participants were lost to follow up, so the total number of participants included in the analysis for short onset preterm labor was 88.

Serum Calponin 1 level was measured by 5 ml of blood sample collected in plain tube from each pregnant woman, which allowed to clot at room temperature. Centrifuge in al-yarmouk hospital laboratory at 2000-3000 RPM mainly for 20 minutes. the human calponin 1 kit used to measure the human calponin 1 level in all collected samples by enzyme linked immunosorbent assay (ELISA). Positive and negative predictive values were compared for the prediction of short onset preterm birth within seven days or more. The standard curve range of kit was 0.05ng/mL - 15ng/mL

Inclusion criteria: pregnant women regardless age & parity, single viable fetus gestational age 28 – 36+6 week determined by LMP and/or reliable obstetrical ultrasound at first trimester. complaining with frequent, intense uterine contraction every 10 minutes, cervical dilatation $\leq$ 3cm, and intact membrane.

Exclusion criteria: ruptured membrane, cervical dilatation > 3 cm. multiple gestation. placenta previa, choroaminitis, polyhydramnios, fetal abnormalities, patients with cervical cerclage, and patients who received tocolytics.

Those patients who fulfilled inclusion and exclusion criteria and agreed to participate in study,

assessed by history, examination, and management of threatened preterm labour which admitted to obstetrical department at al-yarmouk teaching hospital given hydration, corticosteroid and tocolytic agents. After treatment assessment of uterine contractions if subsided then patient kept hospitalized in obstetrical ward but patient who startup active labour referred to the labour suite and followed up until delivery time to determine the gestational age at delivery and record the birth interval from blood sampling till delivery, the pediatrician assessed newborn babies and who need for neonatal care admission.

Statistical analysis

The data analysed by using Statistical Package for Social Sciences (SPSS) version. The data were represented as mean, standard deviation and ranges. Categorical data represented by frequencies and percentages. Independent t-test was used to compare the continuous variables accordingly. Receiver operating characteristic (ROC) curve analysis

was used for deterring the cut off value of serum calponin 1 for risk of short onset preterm birth. A level of P – value was less than 0.05 considered significant

Result

The number of patients in this study was 88. all of them were admitted to obstetrical department of the al-yarmouk hospital confirmed of threatened preterm labor. The distribution of study patients is shown in tables (1). Show patient's age from 17- 38 years (mean 25.25 ± 5.99), And show the highest percent of study patients aged was 20 - 29 years (50%) .Regarding BMI level the highest percent was overweighed (52.3%).About gestational age, we noticed that the highest percent of study patients were > 32 week (64.8%).About parity, we noticed that the highest percent of study patients were multipara (50%).

Regarding mode of birth 75% of study patients were delivered by NVD. The time of delivery in the study patients, about three quarters (73.9%) of the study patients were

delivered within one week after presentation. Regarding NICU admission most of newborns didn't admitted to the neonatal intensive unite.

Table 1: Distribution of study patients by descriptive data, outcome

Variable	Category	No.(88)	Percentage (%)	P.value
Maternal age	<20 20-29 >30	18 44 26	20.5% 50% 29.5%	0.254 0.008 0.121
`BMI	Normal Overweight obese		27.3% 52.3% 20.4%	0.007 0.075 0.107
Gestational age	<32 >32	31 57	35.2% 64.8%	 0.001
parity	Nulliparous Para 1 Multipara	23 21 44	26.1% 23.9% 50%	
Mode of birth	Cs NVD	32 66	25% 75%	
Birth time	< 1 wk > 1wk	65 23	73.9% 26.1%	0.017
NICU Admission	Yes No	24 64	27.3% 72.7%	0.464

The comparison in mean of level calponin 1 according to the time of delivery is shown in table (2). We noticed that mean of level calponin 1 was significantly higher in pregnant women who delivered within one week than those who delivered after one week (0.66 versus 0.53 ng/ml, P= 0.017).

Table 2: Comparison in mean of calponin 1 level according to the time of delivery

Calponin 1 (ng/ml)	Time of Delivery		P- Value
	< One Week Mean ± SD	≥ One Week Mean ± SD	
	0.66 ± 0.17	0.53 ± 0.04	**0.017**

Receiver operating characteristic (ROC) curve analysis was constructed for determination of cut off value of serum calponin 1 biomarker associated with highest sensitivity and specificity to predict of short onset preterm birth. As shown in table (3) and figure (1), the cut-off point of serum calponin 1 was 0.6 ng/ml, 65% sensitive, 100% specific, and 74.1% accurate as a predictor for short onset of preterm birth.

Table 3: Diagnostic accuracy of serum calponin 1 for risk of short-term preterm birth

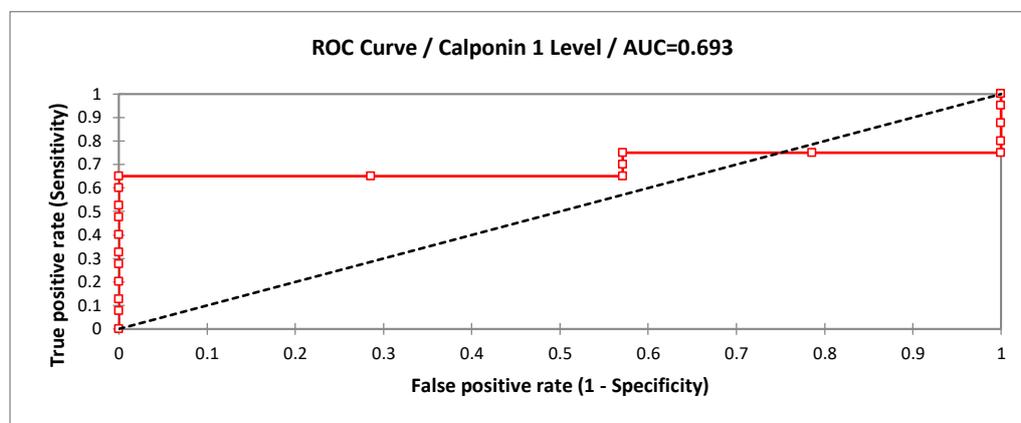| Calponin 1 (ng/ml)	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
	0.6	65%	100%	100%	50%	74.1%

Figure 1: ROC curve for calponin 1 as a predictor of short onset of preterm birth

DISCUSSION

Preterm labour (PTL) remains a major cause of perinatal mortality and long term handicap in surviving infants. the process of uterine contractions leading to a real labor may result in myometrium destruction that may cause increased maternal serum calponin 1 levels which calponin 1 more abundant in smooth muscle of uterus(10).

In the current study, mean and standard deviation (SD) of age was 25.25 ± 5.99 years, ranging from 17

to 38 years and the high percent of study patients aged between 20-29 years (50%), The high percent of study patients was overweight (51.9%),high rate in gestational age >32week (62.5%), also noticed that the high percent of study patients were multipara (50%),Regarding mode of birth 77.3% patient were delivered by NVD and most of newborns didn't admitted to neonatal intensive care unit 72.7%

In comparison to other studies, different results observed in Wing et al study in 2017,as the mean and SD of age was 28.1 ± 5.8 years, ranging from 17–44 years, in regard to gestational age, mean and SD was 29.7 ± 3.0 weeks, Many had a history of a previous term delivery [59.5%]) (11). Van Holsbeke et al study in 2016 found that Average maternal age of women with PTL participated in the study was 29 years and average gestational age at presentation was 29.1 weeks (12).

the average maternal age at testing in Ravi et al study in 2018 was 28.5 years with the average of gestational age at testing was 30.3 weeks (13).

In the present study, the level of calponin 1 significantly high in study patients who delivered within one week than those who delivered after one week (0.66 versus 0.53 ng/ml). Receiver operating characteristic (ROC) curve analysis, found that cut-off point of serum calponin 1 was 0.6 ng/ml, so serum calponin 1 > 0.6 ng/ml is predictive for short onset preterm birth as a large significant area under the curve (AUC= 69.3%). Serum calponin 1 concentration was 65% sensitive, 100% specific, and 74.1% accurate. Furthermore, among patients aged 20 – 29 years, and those who presented at GA > 32 weeks, the level of calponin 1 was significant high in those who delivered within one week than those after (P < 0.05). In comparison to other studies, Cetin and colleagues found a similar result in their study in 2018, as noticed that the levels of serum calponin 1 in maternal blood were riesed in study patients sufferd from PTL who delivered through one week, compared with study patients delivered after one week (P<0.05), while a different results observed in

that the cut-off value of calponin 1 in study patients who delivered through one week was calculated as 2.00 ng/mL (area under curve [AUC] 0.658, confidence interval [CI] 0.53–0.79) with 61.1% sensitivity and 62.2% specificity (14). Another agreement observed in Taema et al study in 2018, in which researchers found that mean and standard deviation (SD) of calponin 1 was significantly high in patients delivered through 1 week from admission (Group-A) and those delivered beyond 1 week from admission (Group-B) (P<0.05), also found that time interval thruogh admission and delivery and level of calponin-1 at admissions were statistically significant positive (0.387, p<0.001). On other hand, cut-off value of serum calponin 1 for prediction of PTL was 1.062 ng/mL (AUC) 0.798, confidence interval 0.726–0.870) with 71.10% sensitivity and 74.8% specificity (15) The prediction of PTL in modern obstetric studies is still a challenging subject. Several studies are attempted in the literatures to predict the

threatened preterm birth. However, these resulted in limited success (16) .

Conclusion

Serum calponin 1 may play an important role at pregnancy as non-invasive predictor for short onset preterm labour in cases diagnosed as threatened preterm labour

Recommendation

Needed larger sample size and longer duration to confirm the standard diagnostic level of calponin 1 biomarker for diagnosis of short onset preterm labour, perform antenatal checkup and testing by other modalities, and take in consideration researches on the genetics or environmental factors (smoking) and their role in the development of preterm labour. Acknowledgment:

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