Research Report

The Rise of Inhibin A Serum Level in Preterm Labor

Kadar Serum Inhibin A Meningkat pada Persalinan Preterm

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Abstract

Objective: The purpose of this study was to measure inhibin A serum level in women with preterm delivery, thus determining any correlation between inhibin A serum and gestational age in preterm delivery.

Method: The design of our study was cross sectional with 36 subjects who came to Dr. Hasan Sadikin Hospital, Bandung and six satellite hospitals in July-August 2011 and met inclusion-exclusion criteria. Inhibin A serum level was measured with ELISA. Inhibin A serum level in preterm labor and was compared using independent t test, and correlation between inhibin A serum level and gestational age in patients with preterm labor was calculated using Pearson correlation test.

Result: Characteristics test in both groups showed that both are homogeneous and comparable. The mean inhibin A serum level in preterm labor was higher (845.733 pg/ml) compared with preterm gestation (568.203 pg/ml) (p = 0.025). There was a significant correlation between inhibin A serum level and gestational age in preterm labor (p = 0.023) with a correlation coefficient of 0.38, indicating a moderate positive relationship.

Conclusion: Inhibin A serum level in preterm labor was higher than preterm pregnancy. In preterm labor, inhibin A serum level increases with gestational age.

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Keywords: preterm delivery, inhibin A serum level

Abstrak

***Tujuan**: Penelitian ini bertujuan untuk mengukur kadar serum inhibin A ibu pada persalinan kurang bulan kemudian mencari hubungan antara kadar serum inhibin A dengan usia kehamilan pada penderita persalinan kurang bulan.*

***Metode**: Rancangan penelitian ini adalah potong silang (cross sectional) terhadap 36 subjek penelitian yang memenuhi kriteria inklusi dan eksklusi yang datang ke RS Dr. Hasan Sadikin Bandung dan enam rumah sakit jejaring periode Juli - Agustus 2011. Kadar serum inhibin A diperiksa dengan teknik ELISA. Perbandingan rerata kadar serum inhibin A antara persalinan dan kehamilan kurang bulan menggunakan uji independen t, dan korelasi antara kadar serum inhibin A dengan usia kehamilan pada penderita persalinan kurang bulan dengan uji korelasi Pearson.*

***Hasil**: Uji karakteristik pada kedua kelompok penelitian menunjukkan kedua kelompok homogen dan dapat diperbandingkan. Rerata kadar serum inhibin A pada persalinan kurang bulan lebih tinggi (845,733 pg/ml) dibandingkan dengan kehamilan kurang bulan (568,203 pg/ml) (p=0,025). Korelasi positif antara usia kehamilan dan kadar serum inhibin A pada persalinan kurang bulan secara bermakna dengan nilai p=0,023 dengan koefisien korelasi 0,38 yang menunjukkan kekuatan korelasi sedang.*

***Kesimpulan**: Rerata kadar serum inhibin A pada persalinan kurang bulan lebih tinggi dibandingkan kehamilan kurang bulan. Kadar serum inhibin A akan meningkat seiring bertambahnya usia kehamilan pada persalinan kurang bulan.*

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***Kata kunci**: persalinan kurang bulan, kadar serum inhibin A*

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INTRODUCTION

Preterm delivery is the main cause of perinatal morbidity and mortality. The cause of preterm delivery is multifactorial. The incidence of preterm labor is ± 7 - 8% of all deliveries and contributes to ± 85% in perinatal deaths.[1]

In New York, USA, 10% incidence of preterm labor is found among the poor, consisting of spontaneous preterm labor (40%), preterm labor with premature rupture of the membrane (40%), and early gestation termination for obstetrics and medical indications (20%).[1] The incidence of prematurity in Indonesia ranges from 10 - 20%, whereas the incidence of prematurity in Dr. Hasan Sadikin Hospital (RSHS) Bandung from January 1998 to December 2000 was 8.2% of all deliveries, the perinatal mortality rate was 53.6%.[2-3,7]

The mechanism of preterm labor is still being debated. Lockwood et al, stated that there were four mechanisms which might lead to preterm labor; Activation of the hypothalamic-pituitary-adrenal axis (HPA) of the fetus and the mother, systemic inflammation or inflammation on decidua and chorioamnion, decidual hemorrhage, pathologic uterine distension such as multiple pregnancy, polyhydramnios, and uterine abnormalities.[4,6,8]

Some research on biomarkers are able to provide information about the pathophysiological mechanisms, which lead to premature delivery, and they are beneficial as detection tools to identify women at high risk for giving premature births.[5] Current researches target a variety of cytokines and extracellular matrix of fetal membranes, cytotrophoblasts, decidua or cervix.[9] Studies of groups of related inhibin proteins is still small levels of inhibin in parturient is very little.

Group of proteins related to inhibin was found while doing research on hypophysiotropic factors that regulate the release of follicle stimulating hormone

(FSH) by the pituitary. Some studies indicated that the localization, the role of biological, physiological and possible involvement of inhibin is more extensive than had been previously thought.[10-11]

During pregnancy, activin and inhibin played a role in embryo-fetal development, and are produced by the placenta, decidua, and fetal membranes, with the placenta as the major producer, maternal serum of activin and inhibin A increases with increasing gestational age.[12] Previous studies suggested a role of activin and inhibin A in the delivery process. Until now, it is unknown for certain whether activin and inhibin levels in maternal serum are influenced by birth or not. Several studies have shown elevated levels of inhibin A in patients of labor at term and preterm.[13,19]

Until now only Small amount of research that have been conducted to find out the relationship between inhibin A and preterm labor. Therefore, further researches are needed to determine whether there are differences in concentrations of inhibin A during pregnancy and preterm labor.

METHOD

Our study design was cross sectional study of thirty-six patients who have met the inclusion- and exclusion-criteria that came to our outpatient clinic at Dr. Hasan Sadikin Hospital Bandung and six satellite hospitals between the periods of July to August 2011. We used independent test 1 to compare the mean serum levels of inhinbin A between labor and preterm pregnancies.

RESULTS

Serum levels examination of inhibin A in 28 - 36 week of pregnant women and parturients had been perfomed in cross-sectional study of 36 patients who have met the inclusion- and exclusion-criteria.

Table 1 showed that there is no difference in patients characteristics based on age, parity, gestational age between 28 - 36 weeks of pregnancy and delivery with p value = 0.426, p = 0.373, p = 0.734 respectively. Therefore, both groups are comparable.

Table 1. Characteristics of the subjects.

Variable	Group						p Value*)
	Preterm delivery (n=18)		Preterm pregnancy (n=18)		Total subjects (n=36)		
	n	%	n	%	n	%	
Age (year)							0.426
< 20	0	0.0	1	5.6	1	2.8	
20 - 25	6	33.3	8	44.4	14	38.9	
26 - 30	5	27.8	4	22.2	9	25.0	
31 - 35	3	16.7	4	22.2	7	19.4	
≥ 35	4	22.2	1	5.6	5	13.9	
Parity							0.373
0	5	27.8	9	50.0	14	38.9	
1 - 3	11	61.1	8	44.4	19	52.8	
≥ 4	2	11.1	1	5.6	3	8.3	
Pregnancy Age (Weeks)							0.734
28 - 30	6	33.3	8	44.4	14	38.9	
31 - 33	7	38.9	5	27.8	12	33.3	
34 - 36	5	27.8	5	27.8	10	27.8	

*) *Chi Square test*

Table 2. Comparison of serum levels of inhibin A between preterm deliveries and preterm pregnancies.

Variable	Group			p Value*)
	Preterm delivery (n=18)	Preterm pregnancy (n=18)	Total subjects (n=36)	
Inhibin A Serum Level				0.025
Mean (± SD)	845.733 (449.922)	568.203 (199.754)	706.96 (370.823)	
Median	815.360	496.940	686.85	
Range	139.500 - 1596.560	272.050 - 933.850	139.500 - 1596.560	

*) *Independent T test*

Table 2 showed that there are significant different levels of inhbin A serum between 28 - 36 weeks of pregnancy and delivery with p value of $p \leq 0.001$. Comparison of inhibin A serum levels between preterm labor and preterm gestation in pregnant women with gestational age of 28 - 36 weeks are explained by Figure 1 below.

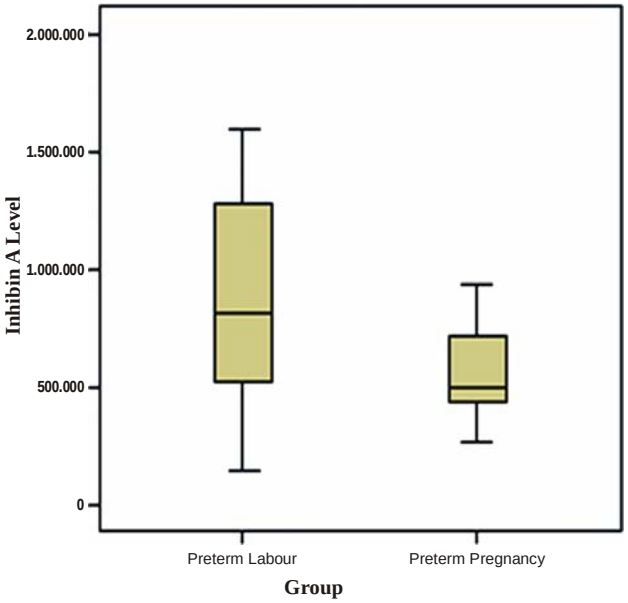

Figure 1. Comparison of inhibin A serum levels between preterm labor and preterm gestation in pregnant women with gestational age 28 - 36 weeks.

According to ROC curve (receiver operating characteristics), the cut off point serum level of inhibin A in preterm delivery is > 698.25 pg/ml.

Table 3 showed that the results of statistical test using Chi Square test at 95% degree of confidence indicated delete a significant relationship between inhibin A serum levels based on ROC curve (receiver operating characteristics) with the incidence of preterm labor with a value of p = 0.019. Validity test of the serum levels of inhibin A serum obtained on the incidence of preterm labor has a sensitivity of 66.7%, specificity 72.2%, 70.6% of positive expected value, expected value of negative 68.4% and an accuracy of 69.4%, the cut off point of > 698.25.

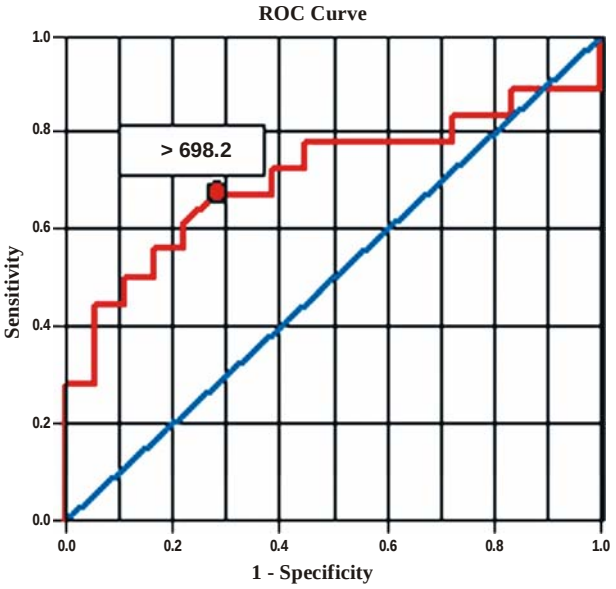

Figure 2. Cut off point on the serum levels of inhibin A in preterm delivery and pregnancy according to ROC curve (receiver operating characteristics).

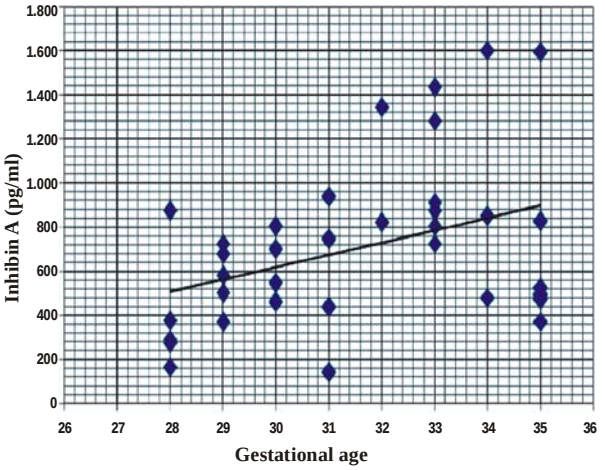

Figure 3. The correlation between gestational age and serum levels of inhibin A in preterm labor.

Table 4. Correlation between pregnancy age and inhibin A serum level in preterm deliveries.

	Correlation coefficient (r_s)	p value
Correlation between pregnancy age and inhibin A serum level	0.38	0.023

*) *Pearson Correlation test*

Table 3. Relationship of inhibin A serum based on ROC curve (Receiver Operating Characteristics) with preterm deliveries incidence.

Variable	Group						p Value*)
	Preterm delivery (n=18)		Preterm pregnancy (n=18)		Total subjects (n=18)		
	n	%	n	%	n	%	
Inhibin A Serum Level							0.019
> 698.25	12	66.7	5	27.8	17	47.2	
≤ 698.25	6	33.3	13	72.2	19	52.8	

*) *Chi Square Test*

Based on Table 4, the results of statistical test using Pearson's correlation test at 95% degree of confidence indicated that there is a positive correlation between gestational age and inhibin A serum levels in preterm labor delete with p-value = 0.023 with a correlation coefficient of 0.38 which indicates medium strength of relationship.

The correlation between gestational age and serum levels of inhibin A in preterm labor can be explained in Figure 3 below.

DISCUSSION

Characteristics of Research Subjects

Mean age of patients with preterm labor in this study was 26 years old and 19 - 39 year age range. The results of this study were similar to studies that have been done before. A research conducted by Hyagriv stated that the average of preterm labor is at 30.8 years old with the age ranged between 18 - 44 years old. Romero et al.[15] stated that the mean age of patients with preterm labor was 30.3 years. Choolani and Anandakumar[16] stated that the mean age in patients with preterm labor is 31 years with age range of 17 - 46 years.

The most parity of preterm labor patients in this study was 1 - 3 (52.8%), and the result is consistent with the Creasy[17] which stated that preterm labor is more common in multiparous.

The risk of preterm labor is higher in women under the age of 18 - 20 years and women over 35 years. This opinion was expressed by Bakketeig. Anna suggested that the risk of preterm labor in multiparous is higher than maternal age factor.[18]

In our study, the spread of confounding factors in both study groups were homogeneous, thus the threat of bias that can occur due to factors of age, parity, and gestational age can be removed. This indicated that both groups of this study are worthy to be compared.

Comparison between Serum Levels of Inhibin A in Premature Delivery and Pregnancy

According to research conducted by Petraglia et al, it was found that elevated levels of inhibin A serum in early pregnancy, is decreasing after 12 weeks of gestation and remain low until 24 weeks of gestation, after which it increases slowly and increases sharply in the third trimester.[10,12]

The elevated levels of inhibin and activin in maternal serum which influenced by delivery are unknown for certain. There are studies that showed elevated levels of inhibin A in labor at term or preterm. However, the result of another study found out that there was no link between labor and increased concentration of Activin A in the serum. This is similar to researches that found an increase and decrease in inhibin A serum both in patients who are in labor or not in labor.[12,19]

According Pleyvak and Lambert, serum levels of inhibin A in women with preterm labor is higher compared to preterm pregnancies when examination of serum levels of inhibin A at 23 - 34 weeks of gestation. Pleyvak et al., showed that the average serum levels of inhibin A in preterm labor was 442.70 with a standard deviation of 366.72, while the average serum levels of inhibin A in preterm pregnancies was 352.00 with a standard deviation of 270.64.[20]

In this study, Table 2 showed that the mean inhibin A serum levels in preterm labor is 845.733 with a standard deviation of 449.922 while the average serum levels of inhibin A in preterm pregnancies is 568.203 with a standard deviation of 199.754. There are significant differences in inhibin A serum levels between preterm labor and preterm pregnancy delete with p-value = 0.025. Inhibin A levels increased in patients with preterm labor, which lead to suspicion that inhibin A serum play a role in the initiation of preterm labor.

Correlation between Inhibin A serum with Gestational Age in Preterm Delivery

During pregnancy the concentration of inhibin A increases with gestational age. Several studies have shown that there is a rise in concentration of inhibin A in an increased release of prostaglandin E2 and oxytocin. The release of proinflammatory mediators, which is followed by elevated levels of inhibin A.[6,8]

Research conducted by Pleyvak et al, found that a correlation with inhibin A serum was more significant in deliveries at gestational age > 31 weeks compared to < 31 weeks.[20]

This study showed that the results of statistical tests using Pearson Correlation test at 95% degree of confidence which lead to indication that there is a positive correlation between gestational age and inhibin A serum levels in preterm labor at Dr. Hasan Sadikin Bandung hospital and hospital networks. And those results were significant with the p value = 0.023 with a correlation coefficient of 0.38 which indicates a medium strength of correlation.

CONCLUSION

The mean inhibin A serum levels in preterm labor is higher than preterm pregnancies. Inhibin A serum levels will increase accordingly to gestational age in preterm labor.

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