IGF-1 Levels Related to Incidence of Macrosomia

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ABSTRACT

*Macrosomia is used to describe a large baby with birthweight 4000 grams or more. Macrosomia incidence has increased over recent decades and is associated with increased maternal and fetal morbidity and mortality. IGF-1 is an important regulator of fetal growth. The objective of this study was to find the relationship between IGF-1 levels with incidence of macrosomia. Study design was correlative with cross-sectional studies. Population were women who delivered macrosomias and normal babies in Prof. Dr. R.D. Kandou Hospital Manado and RW Mongisidi Hospital Manado. Sample of study is population who meet inclusion and exclusion criterias. This study involved 65 women who meet inclusion and exclusion criteria. A total of 48 women gave birth to normal weight babies and 17 women gave birth to macrosomia. Sample characteristics based on general age: 20-34 years (82% macrosomia, 64% normal birth weight), highest parity was multiparous (71%), most frequent maternal education level on macrosomia was elementary school (28%). The most frequent mode of delivery in macrosomia was cesarean section (59%). Most frequent BMI before pregnancy was obesity (53%) in macrosomia and 63% of normal BMI in normal weight. After logistic regression analysis, there was a significant correlation between IGF-1 with the incidence of macrosomia (p = 0048 <0.05), with cut off point 195 ng/mL (sensitivity 88.2%, specificity 97.9%). In conclusion, IGF-1 level was significantly associated with incidence of macrosomia. Analysis result of the relationship between IGF-1 levels with the incidence of macrosomia obtained cut-off point levels of IGF-1 at 195 ng/mL with a sensitivity of 88.2% and specificity 97.9%.(**MOG 2013;21:121-124**)*

Keywords: *IGF-1, macrosomia*

ABSTRAK

*Istilah makrosomia menggambarkan bayi besar dengan berat 4000 gram atau lebih. Insidens makrosomia meningkat dalam beberapa decade terakhir dan terkait peningkatan morbiditas serta mortalitas ibu dan bayi. IGF-1 adalah regulator pertumbuhan fetus. Tujuan dari penelitian ini adalah untuk menemukan hubungan antara kadar IGF-1 dengan kejadian makrosomia. Ini merupakan penelitian korelatif dengan desain cross-sectional. Populasi adalah wanita yang melahirkan makrosomia dan bayi normal di RS Prof Dr RD Kandou Manado dan RS RW Mongisidi Manado. Sampel penelitian adalah populasi yang memenuhi criteria inklusi dan eksklusi. Penelitian ini melibatkan 65 wanita yang memenuhi criteria inklusi dan eksklusi. Sebanyak 48 wanita melahirkan bayi dengan berat badan normal dan 17 wanita melahirkan makrosomia. Karakteristik sampel berdasarkan usia umum: 20-34 tahun (82% makrosomia, berat lahir 64% normal), paritas tertinggi adalah multipara (71%), tingkat pendidikan ibu yang paling sering pada makrosomia adalah sekolah dasar (28%). Cara melahirkan tersering pada makrosomia adalah operasi caesar (59%). BMI paling sering sebelum hamil adalah obesitas (53%) pada makrosomia dan 63% dari IMT normal dalam berat badan normal. Setelah analisis regresi logistik, ada hubungan yang signifikan antara IGF-1 dengan kejadian makrosomia (p = 0048 < 0,05), dengan cut off point 195 ng/mL (sensitivitas 88,2%, spesifisitas 97,9%). Kesimpulannya, kadar IGF-1 terkait secara bermakna dengan kejadian makrosomia. Hasil analisis hubungan antara IGF-1 tingkat dengan kejadian makrosomia diperoleh tingkat cut-off point IGF-1 pada 195 ng/mL dengan sensitivitas 88,2% dan spesifisitas 97,9%.(**MOG 2013;21:121-124**)*

Kata kunci: *IGF-1, makrosomia*

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INTRODUCTION

Macrosomia is a terminology used to describe a large baby, which is a baby with birth weight 4000 grams or more. During the last two to three decades, approximately 15-25% proportion of women with macrosomiawere found in various parts of the world. At Prof. Dr. R.D. Kandou Hospital Manado, incidence of macrosomiawas recorded at 3.73% in 2010.[1,2,3]

The incidence of macrosomia has increased over recent decades and is associated with increased morbidity and mortality of both mother and fetus, such as intrauterine death, labor induction, labor length, asphyxia, infant and

maternal injury, increased operative delivery, postpartum hemorrhage, neonatal hypoglycemia, hyperbilirubinemia and increased use of space-intensive. Long-term impact of macrosomia is the sequel to the neurological, diabetes and cancer. Clinical experience in macrosomia delivery is associated with obstetric and neonatal complications. Therefore, macrosomia becomes a major problem.[4,5,6]

Fetal growth is influenced by several factors, such as genetic factors, hormonal, and environmental. One factor that has been studied frequently is growth hormones that can affect the baby's weight. Insulin-like Growth Factor 1 (IGF-1) is gene product protein that specifically regulate the development of trophoblast cells that form the placenta. IGF-1 is an important regulator of growth of the fetus. Maternal serum IGF-1 level increased progressively throughout pregnancy and is thought to trigger the growth of the placenta which then triggers the fetal growth.[7,8]

IGF-1 present in all cell types in the placenta from gestational age 6 weeks and involved in all stages of placental development and function. IGF-1 increase fibroblast proliferation of placenta. IGF-1 is also known to rescue placental trophoblast and fibroblasts from apoptosis. IGF-1 regulate cytotrophoblast differentiation into syncytiotrophoblast and become extravillous cells. Cytotrofotrofoblas ability to differentiate into syncytiotrophoblast or extravillous trophoblast is very important for the successful development of the placenta.[9,10,11]

IGF-1 is influenced by GH where GH changes can also affect levels of IGF-1. IGF-1 are considered equals to insulin because insulin can bind to receptors, triggering actions such as insulin like reaction and improve insulin sensitivity. Insulin can alter the biologic activity of IGF-1 levels by altering hepatic GH receptor and hepatic IGFBP production. Likewise, most of IGF bind to IGFBP than insulin receptors so insulin sensitivity change indirectly. IGF-1 is very similar to insulin and can lower serum glucose levels, helping intracellular glucose transport and inhibit lipolysis and protein degradation. IGF-1 also increases protein synthesis and positive nitrogen balance, just like insulin.[12,13,14]

MATERIALS AND METHODS

The design of this study is correlative with the approach of cross-sectional studies. The population covered by the study were women who gave birth to macrosomia and normal in delivery room of Prof. Dr. R.D. RS Kandou Hospital Manado and RSU RW Mongisidi Hospital Manado. The sample is a member of the study population who meet inclusion and exclusion criteria. The inclusion criteria were single fetus, definite first day of last menstrual periodand agreement to follow the study (sign the consent form). The exclusion criteria were diabetes mellitus, hypertension in pregnancy, ftus with major congenital abnormalities, obstetric complications and postmaturity pregnancy. After being given an explanation about the research, the subject fills out consent forms that have been available. The research subject is taken as much as 5 cc of blood drawn in the cubital vein using a vacuet tube and then submitted to a laboratory Prodia. Examination of serum IGF-1 levels in this study using immunochemi-luminenscence and instrument used was Immulite 1000.

RESULTS AND DISCUSSION

This study was conducted from January 2010 until March 2011, and by examining levels of IGF-1 in serum. Of 65 subjects, there are 48 women who delivered babies with normal weight and 17 women gave birth to macrosomia. The results was made in the form of table below

Table 1. Study Subjects Distributions

	GROUP	
	Normal Birth Weight	Macro-somia
Age		
≤ 19	8(17)	1(6)
20-34	31(64)	14(82)
≥ 35	9(19)	2(12)
Education		
Elementary	9(19)	5(28)
Junior high	11(23)	4(24)
Senior high	26(54)	4(24)
University	2(4)	4(24)
Parity		
Nulliparous	24(50)	5(29)
Multiparous	24 (50)	12(71)
Mode of Delivery		
Spontaneous	41(85)	7(41)
Vacuum Extraction	7(15)	0
Cesarean Section	0	10(59)
Pre-pregnancy BMI		
< 18.6	5(10)	0
18.6 – 24.9	30(63)	8(47)
> 24.9	13(27)	9(53)

From table 1, the largest age group was 20-34 years (82% macrosomia, 64% normal birth weight), the most frequent parity in macrosomia is multiparous (71%), most frequent level of education on macrosomia is elementary (28%) and high school (54%) in normal birth weight. The most frequent mode of delivery in macrosomia was cesarean section (59%) and spontaneous vaginal delivery (85%) in the normal birth weight. The biggest BMI before pregnancy is obesity (53%) in macrosomia and normal BMI (63%) in the normal birth weight.

Table 2. The relationship of IGF-1 levels with the incidence of macrosomia

Model	Coeficient	p	Result
IGF-1 level	0.225	0.048	significant
Constants	-43,859	0.048	

By using logistic analysis formula, p = 0048 (<0.05) was obtained, a significant relationship between IGF-1 levels with the incidence of macrosomia. The results obtained by logistic regression analysis with the cut off point of IGF-1 levels of 195 ng/mL. With this value, sensitivity of 88.2% and specificity 97.9% obtained.

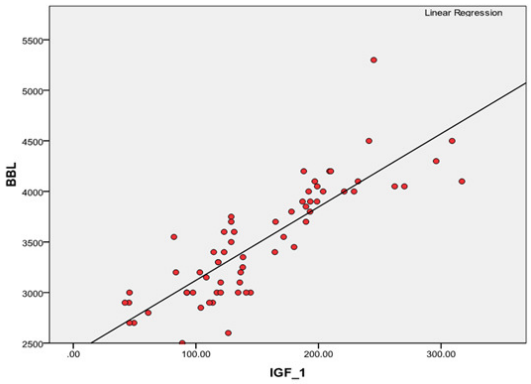

Figure 1. Relationship of IGF-1 levels with birth weight

Results of independent t test showed no significant difference in the average IGF-1 between male fetus and female fetus (p = 0521> 0.05). There is no significant difference found between IGF-1 in primiparous and multiparous (p = 0.53> 0.05).

From table 1, most research subjects is from age group 20-34 years of 14 samples (82%) for mothers with macrosomia and 31 samples (64%) in women with normal pregnancies. This is the same as those studied by Boyne (2003) where the average age of mothers with macrosomia was 26.4 ± 5.1. Levels of IGF-1 in human serum varied according to age and gender. Levels of IGF-1 tends to be low at birth and then increased with age, and reached the peak at the age of puberty and then decreases with increasing age.4,13 From table 1 most research subjects based on the parity is the multiparous group of 12 samples (71%) for mothers with macrosomia. Jaksic (2001) also obtain a majority of mothers with macrosomia were multiparous, as many as 73.33%. This is consistent with the theory which is said to increase the incidence of macrosomia in multiparity.[1,2,8]

Figure 1 shows relationship between IGF-1 levels with birth weight, where r = 0846 or meaningful relationships. By using probability equation models, obtained a 195 ng/mL cut off point.

Table 3. Calculation of sensitivity and specificity cut-off point based on levels of IGF-1 195 ng/mL of macrosomia

IGF-1	Macrosomia		Total
	+	-	
≥ 195	15 (88.2 %)	1	16
< 195	2	47 (97.9 %)	49
Total	17	48	65

Table 4. The correlation between IGF-1 levels and sample distribution

Distribution	Mean IGF-1 Level	p
Female infant	146.93	0.521
Male infant	157.62	
Nulliparous	147.83	0.53
Multiparous	157.78	

From table 1, mothers with normal birth weight babies have a normal BMI before pregnancy which is 30 samples (63%). While in the mother with macrosomia, the most frequent BMI before pregnancy is overweight, as many as 9 samples (53%). At Boyne research revealed macrosomia in patients average pre-pregnancy BMI was 24.6 ± 4.5 kg/m2. This is consistent with the theory which is said that maternal obesity before pregnancy is a predisposing factor of macrosomia occurrence.[1,2,13]

The equation in this study based on logistic regression analysis expressed significant correlation between IGF-1 levels with the incidence of macrosomia (p <0.05). This equation states the higher levels of IGF-1 the greater the chances of macrosomia. From figure 1 can be seen that the relationship expressed higher levels of

IGF-1, the more likely the occurrence of macrosomia. The results obtained by logistic regression analysis with the cut off point of IGF-1 levels of 195 ng/mL. With this value obtained sensitivity of 88.2% and specificity 97.9%.

Boyne have average concentrations of IGF-1 in macrosomia of 265 ng/mL. Meanwhile, the research results of Chiesa (2008) found average levels of maternal IGF-1 in macrosomia is 164 ng/mL. There is a difference between the results of the Boyne, Chiesa, and with a cut off point obtained from this research. This is presumably because IGF-1 levels are influenced by many uncontrolled factors, both in Boyne research and in this research.[11,13]Results of independent t test showed no significant difference in the average IGF-1 between male fetus and female fetus (p = 0521> 0.05) although the average IGF-1 male fetus (157.6 ng/mL) is higher than average IGF-1 female fetus (146.9 ng/mL).Litten (2004) also found that of 987 single fetus has a concentration of IGF-1 and IGFBP-3 in umbilical cord plasma was higher in female fetuses than male fetuses. Although one of the predisposing factors of macrosomia were male fetuses, but this study can not explain the mechanism.[5,9]

The average of IGF-1 in multiparity (157.8 ng/mL) is higher than the average IGF-1 in primiparity (147.8 ng/mL). Multiparity can increase levels of IGF-1 due to increased age, estrogen receptor and insulin resistance. But in this study, no significant difference found between IGF-1 in primiparous and multiparous (p = 0.53> 0.05).[2,3]

CONCLUSION

In research that has been conducted from the period January 2010 to March 2011 obtained that IGF-1 levels was significantly associated with the occurrence of macrosomia. Result analysis of the relationship between IGF-1 levels with the incidence of macrosomia obtained cut-off point levels of IGF-1 at 195 ng/mL with a sensitivity of 88.2% and specificity 97.9%. Examination levels of IGF-1 can be performed in patients who were estimated as macrosomia to support other inspection methods such as clinical examination such as palpation, and ultrasound, which in turn give an effective and efficient management. We suggest that further research is needed with a larger and homogeneous sample so as to improve the accuracy of research.

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