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Correlation of vitamin B12 level with insulin resistance in infant and placenta outcomes☆

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KEYWORDS
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Abstract
Objective: This study aims to assess the correlation of vitamin B12 level with insulin resistance toward the outcome of the baby and the placenta.
Method: This study used a *prospective cohort* study design. The total sampling was 87 people. The samples were pregnant women the second trimester and the third trimester. Data were analyzed using the Chi-Square test and the Spearman test. Pregnant women who were respondents were monitored until birth; then, the examination of the baby's weight and placental weight after the baby was born using a scale was carried out.
Results: The result of this study shows that there is no significant correlation between levels of vitamin B12 and insulin resistance ($\rho = 0.864$, $p > 0.05$), there is no significant correlation between vitamin B12 and infant weight ($p = 0.107$, $p > 0.05$), there is no significant correlation between vitamin B12 and placental weight ($\rho = 0.107$, $p > 0.05$). There is no significant correlation between insulin resistance and infant weight ($\rho = 0.845$, $p > 0.05$), and there is no significant correlation between insulin resistance and placental weight ($\rho = 0.845$, $p > 0.05$).
Conclusion: There is no correlation of vitamin B12 with insulin resistance toward the outcome of the baby and the placenta.

Introduction

The needs of a maternal woman during pregnancy for food elements, such as iron, vitamin C, folic acid, and protein are increasing. If these needs are not fulfilled, the mother will get anemia. A common cause of anemia is lack of nutrients – protein, iron, pyridoxine (vitamin B6), vitamin B12, vitamin C, folic acid, and vitamin E – that play a role in the formation of hemoglobin, either due to lack of consumption or

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due to absorption disorders. Vitamin B12 is needed to activate folic acid in the normal function of the metabolism of all cells, especially digestive cells, marrow bone, and nerve tissue. Folic acid plays a role in the metabolism of amino acids needed in the formation of red blood cells, white blood cells, and their maturation.[1]

Lack of vitamin B12 and folic acid during pregnancy is related to an increased risk of preterm birth, low birth weight, and disruption of fetal growth. Mothers who get adequate folic acid supplementation will increase body weight, decrease the incidence of mental retardation and maternal infections, in contrast to mothers with levels folic acid less than 240 μg/dl the risk of giving birth to an LBW and premature baby increases by more than 200%. In addition, folic acid with a significant requirement of 600 μg/day will affect brain growth by 70% compared to other nutrients. Sources of vitamin B12 can be obtained from meat, tuna, eggs, milk, cheese, and shellfish, while folic acid can be obtained from green vegetables, fruits, cereals, nuts.[2]

Several studies report that a woman who is deficient in vitamin B12 increases the occurrence of insulin resistance and Major depressive disorder (abbreviated as GDM). Vitamin B12 deficiency in a maternal woman is associated with increased adiposity, and ultimately, an increase of insulin resistance and Major depressive disorder (abbreviated as GDM) occurs. This study also states that vitamin B12 deficiency may be an important factor underlying the high risk of diabetes in South Asia, India.[3]

One of the changes that occur in a healthy woman's pregnancy is the resistance of insulin during uptake and glucose utilization. During early pregnancy, normal glucose tolerance increases slightly, and peripheral (muscle) sensitivity to insulin and normal hepatic basal glucose production due to increased maternal estrogen and progesterone hormones in early pregnancy increases pancreatic β cell hyperplasia, so this causes an increase of insulin release. It explains an increase of insulin in early pregnancy is a response to insulin resistance.[4]

During pregnancy, the body's insulin resistance increases three-fold compared to nonpregnancy. In pregnancy, decreased insulin sensitivity is characterized by post-receptor defects that reduce insulin's ability to mobilize SLC2A4 (GLUT 4) from the cell to the cell surface. This might be caused by an increase in hormone-related to pregnancy. Although pregnancy is associated with a rise in β cell mass and an increase of insulin levels, some women cannot increase their insulin production relative to an increase of insulin resistance, thus becoming hyperglycemic and suffering Gestational Diabetes Mellitus (abbreviated as DMG).[4]

Insulin resistance affects other metabolic that can cause overgrowth in the fetus. Besides, the anabolic effect of hyperinsulinemia that characterizes insulin resistance might also explain the increase in fetal growth. Several studies have reported that insulin resistance might be related to adverse pregnancy outcomes including an increase of insulin resistance and an increase of macrosomia risk.[5–7]

Based on this statement, this study aims to assess the correlation of Vitamin B12 and Insulin Resistance toward the outcome of infant and placenta.

Table 1 Characteristic of respondent.

Variable	Frequency (*n*)	Percentage (%)
Vitamin B12		
High	22	25.3
Low	65	74.7
HOMA IR		
Resistance	29	33.3
No resistance	58	66.7
Baby weight		
Normal	71	81.6
LBW	16	18.4
Placenta Weight		
Normal	71	81.6
Abnormal	16	18.4

Method

This research was conducted in the working area of Mother and Child hospital (abbreviated as RSIA) Sitti Khadijah 1 Makassar from March to May 2019. The population in this study were pregnant women in Khadijah Makassar Hospital. The study subject was total sampling, and the criteria of the sample in the study were second trimester and third-trimester pregnant women.

In this study, data from physical examination results and laboratory samples were recorded and collected. The physical examination carried out in the maternal and child health (abbreviated as MCH) room. Blood samples were taken by laboratory staff at RSIA Khadijah 1 Makassar then, blood samples were taken and examined at the laboratory of Hasanuddin University. Pregnant women who were respondents were monitored until birth; then, the examination of the baby's weight and placental weight after the baby was born using a scale was carried out.

Results

Table 1 shows that from 87 respondents (100%), respondents in Vitamin B12 category, high vitamin B12 levels are 22 respondents (25.3%). While respondents with low levels of vitamin B12 are 65 respondents (74.7%). Based on the characteristics of the HOMA IR, it shows that out of 87 respondents (100%), respondents who are resistant are 29 respondents (53.3%). Whereas non-resistance respondents are 58 respondents (66.7%). Based on the characteristics of Infant Weight shows that from 87 respondents (100%), respondents with normal weight category are 71 respondents (81.6%). While LBW respondents are 16 respondents (18.4%). Based on educational characteristics shows that from 87 respondents (100%), respondents with normal placental weight categories are 71 respondents (81.6%). While respondents with abnormal placental weight are 16 respondents (18.4%).

Table 2 shows that from 22 respondents who experience high vitamin B12 7 respondents (31.8%) experience insulin resistance, and 15 respondents (68.2%) do not experience insulin resistance. While 65 respondents who experienced

Table 2 Correlation of vitamin B12 with insulin resistance.

Vitamin B12	Insulin resistance				Total	ρ
	Resistance		Non-resistance			
	n	%	*n*	%		
Height	7	31.8	15	68.2	22	0.862*
Low	22	33.8	43	66.2	65	

*Chi-Square test.

Table 5 Correlation of vitamin B12 level with insulin resistance toward the infant and placenta outcome.

Variable	*r*	ρ
Insulin Resistance	0.019	0.864*
Infant weight	0.202	0.61*
Placenta weight	0.202	0.61*

*Spearman test.

low vitamin B12 22 respondents (33.8%) experience insulin resistance and 43 respondents (66.2%) do not experience insulin resistance. After doing statistical tests using the Chi-Square test, *p*-value = 0.862 means it is higher than ($p > 0.05$). It shows that there is no significant correlation of vitamin B12 with insulin resistance in the working area of RSIA Sitti Khadijah 1 Makassar.

Table 3 shows from 22 respondents who experienced high vitamin B12, 15 respondents (68.2%) experience normal infant weight and seven respondents (31.8%) experience LBW. As many as 65 respondents who experienced low vitamin B12, 56 respondents (86.2%) experience normal infant weight and nine respondents (13.8%) experience LBW. From 22 respondents who experienced high vitamin B12, 15 respondents (68.2%) experience normal placental weight, and seven respondents (31.8%) experience abnormal placental weight. And from 65 respondents who experienced low vitamin B12, 56 respondents (86.2%) have normal placental weight, and nine respondents (13.8%) have abnormal placental weight.

After doing a statistical test using *Chi-Square* test, *p*-value = 0.107 means greater than ($p > 0.05$). It shows that there is no significant correlation between Vitamin B12 and infant weight. And *p*-value = 0.107 means greater than ($p > 0.05$). It shows that there is no significant correlation between Vitamin B12 and placenta weight in pregnancy in the work area of RSIA Sitti Khadijah 1 Makassar.

Table 4 shows that from 29 respondents who experienced insulin resistance, 24 respondents (82.8%) experience normal infant weight, and five respondents (17.2%) experience LBW. From 58 respondents who are not insulin resistant, 47 respondents (81.0%) who experience normal infant weight and 11 respondents (19.0%) experience LBW. Of 29 respondents who experienced insulin resistance, 24 respondents (82.8%) experience normal placental weight and five respondents (17.2%) experience abnormal placental weight. And 58 respondents who are not insulin resistant, 47 respondents (81.0%) experience normal placental weight, and 11 respondents (19.0%) experience abnormal placental weight.

After doing a statistical test using the Chi-Square test, *p*-value = 0.845 means greater than ($p > 0.05$). It shows that there is no significant correlation of insulin resistance with infant weight. And *p*-value = 0.854 means greater than ($p > 0.05$). It shows that there is no significant correlation of insulin resistance with placental weight in the working area of the RSIA Sitti Khadijah 1 Makassar. Table 5, by using the Spearman test shows that none of the 87 study samples correlates with Vitamin B12.

Table 3 Correlation of vitamin B12 with infant weight and placenta weight.

	Infant weight				Total	ρ	Placenta weight				Total	ρ
	Normal		LBW				Normal		Abnormal			
	n	%	*n*	%			*n*	%	*n*	%		
Vitamin B12												
Height	15	68.2	7	31.8	22	0.107*	15	68.2	7	27.3	22	0.107*
Low	56	86.2	9	13.8	65		56	86.2	9	13.8	65	

* Chi-Square test.

Table 4 Correlation of insulin resistance with infant weight and placenta weight.

	Infant weight				Total	ρ	Placenta Weight				Total	ρ
	Normal		LBW				Normal		Abnormal			
	n	%	*n*	%			*n*	%	*n*	%		
Insulin resistance												
Resistance	24	82.8	5	17.2	29	0.845	24	82.8	5	17.2	29	0.845*
Non resistance	47	81.0	11	19.0	58		47	81.0	11	19.0	58	

*Chi-Square test.

Discussion

In this study, we have found that the average of pregnant women who experience vitamin B12 deficiency is 65%. We have found that there is no significant correlation between vitamin B12 and insulin resistance. It may be the existence of an additional mechanism, and other factors linking vitamin B12 to insulin resistance.

This study is in line with research that states that there is no significant correlation of vitamin B12 with Insulin Resistance. The high level of obesity observed may have overshadowed other factors that contribute to insulin resistance.[8]

Although in previous studies, it has been confirmed that vitamin B12 levels correlates with low birth weight and preterm labor but according to Ronnenberg et al.[9] the correlation is determined by adequate folate intake. Low folate at 28 weeks causes the risk of premature birth and low birth weight highly. Although vitamin B12 deficiency is not related to poor obstetric outcomes, a positive correlation is found between maternal vitamin B6 and infant birth weight.[9]

In this study, only a small proportion is overweight. Seeing from the weight status before pregnancy, the average body weight is normal. We argue that, in this study, there are no significant results between insulin resistance and maternal outcomes, which might be due to maternal body mass index before pregnancy and excessive pregnancy weight gain related to an infant weight. Mothers who give birth with excess birth weight may also be caused by factors due to a history of diabetes mellitus (abbreviated as DM) except insulin resistance itself. Our suspicion is reinforced with Sofian's opinion that states the danger of excess weight gain in pregnant women causes large babies and it can complicate labor. After that, it can be a symptom of diabetes mellitus in pregnant women. Besides, we also argue that maternal genetic factors may also specifically affect the growth of the baby.

In this study, most respondents experience low levels of vitamin B12. The decrease in low vitamin B12 levels is also thought to be related to slow vitamin B12 supplementation in pregnancy and non-compliance of respondents in taking supplements. The results of previous studies state that a low level of vitamin B12 has high insulin resistance and affects the weight of the baby and placenta. But the results of the review and analysis of this study, we do not find a significant correlation of vitamin B12 level with insulin resistance and its effect on the outcome of infant and placenta weight.

The incompatibility of this study with previous research might be due to factors from different races, and the criteria in the selection of research samples. The birth weight of a baby depends on the nutrition of the mother and the ability of the placenta to transport nutrients from the mother to her fetus. The placental weight and the size and shape of its surface reflect its ability to transfer nutrients. The mother's weight has a greater effect on the baby's birth weight than the mother's height. The weight of the mother before and during pregnancy greatly influences the outcome of the pregnancy. Women who are underweight before pregnancy tend to give birth faster (prematurely) and give birth to Low Birth Weight Babies (LBW). A mother's weight gain during pregnancy is directly related to her baby's weight, and the risk of giving birth to LBW increases with the lack of weight gain during pregnancy.[10]

The placental weight reflects placental development and function and correlates with maternal age, gestational age, an increase of weight gain during pregnancy, BMI, MUAC. The placenta plays an important role in normal fetal development, and the failure of the placenta to gain weight and function insufficiency can result in fetal disorders.[10]

Conclusion

From the results of research conducted by researchers, it can be concluded that; Vitamin B12 does not correlate with insulin resistance; Vitamin B12 does not correlate with infant and placental outcomes; Insulin resistance does not correlate with infant and placental outcomes. (4) The average level of vitamin B12 is low in normal pregnancy; Low levels of vitamin B12 are common in trimester II and III pregnant women. Better nutritional intake and compliance in taking vitamins need to be considered in order to avoid vitamin B12 deficiency and it is hoped for further and more in-depth research especially in the selection of research samples in different regions.

Conflict of interest

The authors declare no conflict of interest.

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