ISSN: 13412051
Volume 25, Issue 06, June, 2020

COMPETITION BETWEEN MATERNAL AND FETUS THROUGHT HEMOGLOBIN (HB) AND HEMATOCRIT (HCT) IN PARTU, PLACENTA, UMBLICAL CORD BLOOD AND PLACENTA WEIGHT

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ABSTRACT— The iron deficiency often manifests as a sharp decrease in hemoglobin and hematocrit concentrations during the third trimester. It means the amount of oxygen-limited. The competition will arise between mother and fetus. This study was to examine Hemoglobin (Hb) and hematocrit (Hct) levels in partu related to Hb and Hct levels in Placenta, Umbilical Cord, the weight of the Placenta. The study design used was cross-sectional, by measuring hemoglobin and hematocrit levels in partu, Placenta, and umbilical cord. The sample was 100 subjets. Results: The difference of Hb levels between Placenta and Umbilical Cord with Hb in Partu (mild anemia) was 1.6 g /dL (11.3%), 3.9 g /dL (39.8%). ANOVA test continued with LSD test between Hb levels in partu (mild anemia) with Placenta, and Umbilical Cord was significantly different (p =0.004 and p=0.000, CI=95%). The Hct Umbilical cord was 6.3 (14.2%) higher than Hct in partu.There was significant difference (p = 0.000, CI=95%). The difference of placenta weight between anemia (mean Hb = 9.8 g/dL, Hct=35.2%)) and normal (Hb =12.4 g/dL, Hct=39.2%) was 18.4 g (3.9%), 11.75 g (2.17%). This finding showed mild anemia in partu, but it was not anemia in Placenta and Umbilical Cord. In Mild Anemia of maternal, the fetus had been still prioritized to get more supply food and oxygen as showed Hb, Hct, Placenta weight were higher than in partu. However, this finding a prediction that severe anemia in partu will occur in the Placenta and the Umbilical Cord.

KEYWORDS: Anemia, a competition of maternal and fetus, Placenta, umbilical cord.

1. INTRODUCTION

Anemia occurs in many people, especially in adolescents and pregnant women. According to the World Health Organization in 2015, the global prevalence of Anemia in pregnant women (15-49 years) worldwide ranged from 33.5 to 42.6%, and Anemia is one of the indirect causes of maternal mortality. Household Health Survey (SKRT) data in Indonesia in 2012 stated that the prevalence of Anemia in pregnant women was 50.5%(Kementerian Kesehatan, 2015). Anemia is a condition wherein the level of Hemoglobin in the blood is low. Iron deficiency anemia is caused by a lack of iron in the blood. Iron is one of the ingredients for the formation of red blood cells. Not surprisingly, iron deficiency decreases the formation of red blood cells so that it causes Anemia. Pregnancy requires additional iron to increase the number of red blood cells for fetal and placental growth. The need for iron in pregnant women in each trimester is different. Especially in the second and third trimesters, pregnant women need large amounts of iron (Kementerian Kesehatan, 2015). The daily requirement for the First Trimester of pregnancy is relatively small, around 0.8 mg, but will increase drastically to 4 - 5 mg in trimester 2, and more than 6 mg in the third trimester (Bothwell, 2000). An increase in iron demand will result in a decrease in ferritin levels as an ingredient for the

formation of red blood cells. In pregnancy, there is an increase in blood volume that is different in each trimester. Starting in the first trimester of pregnancy increased by 20%, the second Trimester 40%, until the middle of the third trimester, there was an increase in blood volume to nearly 50%(Cunningham FG, 2010). With a relatively rapid increase in blood volume during the second or third trimester, iron deficiency often manifests as a sharp decrease in hemoglobin and hematocrit concentrations (Josipović et al., 2015). Also, placental factors account for 50-70% of cases of antepartum hemorrhage (Sumawan et al., 2013). Excessive blood loss accompanied by loss of iron hemoglobin and depletion of iron stores in pregnancy can be an important cause of iron deficiency anemia in subsequent pregnancies. This condition can increase the risk of death during childbirth, give birth to babies with low birth weight, the fetus and mother are susceptible to infection, miscarriage, and increase the risk of premature births (Health Profile, 2014). (Kementerian Kesehatan, 2015)

Iron intake during pregnancy must be considered because the volume of blood in pregnant women increases. In the third trimester, there is an increase in physiological iron requirements to 3.0-7.5 mg as a result of increased maternal red blood cell mass and increased placental and fetal growth (Bothwell, 2000). So, to be able to continue to meet the needs of mothers in supplying food and oxygen to the fetus through the Placenta, more iron intake is needed. It will be used by the fetus for its growth and development needs, including for brain development, as well as storing it in the liver as a reserve until the baby is six months old. Iron also helps in accelerating the process of wound healing, especially wounds that arise in the process of childbirth (Bothwell, 2000). One of the functions of the Placenta is to channel oxygen to the fetal circulation to support fetal metabolism. The use of oxygen increased significantly due to consumption for pregnant women and fetuses. When the amount of oxygen is limited due to low hemoglobin levels, competition arises between mother and fetus (Murray, 2012). The amount of oxygen is an important factor in the development of placental blood vessel boluses (Huang A et al., 2001). Pregnancy in a healthy condition increases bolus mass (Huppertz B, 2008). If oxygen is low due to low Hemoglobin, it will increase premature birth or low birth weight (Kumar et al., 2013). Anemia in pregnant women causes hypoxia which can lead to spontaneous early births (Allen, 2001) and based on research by Melisa Lelic (2014) (2014) (Lelic et al., 2014), the average delivery is one week earlier, and babies are born shorter, and babies weigh less. A full-term baby with a birth weight of 4000 grams contains 320 mg of iron, while a term baby contains less than 50 mg of iron (Parmono B, Sutaryo, Ugrasena IDG, Windiastuti E, n.d.). In anemic patients due to iron deficiency (smaller size of red blood cells), the value of Hct will be measured lower because microcytic cells accumulate in smaller volumes even though the number of red blood cells looks normal. The developing fetus takes all the iron it needs from the mother, regardless of how much iron is stored in the mother's blood. Hemoglobin levels that contain lots of iron in the mother during pregnancy will be widely used for fetal needs through the Placenta [10]. This situation indicates that pregnant women can develop Anemia, but that may not occur in the Placenta or umbilical cord. However, if hemoglobin and hematocrit levels continue to decrease in pregnant women, there will also be Anemia in the Placenta or umbilical cord. This research will study this. In addition, how does Anemia in pregnant women affect placental weight? This must be observed to ensure fetal growth. The purpose of this study was to examine changes in Hemoglobin (Hb) and hematocrit (Hct) levels in pregnant women before delivery for changes in Hb levels, Hct placenta and Umbilical Cord in newborns baby. In addition, we would like to examine how Anemia affects the weight of the Placenta.

2. Methods

The study design used was cross-sectional, by measuring maternal Hemoglobin and hematocrit levels before delivery and dependent variables (placental weight, Hemoglobin, and hematocrit level of Placenta and

umbilical cord). The study was conducted at Cibabat Cimahi Hospital Indonesia. The sample was all pregnant women who delivery in August to October, were 100 pregnant women. Inclusion Criteria: Pregnant women with 3rd-trimester pregnancy who would like delivery soon and single pregnancy. Exclusion criteria: Pregnant women without premature birth and cesarean section. Informed consent had been obtained from each patient before the investigations were undertaken. Measurement of hemoglobin levels used the cyanmethaemoglobin method. Hb and Hct would be measured in partu, the Placenta, and the umbilical cord. The Placenta is also weighed.

How to draw blood in the Placenta to measure hemoglobin and hematocrit levels:

1. Place the Placenta in a large plastic container and clean enough blood on the outside.
2. Weigh the Placenta by using the scales in grams.
3. Measure the length and width of the Placenta. In the middle of Placenta, determined the crossing point of the length and width of the Placenta.4. Slice on the cross-section and not translucent until the bottom (about 5 mm depth)
5. Take blood out of the deep tissue to measure Hemoglobin and hematocrit.

Measurement of hematocrit levels used micro methods, which later after centrifuge, it was read by a hematocrit reader. The weight of the Placenta is weighed with accuracy 1 gram.

3. RESULTS AND DISCUSSION

3.1 Characteristics of Subjects

Respondents in this study were pregnant women in the third trimester who would like delivery. Characteristics of respondents include age, number of children born to mothers, gestational age at delivery Based on the age category, a mother who is ready to give birth is over the age of 20 years. The results can be seen in table 1.

Table 1. Maternal Age

Maternal age	n	%
< 20 years old	8	8,0
20 - 29 years old	40	40,0
30 - 35 years old	33	33,0
36 - 40 years old	14	14,0
> 40 years old	5	5,0
Total	100	100,0

Table 1 shows that there is still eight maternal age (8%) who again deliver under 20 years. That would have the risk of increased maternal and child mortality during childbirth. According to the achievement of sufficient physical, mental, and social function maturity of prospective mothers is at the age of 20-29 years, which is the age readiest to give birth. Maternal age 30-40 years reaches 47%, and this also has a risk in giving birth. There are still five people who give birth over 40 years. Increasing age cause risk of childbirth which contributes to the maternal and child mortality rates during delivery and also the occurrence of Asphyxia, which is a state of respiratory failure in newborns at both the age of young birth (<20 years) and old (> 35 years) (Ekasari, 2015). Parity will affect the health of the child and the mother. Mothers who have more children need to pay attention to health, including food so that it requires greater costs. The number of

children can be seen in table 2.

Tabel 2. Parity

Parity	n	%
1 – 2 children	61	61,0
3 - 4 children	32	32,0
5 – 7 children	7	7,0
Total	100	100,0

Table 2 shows that mothers have 1-2 children (61%), and there are still mothers who have up to 7 children. According to Sari H, et al. (2014), the more children they have, the less educated mothers generally (H et al., 2015). According to Qurniyawati, E (2015), Mothers who give birth to more than two children, then 4.58 times, are a risky birth (Qurniyawati et al., 2010). Age at the time of childbirth represents the number of months in labor. Details of gestational age are as follows.

Table 3. Gestational age

Age of pregnancy	n	%
< 36 weeks	16	16,0
36 weeks	48	48,0
37 - 42 weeks	35	35,0
> 42 weeks	1	1,0
Total	100	100,0

Gestational age is usually at the period of 37 weeks. Data shows that many mothers give birth at 36 weeks (48%), but still have a big chance of a normal delivery because there is a different Estimated Birth Day (HPL). There were still preterm births that are less than 36 weeks by 16%.

3.2 COMPARISON OF HB LEVES IN PARTU WITH HB PLACENTA AND UMBILICAL CORD LEVELS

Overview of Pregnant women who would like delivery with Anemia (by measuring Hb) and how the development of Hb levels in the Placenta and Umbilical Cord. The data in Feature1 compares changes in hemoglobin levels in the anemic and non-anemic categories and their changes up to the Umbilical Cord. The number of samples of pregnant women who were not anemic was 66 people, and Anemia was 34 people.

ISSN: 13412051
Volume 25, Issue 06, June, 2020

Feature 1. Hb Levels in partu (with Anemia and Non-Anemia), Placenta, and Umbilical Cord.

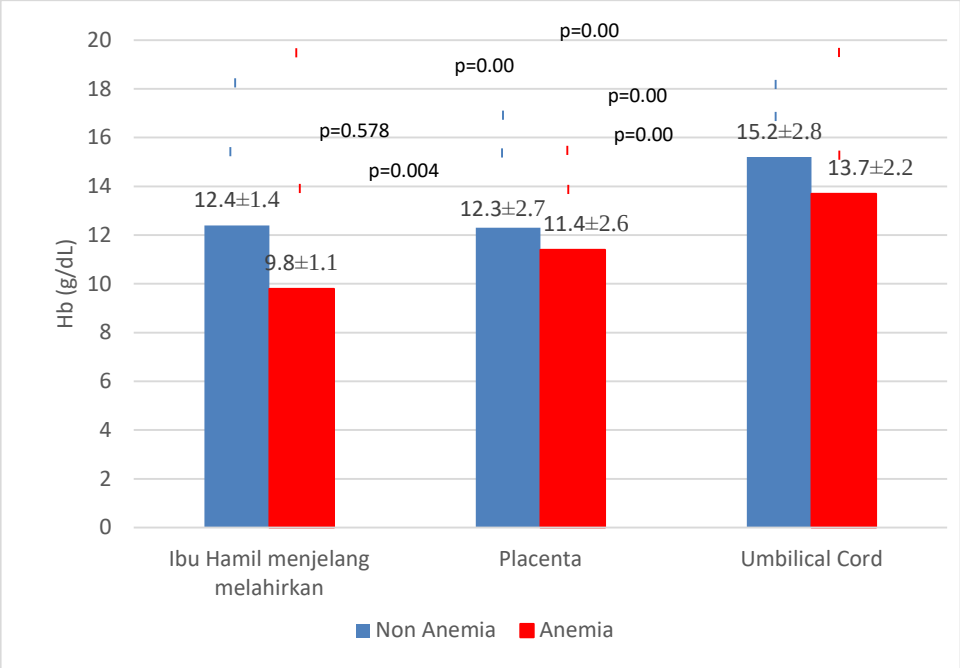


Figure 1 is a comparison of changes in normal hemoglobin levels and Anemia in partu to Hb Placenta and Umbilical Cord levels. Statistical test with Kruskal Walis there was no difference between Hb levels of non-anemic in partu with placental Hb levels (p = 0.578). Hb levels in partu (non anemic) and placenta against Hb Umbilical cord were significantly different (p = 0.000) and (p = 0,000). The statistical test used Anova and continued with the LSD test; between the Hb levels in partu with anemia, group were with significantly different placental Hb levels (p = 0.004) and on umbilical cord Hb levels (p = 0,000). There is no difference in the average Hb levels of non-anemia in partu with non-anemic placental Hb levels. The level of Hb Placenta non-anemia to Hb Umbilical cord non-anemia level increased 2.9 gr /dL (23.6%) and significantly different (using the Kruskal Wallis statistical test) (p = 0.000). That showed Hb for the fetus through the umbilical cord takes precedence over maternal and placental Hb. If a pregnant woman has mild anemia, what happens to the placental Hemoglobin and umbilical cord levels? Is it still anemic, or is the body trying to prioritize the fetus to prevent anemia? Feature 1 also shows Hb levels in partu with mild anemia and placental and umbilical cord Hb levels. Mothers who suffered mild anemia (in partu), but hemoglobin levels in the Placenta and umbilical cord were not anemic. Placental Hb and Hb in partu differed by an average of 1.6 g/dL (11.3%). Umbilical Cord Hb with Hb in partu differed by an average of 3.9 g/dL (39.8%). Statistical tests with Anova and continued with LSD test between Hb levels (mild anemia) in partu with placental Hb levels were significantly different (p = 0.004). Moreover, the average levels of Hemoglobin in partu with mild Anemia and Placenta compared to umbilical cord hemoglobin levels, and the two were significantly different (p = 0.000). These showed that although pregnant women in partu with mild anemia, but placental Hb and umbilical cord did not have anemia.

During pregnancy, there is also an increase in maternal erythropoietin production. That causes the red blood cell mass to increase slightly compared to the increase in plasma volume, ultimately reducing the concentration of Hemoglobin (Chandra et al., 2012). Lack of maternal hemoglobin levels in pregnant women can also cause a lack of oxygen flow. As is known that one of Hemoglobin can function to bind

oxygen. Although the oxygen content of blood in pregnant women is low, it turns out that the Placenta does not lack because it is a reservoir so that it remains sufficient for fetal oxygenation (Carles et al., 2003). Low hemoglobin levels can also show iron deficiency when there is a mild iron deficiency, the expression of Transferrin Receptor 1 (TFR1) in the placenta increases while Ferroportin (FPN) does not change. Low TFR1 as a compensation mechanism to continue supporting the availability and delivery of iron to the fetus (Li et al., 2008). The mechanism for the flow of iron from the mother to the fetus is first started from iron from the mother's blood circulation and then carried by Iron-transferrin (Fe-Tf). Second, the Fe-Tf is bound by transferrin receptor 1 (TFR1), which is located on the apical surface of the syncytiotrophoblast in the Placenta (Bastin et al., 2006). In the Placenta, it turns out that there is a protein as a place for storing iron, Ferritin. Ferritin is also found in fetal endothelial tissue (Bastin et al., 2006). Anemia due to iron deficiency will be inversely proportional to Hepcidin levels. Hepcidin is a hormone that plays a role in iron metabolism in the body. Anemia in pregnant women shows a stable level of Hepcidin but a decrease in Ferroportin levels in the Placenta. The stability of Hepcidin can increase iron absorption as a consequence of Anemia. It also shows that in anemic conditions in pregnant women, the body still prioritizes the availability of sufficient blood for the baby. Other studies have shown that the average maternal hemoglobin concentration is 11.14 ± 1.39 g /dL and it turns out that the average neonatal hemoglobin level can reach 16.34 ± 2.01 g / dL (Timilsina et al., 2018) and that includes healthy category (RD, 2005).

3.3 COMPARISON OF HB LEVES IN PARTU WITH HB PLACENTA AND UMBILICAL CORD LEVELS

Anemia is not only based on Hemoglobin but also on hematocrit levels. Hematocrit describes the red blood cell fluid, which is important for pregnant women.

Feature 2. Hct Levels in partu (with Anemia and Non-Anemia), Placenta and Umbilical Cord.

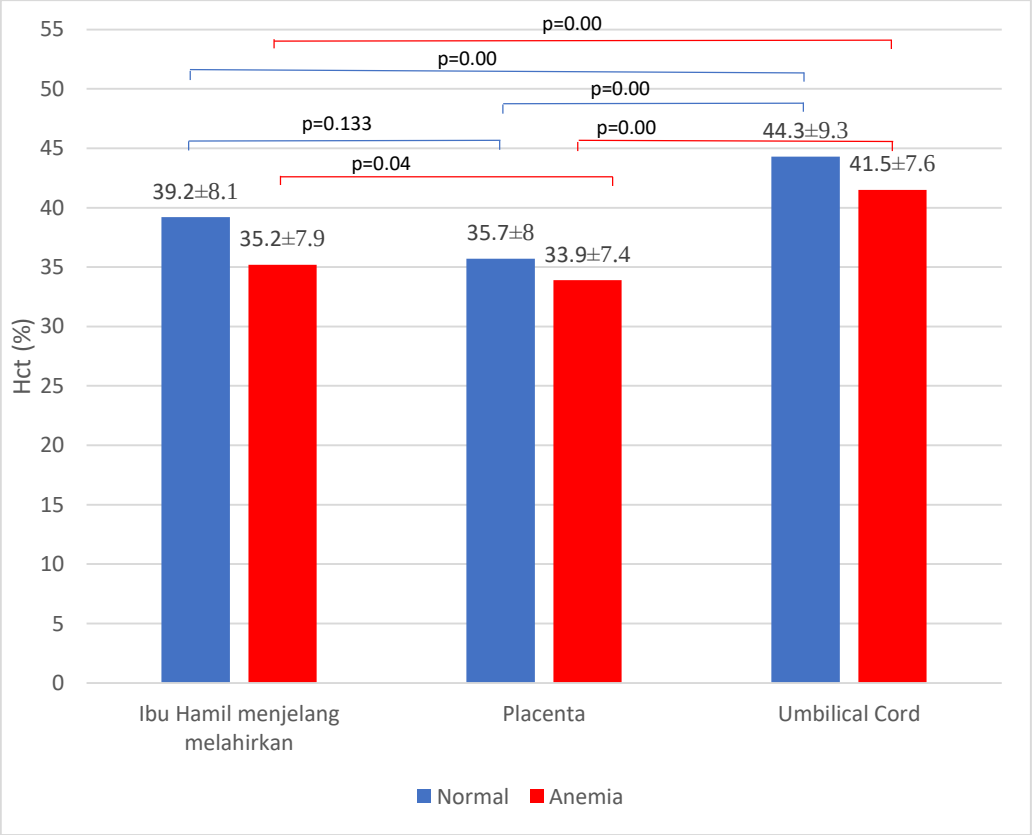


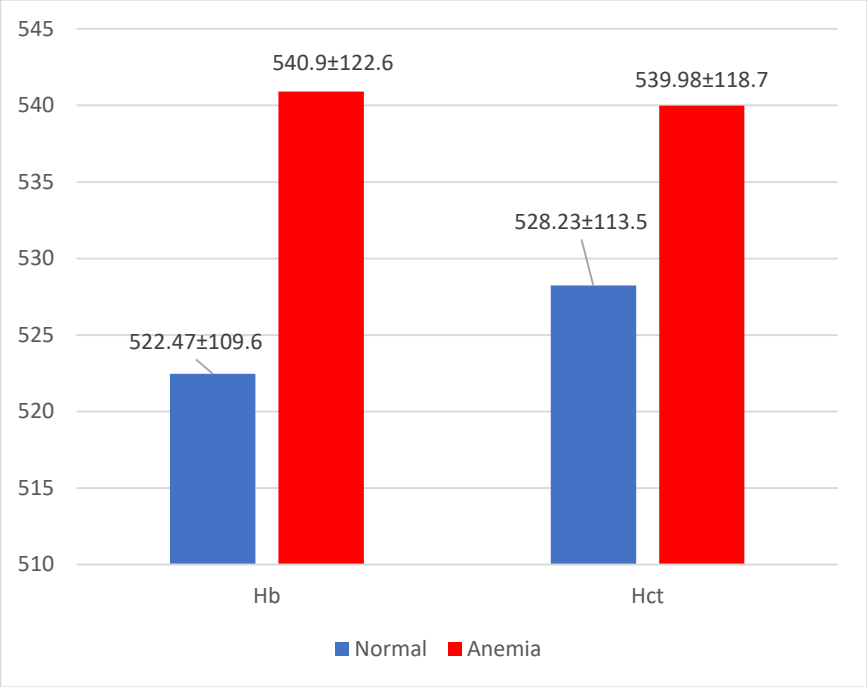
Figure 2 is a comparison of the categories of Anemia and non-anemia in partu (based on hematocrit examination) with the Hct placenta and Umbilical cord. The results in the Hct category of non-anemic pregnant women turned out to mean placental Hct lower than the average Hct in partu, and the statistical test results of this difference were not significant. Hct Umbilical cord (non-anemic maternal) was 8.6 (24.1%) higher than Hct Placenta. Statistical test results between Hct in partu, Hct Placenta to Hct Umbilical cord were both significant (p = 0.00, CI=95%). If in the condition of Anemia based on hematocrit levels it turns out that the average Hct of the Placenta is a little bit lower than the average Hct in partu which is -1.3% (3.9%) and the statistical test results of this difference are significant (p = 0.04, CI=95%). Hct Umbilical cord is 6.3 (14.2%) higher than Hct in partu. Statistical test results between Hct in partu Hct placenta to Hct Umbilical cord were both significant (p = 0.00, CI 95%). In the condition of pregnant women without Anemia, the difference is not significant. The amount of fluid volume in pregnant women affects hematocrit levels. Based on the research of Hasegawa J, Nakamura M, et al. (2014), there was no change in Trimester 1 placental volume in anemic and non-anemic pregnant women. In the third trimester of pregnancy, oxygen demand increases for fetal growth (Hasegawa et al., 2014). The fetus craves nutrition and oxygen. At the time of childbirth, the mother will lose a lot of blood. For the fetus to remain fulfilled with nutrients and oxygen and reduce the effects of blood loss, there is an increase in blood volume (plasma and red blood cells). This also facilitates blood flow to the uterus and Placenta. (Lester, 2018) Changes in the volume of blood affects hematocrit levels. During pregnancy, there is also an increase in cardiac output. It is to fill the circulation of the uteroplacental and the needs of the fetus to develop (Oliveira & Abdel-Razeq, 2018). The increase in plasma volume is also associated with increased activity of the renin plasma, as a response to system vascular caused by systemic vasodilation and increased capacity of vascular (Bernstein et al., 2001). An increase in blood volume in addition to influence Hematocrit levels but also changes the availability of iron. In the third trimester of pregnancy, levels of Hepcidin in the blood is low. The consequence will increase the iron absorption and availability of iron to the Placenta, which will be transported to the fetus optimally (Fisher & Nemeth, 2017). Moreover, iron levels in the umbilical cord is associated with also with the levels of Hepcidin umbilical co (Rehu et al., 2010). Hepcidin is the master regulator of the metabolism of iron.

Feature 1 and 2 show that Hb and Hct levels with mild Anemia, apparently in the Placenta and umbilical cord, Hb levels and Hct were higher. The data also showed that the levels of Hb and Hct of the Placenta and umbilical cord were decreased, if the Hb and Hct levels of in partu also low. This finding also illustrates that if the condition of pregnant women with severe Anemia will also occur in the Placenta and in the Umbilical Cord. The body is no longer able to adjust to severe Anemia. So, we need treatment for pregnant women with mild Anemia in order not to be severe Anemia. In severe anemia levels decrease Ferroportin, which may result in reduced iron availability to be transported to the fetus (Sangkhae et al., 2020). Pregnant women with Anemia may also occur hypoxia. Hypoxia can cause a lack of oxygen flow to the placental tissues. So hypoxia will slow down fetal growth and can be a risk factor of premature arterial hypertension and endothelial dysfunction that can develop into cardiovascular disease. (Universités et al., 1987) If severe Anemia occurs in pregnant women, it can also trigger the occurrence of vasodilation of the fetal brain (Stefanovi et al., 2005)

3.4 RELATION OF ANEMIA IN PARTU TO PLACENTAL WEIGHT

In this section, we describe how Anemia in partu (Hb and HCT) can affect the weight of the Placenta.

Feature 3. The weight of Placenta based on the level of Anemia (Hb and Hct)



On Figure 3 is to describes the comparison between anemia category in partu (based on examination of Hemoglobin and Hematocrit) with the weight of the Placenta. In Partu anemia, the weight of the Placenta was higher than no-anemia. The difference of placenta weight between anemia (mean Hb = 9.8 g / dL) and normal (Hb = 12.4 g / dL) was 18.4 g /dL(3.9%). Based on the Mann Whitney statistical test, the difference was not significant (p = 0.834). The difference of placenta weight between anemia (mean Hct = 35.2%) and normal Hct (39.2%) was 11.75 grams (2.17%). Based on the Mann Whitney statistical test the difference was not significant (p = 0.647). These results indicate that the weight of the Placenta with anemic pregnant women with Hb and Hct examination showed higher placental weight in the anemia group. Based on Stangret's research, Aleksandra (2017), if hemoglobin levels are low, the density of Vascular Placenta will increase 2-fold as an adaptive response due to low Hb. The increased placental density results in increased placental weight. Based on Larsen's research, S (2016) Hemoglobin levels <9 g /dL and higher placental weights than hemoglobin levels 9-13.5 g / dL. According to Michailidis research, G.D (2002) that there is an inverse relationship between hematocrit levels with placental growth. In the third Trimester, the Placenta adjusts to the severity of Anemia by thinning the villous membrane so that normal diffusion is maintained. Anemic Placenta can also cause higher terminal villous surface density values, including volume density and absolute volume of terminal villous capillaries compared with mothers who are not anemic (Lelić et al., 2015). Our results showed that placental weight in the anemic group of mothers was higher than in the non-anemic group of pregnant women. Placental weight can be associated with an increase in the volume of the center of the villous tree (Buehlmeyer et al., 2019). The weight of the Placenta is also closely related to the bodyweight of the newborn baby (Panti et al., 2012).

4. CONCLUSION

The levels of Hb and Hct in partu with mild Anemia leading to delivery were lower than the Hb and Hct levels in the Placenta and umbilical cord. Placental weight with mild Anemia was also higher than those without Anemia. That showed that the mother's body prioritizes the needs of her fetus than the mother, especially at the level of mild Anemia. Hb and Hct in partu with mild Anemia caused Hb and Hct of the

Placenta, and umbilical cord also decreased. It means if the level of Hb and Hct in partu decline then the level of Hb and Hct placenta and umbilical cord also decreases. So, when it comes to severe Anemia, Hb and Hct umbilical cord will also be lower so it can be ensured that severe Anemia is insufficient oxygen and nutrients for the fetus. The opportunity to improve anemia status of the mother is maximum in the condition of mild Anemia, so that it does not affect the newborn. Health workers must take care of pregnant women so that Hb and Hct levels do not decrease to severe Anemia. If this happens, it will be dangerous for the fetus.

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