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Milk supplementation increases mid-upper arm circumference and haemoglobin level among pregnant women in Kupang, Indonesia: Evidence from a regression discontinuity design

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ABSTRACT

Introduction: The high prevalence of chronic energy deficiency (CED) and anaemia among pregnant women in Indonesia is worrying. Nusa Tenggara Timur (NTT) is one of the provinces in Indonesia with the highest prevalence of CED. This study aimed to determine the effect of fortified milk supplementation on changes in mid-upper arm circumference (MUAC) and haemoglobin level among pregnant women. **Methods:** This quasi-experimental study was conducted in three locations of Community Health Centers in NTT from May to August 2019. Purposive sampling was used to recruit 69 pregnant women who were divided into two groups based on haemoglobin levels; the intervention group consisted of 31 pregnant women with haemoglobin levels below 11 g/dL, and control group consisted of 38 pregnant women with haemoglobin levels above 11 g/dL. Intervention group was provided with fortified milk supplementation, while control group received education about prevention of CED and anaemia. Data were analysed using regression discontinuity design with haemoglobin of 11 g/dL as cut-off. **Results:** Using regression discontinuity method, we were able to determine the effect of milk supplementation based on haemoglobin levels and confirm the result that milk supplementation significantly increased MUAC by 4.69 cm. Despite no discontinuity found, a positive increase of 0.98 g/dL in haemoglobin level was important to note. **Conclusion:** Milk supplementation of 300 kcal/day for three months significantly increased MUAC and to some extent, increased haemoglobin level. Thus, it should be considered when planning nutrition programmes to improve the nutritional status of pregnant women.

Keywords: haemoglobin level, milk supplementation, MUAC, pregnant women, regression discontinuity design

INTRODUCTION

Chronic energy deficiency (CED) and anaemia are considered as serious public health concerns, especially among pregnant women, due to their effects on pregnancy and pregnancy outcomes. CED and anaemia in pregnant women have been found to negatively affect pregnancy outcomes, such as imposing higher risks of intrauterine growth retardation (IUGR), low birth weight, and short birth length, which can further cause undernutrition throughout childhood, as well as reduced mental

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and motor skills development (Black *et al.*, 2008; Ahmed, Hossain & Sanin, 2012).

Globally, maternal undernutrition remains common in lower- and middle-income countries (LMIC), including South East Asia (Black *et al.*, 2008). Pregnant women are known to be susceptible to iron deficiency and global data have shown minor changes in the prevalence of anaemia in women of childbearing age from 31.6% to 32.8% in 2000–2016 (Global Nutrition Report, 2018). Anaemia in pregnant women increases the risks of perinatal and neonatal mortality, as well as low birth weight (Rahman *et al.*, 2016).

The high prevalence of CED and anaemia among pregnant women in Indonesia is a worrying phenomenon. The prevalence of CED in pregnant women has decreased from 24.2% in 2013 to 17.3% in 2018, whereas in the same period, the prevalence of anaemia in pregnant women has dramatically increased from 37.1% to 48.9% (Ministry of Health of the Republic of Indonesia, 2018), possibly due to increasing prevalences of both chronic and acute deficiencies of macro- and micronutrients, as well as the high prevalence of hookworm infection. In the long term, high prevalence of low birth weight may increase the risks of children developing chronic diseases throughout adulthood and later life, such as coronary heart diseases, hypertension, type 2 diabetes, and metabolic syndrome (Marciniak *et al.,* 2017).

Data on consumption patterns of pregnant women in Indonesia have shown that there are large number of pregnant women who do not meet the Indonesia Recommended Dietary Allowance (RDA) throughout pregnancy. Approximately 70-80% of pregnant women in both village and city do not meet their energy and protein requirements (Ministry of Health of the Republic of Indonesia, 2014). This situation is exacerbated by the number of women of childbearing age who enter pregnancy with poor nutritional status. Based on the Basic Health Research data (2018), the prevalence of CED in pregnant and non-pregnant women in Indonesia is quite high at 17.3% and 14.5%, respectively (Ministry of Health of the Republic of Indonesia, 2018). If this situation is not resolved immediately, Indonesia will experience a crisis of human resources in terms of nutrition and intellectual capacities. One way to overcome CED and anaemia in pregnant women of Indonesia is to provide food supplementation containing energy and iron for this vulnerable population.

This study was conducted among pregnant women in Nusa Tenggara Timur (NTT). CED and anaemia are highly prevalent among pregnant women in NTT, which has the highest prevalence of CED in women of childbearing age in Indonesia - 36.8% in pregnant women and 32.5% in non-pregnant women (Ministry of Health of the Republic of Indonesia, 2018). The study aimed to determine the effect of fortified milk powder supplementation on changes in anaemia and CED rates in pregnant women. Supplementation of milk for pregnant women was chosen because fortified milk powder is rich in energy and iron (both are associated with anaemia), with practical preparation and manufacture, is easily consumed by pregnant women, and can be obtained at a relatively affordable price.

MATERIALS AND METHODS

The quasi-experimental study was conducted in Kupang Regency, NTT Province in the eastern part of Indonesia, with study sites in three selected Community Health Centers (Puskesmas), namely Naibonat Health Center-East Kupang District, Oesao Health Center-East Kupang District, and Tarus-Kecamatan Kupang Tengah District Health Center. The selected Health Centers were within the Sehati Midwives Group (our partner in this study) working area and selection was advised and consulted by NTT Province Health Office. Purposive sampling was used in this study where all eligible subjects in the three health centres were included as samples. The inclusion criteria of the study were pregnant women that frequently went to these selected community health centres, did not have physical and mental disorders, did not have any specific diet such as vegan diet, and was self-reported as not having lactose intolerance or milk allergy.

The number of pregnant women recruited at the start of the study was 108 pregnant women, with 54 pregnant women in each group. Both groups comprised women with haemoglobin levels below 11 g/dL, which is based on the World Health Organization (2011) reference cut-off for anaemia among pregnant women. During the study period, the number of pregnant women was reduced to 31 in the intervention group and 38 in the control group. The drop-outs in the intervention group was caused by two people having miscarriages, two people moved houses, two gave births, two people went to another place when data were collected, and 15 pregnant women who had haemoglobin levels >11g/dL but received milk supplementation due to field situation. In the control group, the drop-outs were due to six miscarriages, one who moved to a new house, two returned home, six went to another place during data collection, and one gave birth. Per protocol analysis was conducted on a total of 69 pregnant women who completed the study.

The outcomes were post-intervention haemoglobin level and mid-upper arm circumference (MUAC) calculated as g/dL and cm, respectively. Calculated using the RD package for STATA, the power of this study was 75%, slightly lower than the expected power of 80%, due to drop-out of respondents that were mainly related to moving to other places as reasons for not continuing their participation.

In the intervention group, supplement was given to pregnant women in the form of two cups of milk (one cup contained one sachet of 35 g powdered milk diluted in 180 ml lukewarm water) containing 17 mg elemental iron per day and total energy of 300 kcal/day. In addition, the protein content of a sachet of powdered milk was 6 g, fat 3.5 g, carbohydrate 22 g, and both iron and calcium 25% of the Indonesia RDA. Milk supplementation was provided to pregnant women in person from house-to-house. Pregnant women drank the milk every morning and evening under the supervision of the cadre. In the control group, milk supplementation was not provided, but participants received education about CED and anaemia, preventive measures, and efforts to overcome them. The education was provided at the beginning of the study for both intervention and control groups. The two groups were followed for a three-month period (June–September 2019). Measurements of anthropometry (body weight, MUAC) and haemoglobin level were conducted at four time points: T0 - Baseline in June 2019, T1 - July 2019, T2 - August 2019, and T3 - Post-intervention in September 2019. Measurements were conducted by the local Puskesmas' midwives. When a mother gave birth, the weight and length of the infant were measured and recorded by the midwives.

The instruments used in this study included a pre- and post-test knowledge questionnaire for pregnant women, an intervention monitoring form, a weight measurement tool (digital scale with 0.1 kg accuracy), a MUAC flexible measuring tape, blood collection equipment for haemoglobin examination using quick-check tool, interview guide for 24-hour dietary recall, as well as measuring devices for infants' weight and length (length board). Training was provided by the research team to the data collectors, namely 21 cadres under the care of a local partner "Sehati" midwives group. The responsibilities of cadres involved distributing and providing milk supplementation to pregnant women twice a day (morning and evening), every day for 12 weeks (three months, from June to August 2019), ensuring that milk supplementation was consumed by pregnant women, recording the monitoring form for milk drinking (throughout the intervention), and providing a monitoring form at the end of the intervention to the Puskesmas' midwives. To assess nutrient intakes, 24-hour food recalls were carried out at baseline and post-intervention by two research assistants who were D3 graduates from the State Health Polytechnic of the Ministry of Health, Kupang. Measurements of haemoglobin level, body weight, and MUAC were conducted by midwives who had been trained to use the Quick-check Haemoglobin Testing System (ACON), Camry brand step scale, and MUAC tape. Pre- and post-test trainings were provided to trainees to ensure the competency of enumerators. Prior to data collection, all prospective respondents were given information about the research mechanism and informed consent was obtained through verbal and written forms. All information collected about the respondents during the study were stored anonymously in a database protected by password.

Regression discontinuity (RD) design was used in the analysis with basic components: a score to define a cut-off point as threshold, an intervention, and outcomes. This design's main advantage is its simplicity in estimating causal effects, assuming that the threshold value distribution of intervention cannot be manipulated by subjects and covariates are evenly distributed both above and below the threshold through continuity assumption (Bor *et al.*, 2014). This design then allowed us to see the valid causal effect of milk supplementation on outcomes by giving milk supplementation to only anaemic pregnant women, while non-anaemic women received no intervention as they were part of the control group.

In a situation where intervention affects the outcomes, the RD design allows us to isolate the effect of milk supplementation on haemoglobin level and MUAC due to the use of sharp design in which our haemoglobin scores on baseline were continuously distributed and discontinuity around the threshold of 11 g/dL was found, had only one cut-off, and the distribution of intervention and control groups were clear in the threshold (Cattaneo, Idrobo & Titiunik, 2019). We used first degree local polynomial approach with CCT mean squared error minimising bandwidth choice, triangular kernel, and data were statistically analysed using STATA 14.1 (StataCorp, 2015) with rdrobust and rdmulti package along the STATA module to confirm the procedures were correct (Cattaneo *et al.*, 2019).

This study obtained ethical approval by the Institute of Research and Community Service at Atmajaya Catholic University (Letter of Approval No.0617/III/LPPM-PM.10.05/05/2019 dated 24 May 2019). Written informed consent was obtained from all subjects.

RESULTS

At baseline, the mean age of mothers in the intervention group was younger (27.3 years old) compared to the control group (30.2 years old). However, the difference was not significant and both intervention and control groups were within the same age group (according to WHO) and as a result, the age difference did not affect study findings. Table 1 shows the proportion of mother's age between intervention and control groups. Social and economic characteristics of subjects in both groups could be assumed to be relatively similar since they came from the same catchment area of health centres. This similarity was also reflected as no significant difference was found on knowledge and attitude scores at pre-test and post-test (Table 2). The mean maternal haemoglobin level in the intervention group was 10.0±1.7 g/dl and the control group was 12.2±1.1 g/dl. Mean weight and MUAC of pregnant women in the intervention group were 48.5±9.5 kg and 23.3±3.0 cm, respectively, while in the control group, they were 54.6±7.8 kg and 26.4±2.2 cm, respectively. Weight gain in the two groups were not statistically significant (Table 2), so we decided to use MUAC as an indicator of CED since it was not as easy to change as weight. Consistent to the intention of using RD design, the control group had better values of haemoglobin, MUAC, and weight than the intervention group.

The results of nutrient consumption analysis (Table 3) showed that there were significant differences ($p<0.05$) in nutrient consumption between baseline

Table 1. Distribution of respondents' characteristics by treatment group

Variable	*Group*				*p-value*
	Intervention		*Control*		
	n	*%*	*n*	*%*	
Age					
<35 years	27	87.1	29	76.3	0.36
>35 years	4	12.9	9	23.7	
Infant birth weight					
<2500 gram	1	3.2	2	5.3	0.17
>2500 gram	30	96.8	36	94.7	
Infant birth length					
<46 cm	1	3.2	0	0.0	0.45
>46 cm	30	96.8	38	100.0	

Table 2. Baseline and post-intervention measurements by treatment group

Variable	*Group*				*p-value*
	Intervention		*Control*		
	n	*mean*	*n*	*mean*	
Mother's weight (kg)					
Baseline	31	50.1	38	55.2	0.03
1st measurement	31	52.7	38	57.7	0.03
2nd measurement	31	55.3	38	60.7	0.02
Post-intervention	31	55.9	38	61.9	0.01
Δ Mother's weight (kg)					
Baseline-1st measurement	31	2.5	38	2.5	0.92
1st-2nd measurement	31	2.6	38	3.0	0.47
2nd measurement- post-intervention	31	0.6	38	1.2	0.39
Knowledge (score)					
Pretest	31	13.5	38	12.9	0.56
Posttest	31	15.5	38	14.9	0.59
Attitude (score)					
Pretest	31	75.6	38	74.4	0.56
Posttest	31	76.7	38	76.4	0.87

and post-intervention in the intervention group, with an average energy difference of 306 kcal, fat 20.9 g, iron 4.1 mg, and calcium 426.4 mg; whereas in the control group, significant differences (p<0.05) between the values of nutrient consumption at the beginning and end of the study period were seen in energy and fat, with an average difference of 636 kcal and 24.3 g, respectively.

Figure 1a exhibits that the RD effect in haemoglobin level of the intervention group increased by 0.98 g/dL with milk supplementation. This RD effect represented an increase of 9.5% relative to the control group, but no significant discontinuity effect was found in the haemoglobin level outcome (p=0.15).

Discontinuity was found in MUAC (p<0.05) where RD affected the intervention group by 4.7 cm higher than the control group. The effect represented 16.4% relative to the control group above the threshold and this effect was statistically significant (p=0.035) (Figure 1b). Table 4 summarises the discontinuity of the outcomes with haemoglobin level of 11 g/dL as cut-off.

DISCUSSION

The consumption data apparently exhibited that the intervention group experienced a significant increase in the consumption of energy, carbohydrate, protein, fat, iron, and calcium; whereas in the control group, the increase was only in energy and fat consumption. This showed that giving milk to pregnant women can significantly increase the consumption of several nutrients. However, this study showed that in general, the daily nutrients consumption of pregnant mothers was very low, especially micronutrients. Based on the Indonesian RDA, the consumption of iron and calcium in pregnant mothers in the intervention group only met 42.6% and 57.4% of the RDA; whereas in the control group, it was even lower at 30.4% and 29.9% of the RDA,

Table 3. Analysis of respondents' daily nutrient consumption by treatment group

Nutrients	*Type of groups*							
	Intervention (n=31)				*Control (n=38)*			
	Baseline	*Post-intervention*	*Δ Mean*	*% RDA*	*Baseline*	*Post-intervention*	*Δ Mean*	*% RDA*
Energy (kcal)	1282±530	1588±525	306*	62.0	1404±602	2040±1763	636*	80.0
Carbohydrate (g)	192.8±83.9	210.7±79.9	17.9	52.7	226.7±99.9	224.5±101.4	2.3	56.1
Protein (g)	46.3±21.8	57.2±19.7	10.9	81.7	55.5±34.3	66.5±48.2	11.0	95.0
Fat (g)	37.1±25.1	57.9±25.8	20.9*	85.7	42.1±26.8	66.3±58.6	24.3*	98.2
Iron (mg)	6.5±3.8	10.6±3.7	4.1*	39.3	8.5±8.7	8.3±5.3	0.2	30.7
Calcium (mg)	276.3±197.5	702.7±371.3	426.4*	58.6	352.3±231.2	374.4±326.3	22.1	31.2

*p<0.05, paired t-test

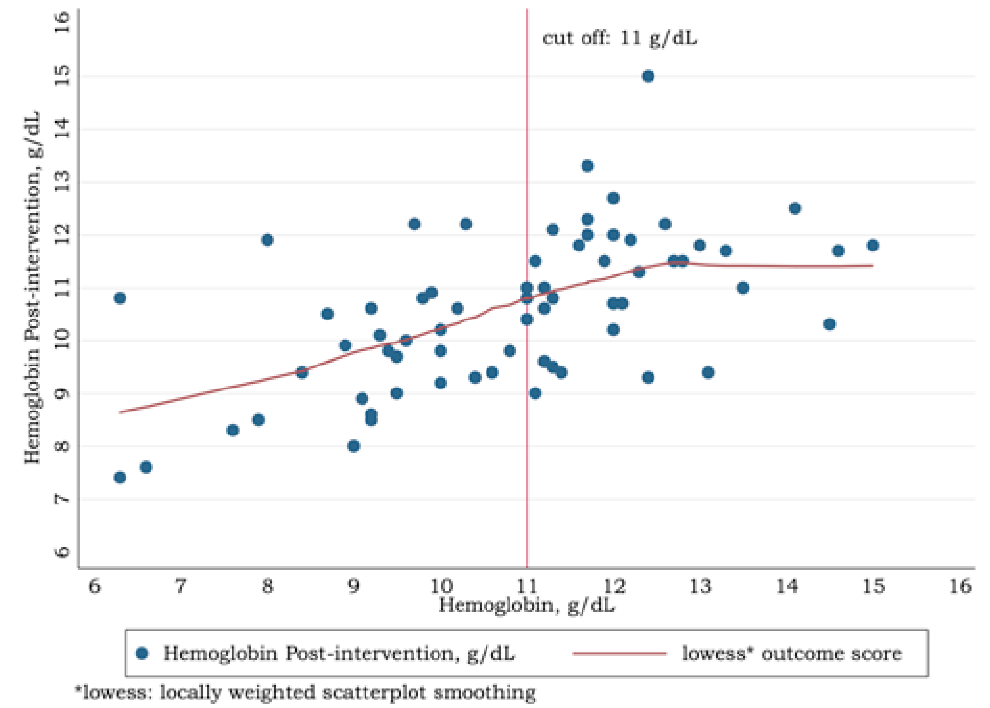

Figure 1a. Regression discontinuity analysis on post-intervention haemoglobin level (g/dL)

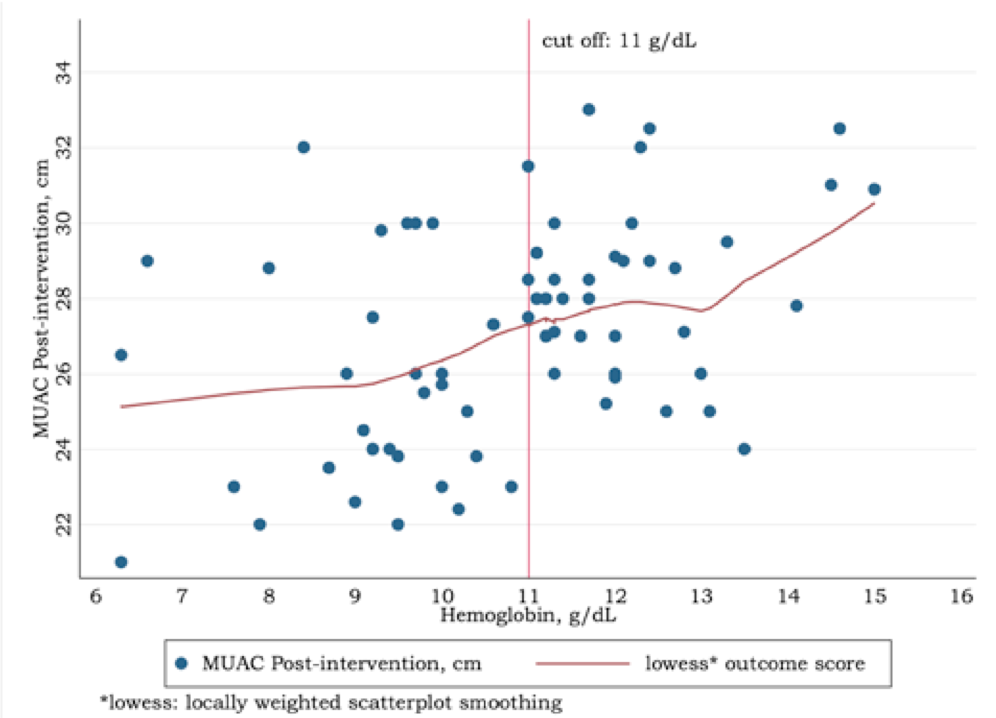

Figure 1b. Regression discontinuity analysis on post-intervention MUAC (cm)

Table 4. Effect size on outcomes based on discontinuity regression

Outcome	*Effect size (95% CI)*	*Relative percentage (%)*	*p-value*
Haemoglobin (g/dL)	0.98 (-0.35 to 2.32)	9.5	0.15
Mid-upper arm circumference (cm)	4.69 (0.33 to 9.06)	16.4	0.04

respectively. All women in this study were distributed with iron-folate tablets from the government, but the recall conducted in this study did not reveal iron supplementation reported by subjects. However, based on information from midwives, no compliance problems have been reported regarding iron-folate consumption.

The low consumption of iron in pregnant women is concerning. During pregnancy, iron is required for both mother and foetus. The urgency of increasing iron status in mothers is to maintain blood volume expansion during pregnancy. Failure to expand maternal plasma volume can result in unwanted pregnancy outcomes, such as premature birth, pre-eclampsia, and foetal growth restriction (Vricella, 2017). The lack of expansion in blood volume during pregnancy can also result in a decrease in cardiac output, which is associated with a decrease in uterine blood flow that can ultimately lead to growth retardation in the foetus (Soma-Pillay *et al.*, 2016). According to Mecacci *et al.* (2015), nutritional supplementation, such as iron in milk, for pregnant women is needed in sufficient quantities for foetal development and prevention of the effects of anaemia. In addition, iron fortified foods, including milk, are considered as a promising approach to prevent iron deficiency anaemia in pregnancy in developing countries because they are relatively accessible and cost-effective (Osungbade & Oladunjoye, 2012).

In this study, milk supplementation could increase haemoglobin level, although not significant and the increase was relatively low. The modest effect of milk supplementation on haemoglobin levels in this study could be explained in a couple of ways. Firstly, maternal anaemia in pregnancy is related to many factors including infections, inappropriate health seeking behaviour, and poverty (Stoltzfus, 2011). In this context, as pointed out by Steketee (2003) considering the tropical climate, poor sanitation and hygiene, it is very possible that hookworm infestation was prevalent among pregnant women in the study area. In 2014, it was reported that in the East Nusa Tenggara rural areas, the prevalence of hookworm infection reached 53.5% (Sungkar *et al.*, 2015). Blood loss caused by hookworm infestation can range from 0.05 mL/day to 0.25 mL/day, depending on the type of nematodes (Steketee, 2003). Secondly, the dietary pattern outside supplementation was based mostly on plant origin foods and less animal source foods. Thus, the low dosage of fortified iron provided by milk supplement (i.e. 17 mg, only 25% of RDA) might have been insufficient to give a significant effect since the iron provided by daily consumption was low, especially among the intervention group. In addition, women who entered pregnancy with undernourished condition is unlikely to improve their nutritional status due to additional demand of the foetus (Ahmed *et al.*, 2012). Thus, food supplementation for malnourished pregnant women can have a significant role in the body's physiological and metabolic requirements, both for themselves and their foetus. Although during pregnancy the body can work in such a way as to compensate for the state of deficiency or excess of certain nutrients, a pregnant woman will not be able to provide essential nutrients for her foetus if she herself is deficient (Koenig, 2017). This can be a targeted focus for intervention in populations of pregnant women vulnerable to nutrient deficiencies.

Recently, Lipoeto, Masrul & Nindrea (2020) found in their study that after controlling for age, dietary pattern, parity, education level, iron supplementation, health knowledge, prenatal care, health status, and comorbidity, the dominant significant factor for anaemia was chronic energy deficiency. Furthermore, Lipoeto *et al.* (2020) stressed that a reduction in chronic energy deficiency may also reduce anaemia. This might explain why haemoglobin level increase was modest, but MUAC increase was significant since the correction on energy deficiency came first, followed by the increase in haemoglobin level. If a longer duration of intervention was applied, it is not impossible that we can see a higher increase in haemoglobin level.

This study found a significant increase in MUAC in both groups. This is expected and in accordance with the physiological changes in pregnancy, namely the increase in maternal weight due to the development of maternal and foetal body tissues. Regression discontinuity analysis showed that there was a significant effect of milk supplementation on MUAC with relative percentage of 16.4% and an effect size of 4.69 cm higher in intervention group compared to controls. This is in line with Papathakis, Singh & Manary (2016)'s findings that food supplementation can increase MUAC and gestational weight, which can have a positive effect on foetal growth and development. Likewise, according to Heppe *et al.* (2011), milk consumption during pregnancy is associated with an increase in foetal weight and birth weight. A longitudinal study in India showed that milk consumption in the second trimester of pregnancy was positively associated with an increase in placental weight (Rao *et al.*, 2001). There is a tendency that the best effect on foetal growth occurs when milk supplementation is provided in the last trimester. According to Melnik *et al.* (2015), milk is the strongest predictor of increased maternal weight gain during the last trimester. Increased weight in placenta because of milk consumption not only increases nutrient transfer to the foetus, but can also increase maternal blood sugar levels, which will increase foetal growth and birth weight (Melnik *et al.* 2015). Maternal diet for stimulation of smooth transfer of nutrients and uteroplacental blood supply is therefore important to be considered to support foetal growth (Burton & Jauniaux, 2018).

In this study, milk supplementation in the amount of 300 kcal/day for three months had a positive effect on pregnant women with anaemia in terms of MUAC and haemoglobin levels. The energy content of the provided supplement was relatively modest and on the lower side compared to other studies which usually ranged around 300-1000 kcal/day (Liberato, Singh & Mulholland, 2013). Moreover, Ahmed *et al.* (2012) suggested an energy content of 700 kcal/day for supplementing undernourished pregnant women. However, despite the minimal energy content, this study found that milk supplement had a significant effect on MUAC. This might be related to the fact that undernourished women will benefit more from the supplementation compared to normal women (Jackson & Robinson, 2001). Another important note is the contribution of 16% protein towards total energy of the milk supplement. Protein-energy balance in food supplement to treat CED is an important consideration for the supplement to be effective and it is supposed to be under 25% (Jackson & Robinson, 2001) or more recently, under 20%, as excessive energy contribution from protein may do more harm than good to the foetus's growth (Liberato *et al.*, 2013).

Interventions to support foetal growth are crucial for vulnerable groups with CED to avoid the potential long term impacts of prenatal growth optimisation as a risk factor for foetal programming of metabolic syndrome such as diabetes, hypertension, and heart diseases (Marciniak *et al.*, 2017). Therefore, milk supplementation for population of pregnant women that are prone to energy and iron deficiency is considered suitable for population with high prevalence of CED.

Huynh *et al.* (2018) showed that efforts to improve the nutritional status of mothers through milk supplementation had a positive effect on the nutritional status of pregnant women preparing for the requirement of fat storage for lactation. A study by Zhang *et al.* (2018) among 228 pregnant women in Vietnam showed that there was a sustained effect of maternal milk supplementation which not only contributed to foetal growth and development, but also better exclusive breastfeeding. Two studies of milk supplementation intervention for lactating mothers for three months in Beji and Cipayung Subdistricts in Depok and East Jakarta, Indonesia showed consistently high success rates of exclusive breastfeeding for six months (more than 80%) (Fikawati, Syafiq & Mardatillah, 2017; Fikawati *et al.*, 2019). Furthermore, to support exclusive breastfeeding for six months, as well as the optimal growth and development of children, continuous milk supplementation from pregnancy to lactation is to be provided.

The limitation of this study was related to the lack of maternal height measurement and no pre-pregnancy body mass index values could be obtained as indicators of maternal nutritional status. The limited time of the study also caused the study to lack monitoring of accurate pregnancy outcome measurements, such as birth weight and infant's length. We also noted that despite similar levels of compliance among mothers regarding iron and folate supplementation in both groups, this should be included in the questionnaire and be reported in future. Another limitation was that the sample size could be increased to obtain higher power although the power of this study was considered as sufficient. The study could not reach mothers who did not come to the measurement site because of incomplete addresses. Thus, it is possible that the actual situation is even worse.

CONCLUSION

Using RD method, we were able to determine the effect of milk supplementation based on haemoglobin level and confirm the result that milk supplementation was able to significantly increase MUAC by 4.69 cm, and despite no discontinuity found, a positive increase of 0.98 g/dL in haemoglobin level was important to note. Provision of supplementation targeted to pregnant women is recommended to ensure adequate intakes of both macro- and micronutrients which could not be provided by daily food intakes.

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Authors' contributions

AS, conceptualised and designed the study, prepared the analysis and draft of the manuscript, and reviewed the manuscript; SF, advised on data analysis and interpretation, and reviewed the manuscript; NPM, data analysis and interpretation, assisted in drafting of the manuscript, and translated the manuscript; M, conducted the field study and led the data collection in Kupang District.

Conflict of interest

None.

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