Original Article

Effect of Maternal Multi-Nutrient Deficiencies on Fetal Growth: A Cohort Study

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ABSTRACT

OBJECTIVE: This study aims to examine the impact of nutritional deficiencies during pregnancy on fetal development by analyzing the relationship between nutritional status and prenatal fetal development.

METHODOLOGY: This cohort study was conducted from April to August 2025 with a sample of 92 pregnant women from all health centres in Bogor City Indonesia. The purposive sampling technique was used to determine the sample with strict inclusion and exclusion criteria. The study variables were maternal age, body mass index, and estimated fetal weight. Several tests were used for data analysis, including ANOVA, the Kruskal–Wallis test, and linear regression.

RESULTS: The findings revealed significant differences in calcium intake (82.6%), iron (91.3%), and protein (54.3%). Between the MMA and IFA groups, there was a significant difference in calcium intake, with p-values of 0.033 and 0.024, respectively. These findings confirm that calcium intake is crucial for fetal growth. Further analysis showed that fetal weight increased significantly in the MMS group, with a β value of 3383.64 and a p-value of 0.027.

CONCLUSION: This study confirms that calcium has a crucial role in fetal development, especially in the MMS group.

KEYWORDS: Multi-Nutrient Deficiencies, Fetal Growth, Maternal Nutrition, Supplementation Types, Calcium Intake

INTRODUCTION

Micronutrient deficiencies are a global problem of grave concern. Almost 40% of pregnant women worldwide suffer from anemia. Anemia is primarily caused by insufficient iron intake during pregnancy[1,2]. Research shows that micronutrient supplements are needed to prevent complications during pregnancy. This is especially true in developing countries where pregnancy complications are more common[3,4].

Nutritional deficiencies, including iron, folate, and iodine, significantly impact pregnancy outcomes globally. For example, the prevalence of folate deficiency remains very high, particularly in developing regions, where surveys indicate that up to 55% of pregnant women were affected before grain fortification measures were implemented, and has decreased significantly since[5]. Iron deficiency, which primarily causes anemia, is associated with a higher risk of low birth weight and preterm birth[6]. Furthermore, iodine deficiency is reported to affect a large proportion of the population, with pregnant women particularly vulnerable due to their increased iodine requirements[7]. Iodine deficiency during pregnancy can lead to serious cognitive impairment and severe hypothyroidism in offspring[8].

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Fetal growth restriction (FGR) is the impact of insufficient nutritional intake during pregnancy, whether from macro or micronutrients[9]. Previous research has shown that nutrient availability during pregnancy significantly influences fetal growth and development. Placental nutrient transfer also plays a crucial role in fetal development[9]. There is a clear relationship between the mother's body composition and fetal development[10].

It is also known that deficiencies of essential minerals and vitamins can worsen and cause complications (hypertension and gestational disorders)[4]. The leading cause of anemia in pregnant women is a lack of iron intake, which increases the risk of premature birth and developmental disorders in babies, especially in cognitive matters[2]. Another equally essential nutrient is iodine. A lack of this nutrient can affect the development of the fetus's brain and nervous system[11]. Eating habits are often influenced by the mother's education and awareness of nutrition[12]. Enhanced nutritional knowledge correlates with improved dietary choices, as observed in studies where targeted education increased food literacy among pregnant women, resulting in diversified diets rich in essential nutrients[13].

The aim was to analyze the effects of maternal deficiencies in multiple nutrients during pregnancy on fetal development. The cohort study allows longitudinal assessment of maternal nutrition and fetal growth, providing more robust evidence compared to cross-sectional studies.

METHODOLOGY

Study Design and Sampling

This cohort study was conducted from April to August 2025 at all community health centres in Bogor City. All participants were recruited from primary health centres across the study sites and met predetermined inclusion and exclusion criteria. Inclusion criteria included willingness to undergo anthropometric measurements, fetal weight estimation, dietary assessment, and a singleton pregnancy. Sample exclusion criteria included comorbidities and incomplete data.

Sample Size Calculation

The confidence level was set at 95% with a power of 80%. The expected proportion in the exposed group was P_2 = 64.8% = 0.648. The assumed outcome proportion was P_1 = 36% (0.36), and the RR value was 1.8.

Sample:

$$n_{\text{per group}} = \frac{[Z_{\alpha/2}\sqrt{2\bar{P}(1-\bar{P})} + Z_{\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}]^2}{(P_1-P_2)^2}$$

$$\bar{P} = (P_1 + P_2)/2$$

Variables

The primary variable in this study is the estimated fetal weight. Meanwhile, the predictor variables were pre-pregnancy body mass index, second-trimester hemoglobin levels, and maternal age. Nutritional status was measured as adequate, sufficient, or excessive.

Supplementation Classification

The samples were divided into two groups: MMS and IFA. One group received multivitamins and minerals (MMS), while the other received iron and folic acid (IFA).

Data Collection and Analysis

Variables are displayed as Mean ± SD / Median (IQR) values and frequencies and percentages.

Bivariate Analyses

Analysis of Variance (ANOVA) or the Kruskal–Wallis test was used as a bivariate analysis

Multivariate Analyses

Multivariate testing was performed using a linear regression model. Several models were adjusted for supporting variables such as pre-pregnancy BMI, maternal age, and Hb T2 levels. Several terms, such as nutritional intake × type of supplementation, were also included to explore the potential for effect modification. A threshold of $\alpha = 0.05$ was set for statistical significance testing. The Hosmer-Lemeshow test and the pseudo R^2 value were used to determine the suitability of the regression model.

Ethical Considerations

This research has received ethical approval from IBN Khaldun University, Bogor, Indonesia, with letter No. 018/K.11/KEPK/FIKES-UIKA/2025.

RESULTS

Table I shows that the interquartile range (IQR) of maternal age was 23–34 years. The median maternal hemoglobin level was 11.75 g/dL (IQR: 10.80–12.40). The estimated fetal weight in the second trimester was a median of 341 g (IQR: 181–928 g).

Table I: Participants' Characteristics

Variable	Mean ± SD / Median (IQR)
Maternal age (years)	28.00 (23.00 – 34.00)
Hemoglobin in 2nd trimester (g/dL)	11.75(10.80 – 12.40)
Estimated Fetal Weight T2 (grams)	341.00(181.00-928.00)

Table II shows that the majority of samples were deficient in protein, fiber, sodium, potassium, energy, carbohydrates, calcium, and iron. Meanwhile, regarding vitamins, the majority were deficient in vitamin C, retinol, and beta-carotene.

Table II: Characteristics of Participants

Variable	Category	n	%
Energy intake	Inadequate	72	78.3
	Adequate	12	13.0
	Excessive	8	8.7
Protein intake	Inadequate	50	54.3
	Excessive	30	32.6
	Adequate	12	13.0
Fat intake	Inadequate	40	43.5
	Excessive	33	35.9
	Adequate	19	20.7
Carbohydrate intake	Inadequate	76	82.6
	Adequate	10	10.9
	Excessive	6	6.5
Fiber intake	Inadequate	91	98.9
	Excessive	1	1.1
Calcium intake	Inadequate	76	82.6
	Excessive	12	13.0
	Adequate	4	4.3
Phosphorus intake	Excessive	57	62.6
	Inadequate	20	22.0
	Adequate	14	15.4
Iron intake	Inadequate	84	91.3
	Adequate	4	4.3
	Excessive	4	4.3
Sodium intake	Inadequate	80	87.9
	Excessive	9	9.9
	Adequate	2	2.2

Potassium intake	Inadequate	86	93.5
	Excessive	4	4.3
	Adequate	2	2.2
Copper intake	Excessive	51	55.4
	Inadequate	38	41.3
	Adequate	3	3.3
Zinc intake	Inadequate	73	79.3
	Adequate	10	10.9
	Excessive	9	9.8
Thiamine intake	Inadequate	82	89.1
	Excessive	8	8.7
	Adequate	2	2.2
Riboflavin intake	Inadequate	62	67.4
	Excessive	21	22.8
	Adequate	9	9.8
Niacin intake	Inadequate	63	68.5
	Excessive	21	22.8
	Adequate	8	8.7
Vitamin C intake	Inadequate	75	81.5
	Excessive	14	15.2
	Adequate	3	3.3
Retinol intake	Inadequate	92	100
Beta-carotene intake	Inadequate	92	100
Total carotene intake	Inadequate	90	98.9
	Adequate	1	1.1
Vitamin A intake	Inadequate	69	75.0
	Excessive	18	19.6
	Adequate	5	5.4

Note: *Values are presented as mean ± SD or median (IQR) for continuous variables and n (%) for categorical variables. MMS, Multiple Micronutrient Supplementation; IFA = Iron and Folic Acid Supplementation*

With p-values of 0.033 and 0.024, respectively, a difference in calcium intake was found between the two groups (IFA and MMS). Other nutrients did not show a significant relationship. Further details are shown in **Table III**.

Table III: Relationship between nutritional intake and estimated fetal weight

Nutrient	Group (Supplement)	ANOVA p-value	Kruskal–Wallis p-value
Energy	MMS	0.854	–
	IFA	0.875	–
Protein	MMS	0.206	0.543
	IFA	0.397	0.469
Fat	MMS	0.328	0.416
	IFA	0.146	0.328
Carbohydrate	MMS	0.920	–
	IFA	0.083	–
Calcium	MMS	0.033	–
	IFA	0.024	–
Phosphorus	MMS	0.599	0.433
	IFA	0.171	0.238
Iron	MMS	0.385	–
	IFA	0.332	–
Sodium	MMS	0.303	–
	IFA	0.127	–
Potassium	MMS	0.673	–
	IFA	0.178	–
Copper	MMS	0.775	–
	IFA	0.963	–
Zinc	MMS	0.431	–
	IFA	0.632	–
Thiamine	MMS	0.317	–
	IFA	0.386	–
Riboflavin	MMS	0.958	0.681
	IFA	0.052	–
Niacin	MMS	0.472	0.388
	IFA	0.754	–
Vitamin C	MMS	0.164	–
	IFA	0.737	–
Vitamin A	MMS	0.299	–
	IFA	0.288	–

Note: MMS = Multiple Micronutrient Supplementation; IFA = Iron and Folic Acid.

Table IV shows that the Multiple Micronutrient Supplementation (MMS) group showed a significant increase in EFW (β=3383.64, p=0.027) compared to the Iron and Folic Acid (IFA) group. Maternal age (β=21.49, p=0.042) and second-trimester haemoglobin levels (β=60.43, p=0.011) also showed significant effects. However, pre-pregnancy Body Mass Index (BMI) did not show a significant effect (p=0.898). The Hosmer–Lemeshow value of the regression model indicated a good fit (p=0.68), and the Pseudo R^2 was 0.35, indicating that the model could explain 35% of the variation in EFW.

Figures 1 and 2 highlight calcium as the key nutrient influencing estimated fetal weight (EFW) in the second trimester. Excessive calcium intake was significantly associated with higher EFW, whereas inadequate intake showed a borderline effect.

Table IV: Multivariate linear regression of nutrient intake categories and estimated fetal weight (EFW) in trimester 2

Nutrient	Variable	β	SE	95% CI		p-value
				Lower	Upper	
Calcium	Inadequate vs. Adequate	1538.35	779.33	53.26	3129.96	0.038
	Excessive vs. Adequate	2404.02	796.91	776.51	4031.53	0.005
	IFA group	2937.18	1260.18	1123.11	5510.81	0.013
	MMS group	3383.64	1285.73	757.82	6009.46	0.027
	Maternal age	21.49	10.13	0.81	42.19	0.042
	Pre-pregnancy BMI	2.07	16.03	0.34	10.11	0.898
	Hb T2	60.43	22.15	15.19	105.66	0.011

Note: MMS = Multiple Micronutrient Supplementation; IFA = Iron and Folic Acid;
Hb T2 = Haemoglobin in the second trimester. Diagnostic Test
Hosmer-Lemeshow test: p=0.68 Pseudo R2 (Nagelkerke)= 0.35

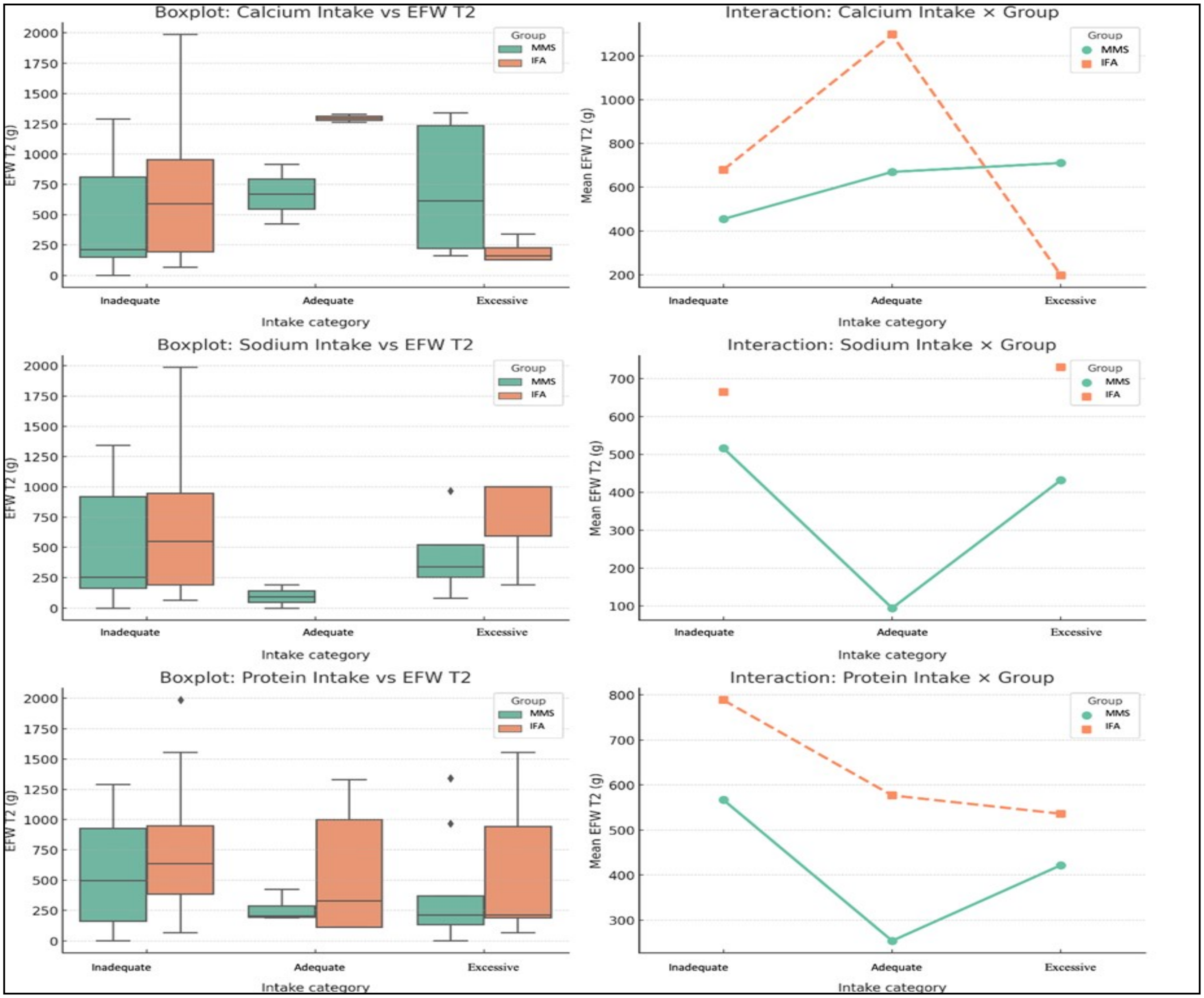

Figure 1: Relationship between nutrient intake categories and estimated fetal weight (EFW) in the second trimester, loading by supplementation group (MMS vs. IFA), as shown by boxplots (left panel) and interaction diagrams (right panel)

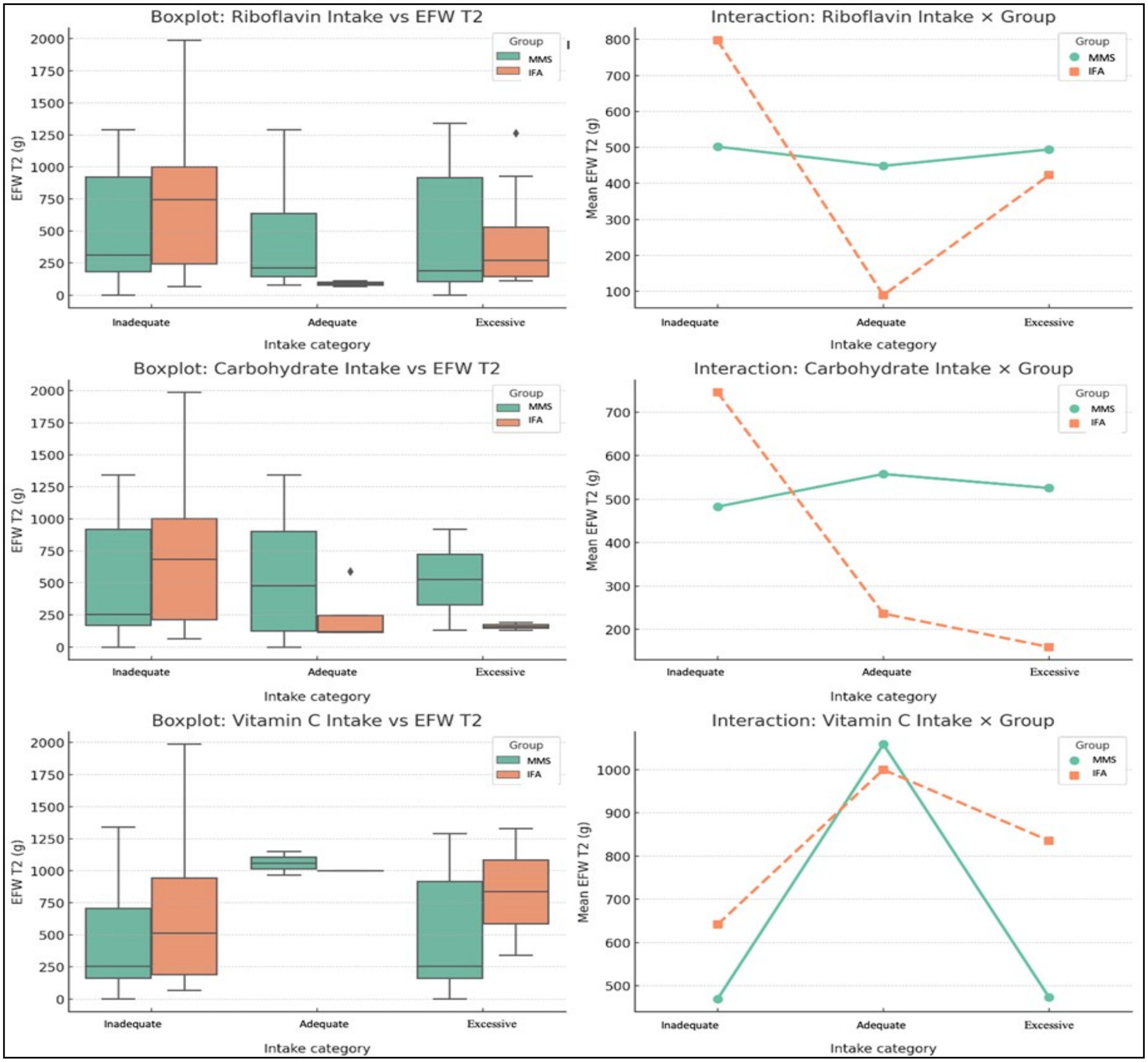

Figure 2: Stratified by supplementation group (MMS vs. IFA), boxplots (left panels) and interaction plots (right panels)

DISCUSSION

Table I shows that the study participants were at optimal reproductive age. The study findings indicated deficiencies in essential nutrients during pregnancy in both the MMS and IFA groups. This age range is generally associated with lower obstetric risk[14]. Results showed that the average haemoglobin level in pregnant women in the second trimester was approximately 11.75 g/dL. This figure indicates anemia, which can negatively impact both the mother and the fetus[15].

Nutritional deficiencies contributing to anemia, such as iron and vitamin B12 deficiency, are prevalent in this demographic, further complicating pregnancy outcomes[16]. Maintaining hemoglobin levels above 11.0 g/dL is essential, as recommended by WHO guidelines, to mitigate risks during pregnancy[17]. Furthermore, interventions addressing micronutrient deficiencies have been shown to improve hemoglobin levels, thereby enhancing maternal health and fetal development[18]. The implications of these findings underscore the need of proactive nutritional management in pregnant women, especially those with signs of anaemia.

The findings in **Table II** indicate that macro- and micronutrient deficiencies occurred in both groups. **Table II** shows that 91.3% suffered from iron deficiency, 78.3% from energy deficiency, and 54.3% from protein deficiency. It is known that the health of the fetus and mother is highly dependent on the fulfilment of these nutritional needs[19]. Malnutrition can occur for various reasons, including the placenta's inability to adequately deliver nutrients to the fetus. This, of course, is dangerous for the health of both the fetus and the mother[20]. The importance of maintaining food quality needs to be a serious concern rather than just paying attention to quantity[21]. Calcium intake has been associated with improved fetal growth, reinforcing the need of dietary supplementation to prevent adverse pregnancy outcomes such as low birth weight and preterm birth[22]. Maternal age and stable haemoglobin levels are key determinants of fetal growth, underscoring the importance of tailored nutritional interventions during this critical period[23]. Thus, a multi-faceted approach to prenatal nutrition is essential for optimizing outcomes.

Table III shows the importance of calcium intake. It is known that adequate calcium intake can increase estimated fetal weight in both groups. Previous research also showed that calcium can affect fetal growth and development[24]. A comprehensive approach to fetal nutritional intake is needed. The increase in fetal growth associated with MMS may be explained by insulin-like growth factor, which is positively affected by a healthy calcium intake, as this study shows[25].

Table IV shows that maternal age, second-trimester haemoglobin levels, and calcium intake are key factors in improving fetal development and growth. Qualitative (specific nutrient interactions) and quantitative (calorie intake) dimensions must be a shared concern to reduce the risk of preterm birth and low birth weight[26]. It is widely known that maternal diet and nutritional adequacy can improve the health index of the fetus and baby[27].

Although calcium is a key nutrient for optimal fetal growth, other nutrients, such as protein and natrium, do not show a consistent relationship across supplement groups, as demonstrated by **Figures 1 and 2**, which highlight the close relationship between nutritional needs and Exclusive Breastfeeding. The results of this nutrient effect study illustrate the importance of personalized diet recommendations in prenatal care that consider the needs of various populations and the interactions between dietary components[20]. Calcium is a crucial factor for optimal fetal growth. Previous research has also shown that low calcium intake can impact the incidence of complications and preeclampsia, especially in populations with limited food access[28].

The findings presented in **Table IV** show a significant positive association between Multiple Micronutrient Supplementation (MMS) and estimated fetal weight (EFW), with a beta coefficient (β) of 3383.64 ($p=0.027$). This indicates that, controlling for other factors, MMS is associated with a substantial increase in EFW compared to the Iron and Folic Acid (IFA) group. However, the cited references do not specifically support this claim regarding MMS and EFW. Maternal age and haemoglobin levels also significantly impact EFW, with β values of 21.49 ($p=0.042$) and 60.43 ($p=0.011$), respectively, suggesting that older maternal age and higher haemoglobin levels during the second trimester improve fetal growth outcomes. The existing literature generally supports the association between maternal age, Haemoglobin, and fetal growth, but requires specific citations that directly address these findings.

In contrast, pre-pregnancy Body Mass Index (BMI), as reflected in a β of 2.07 ($p=0.898$), did not show a significant association, suggesting that BMI may not be a dominant factor influencing EFW in this cohort. This observation is consistent with several studies showing a limited impact of BMI on fetal weight. The goodness-of-fit of the model, indicated by a Hosmer–Lemeshow p-value of 0.68 and a pseudo-R^2 of 0.35, confirms its adequacy in explaining variability in EFW outcomes. The emphasis on dietary micronutrient intake during pregnancy is noteworthy, although additional support from high-quality studies specifically documenting this association is needed.

Calcium is a critical nutrient for fetal growth and development, particularly influencing bone formation and overall fetal health. It is essential in the later stages of pregnancy, when approximately 80% of calcium transfer occurs to the fetus during the third trimester, highlighting its significant role in skeletal mineralization and in preventing pregnancy-related complications[29]. Adequate maternal calcium levels are vital, as deficiencies can lead to serious outcomes such as fetal growth restriction and preterm birth[4]. Moreover, calcium's impact extends beyond bone health; it is involved in critical physiological processes, including cell signalling and the regulation of hormonal regulation, which are integral during embryonic development and maternal adaptations throughout pregnancy. Insufficient calcium can exacerbate anemia and overall energy deficiencies, further compromising the health of both the mother and fetus[30]. Thus, addressing calcium deficiency through appropriate supplementation is paramount for ensuring optimal fetal growth and reducing the risk of adverse pregnancy outcomes.

CONCLUSION

Calcium plays a vital role in fetal growth and development. A high prevalence of micronutrient deficiencies, including iron, protein, and energy, was observed among pregnant women. Multiple micronutrient supplementation may improve fetal growth outcomes compared to iron–folic acid supplementation alone .

Ethical permission: IBN Khaldun University, Bogor, Indonesia, ERC approval letter No. 018/K.11/KEPK/ FIKES-UIKA/2025.

Conflict of interest: There is no conflict of interest between the authors.

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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Pertiwi FD: Design, Revision, analysis, approval
Prastia TN: Design, Revision, analysis, approval
Jayanti R: Design, Revision, analysis, approval
Rohmaeni Y: Design, Revision, analysis, approval

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