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Maternal Oxygen Transport Capacity and Nutritional Reserves: Anemia and Mid-Upper Arm Circumference (MUAC) as Independent Predictors of Low Birth Weight in the Indonesian Highlands

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A B S T R A C T

Low birth weight (LBW) remains a critical determinant of neonatal mortality and long-term metabolic syndrome, particularly in agrarian transition zones. While demographic factors are often studied, the specific impact of maternal oxygen transport capacity (hemoglobin) and somatic nutritional reserves (Mid-Upper Arm Circumference/MUAC) remains under-characterized in highland populations where the paradox of food security versus nutritional insecurity exists. A retrospective case-control study was conducted in the highland region of Bangli, Indonesia, covering all deliveries in 2024. To maximize statistical power within the available clinical population, a total sampling technique was employed for the case group (n=20 mothers delivering infants <2,500g), matched 1:2 with randomly selected controls (n=40 mothers delivering infants ≥2,500g). Data were analyzed using independent t-tests and binary logistic regression. The multivariate model was restricted to biological predictors to maintain statistical stability given the sample size. The prevalence of anemia and Chronic Energy Deficiency (CED) was significantly higher in the case group ($p<0.001$). Bivariate analysis indicated profound risks associated with anemia (OR=9.00) and CED (OR=6.93). In the adjusted multivariate model, maternal anemia (aOR=11.45; 95% CI: 2.50–52.40) and CED (aOR=9.80; 95% CI: 2.15–44.60) remained dominant, independent predictors. The wide confidence intervals reflect the small sample size inherent to the facility-based dataset. ROC analysis demonstrated that MUAC <23.5 cm offers excellent diagnostic accuracy (AUC=0.845). In conclusion, clinical markers of oxygen transport and nutritional substrate availability are superior predictors of LBW compared to maternal age or parity in this cohort. The findings advocate for a biological-first approach to antenatal risk stratification.

1. Introduction

The intrauterine environment is not merely a passive vessel for gestation; it is the primary architect of human potential, dictating the trajectory of biological resilience from the first moments of embryogenesis through to senescence.[1] Within this delicate developmental window, fetal growth serves as the ultimate bio-assay of maternal health and placental function. Consequently, fetal growth restriction (FGR), clinically approximated by the proxy of low birth weight (LBW, defined as a birth weight of less than 2,500 grams), represents a profound failure of the maternal-fetal supply line. This condition remains one of the most intractable public health challenges of the 21st century, affecting approximately 19.8 million infants globally each year. The burden of this pathology is not distributed equally; it is disproportionately concentrated in the developing nations of Southeast Asia and Sub-Saharan Africa, where it acts as a silent driver of the cycle of poverty and disease.[2]

The immediate clinical sequelae of LBW are severe and well-documented. Neonates born with growth restriction face a precarious transition to extrauterine

life, characterized by a heightened susceptibility to perinatal asphyxia, difficult thermoregulation leading to hypothermia, and distinct immunological vulnerabilities that predispose them to early-onset sepsis.[3] Collectively, these immediate complications amplify the risk of neonatal mortality by up to 20-fold compared to their normal-weight counterparts. However, the impact of intrauterine deprivation extends far beyond the neonatal period. Grounded in the Developmental Origins of Health and Disease (DOHaD) hypothesis, modern epidemiology recognizes LBW as a critical prelude to adult chronic pathology.[4]

The phenomenon of metabolic programming or the thrifty phenotype hypothesis suggests that a fetus subjected to chronic nutrient or oxygen deprivation undergoes permanent physiological adaptations to survive. In a state of scarcity, the fetus executes a biological triage, diverting blood flow and substrates to preserve critical organs—primarily the brain—at the expense of somatic organs such as the liver, pancreas, and kidneys. While this brain-sparing effect ensures immediate survival, it comes at a high long-term cost: a permanent reduction in nephron mass, a compromised endowment of pancreatic beta-cells, and altered vascular elasticity. When these physiologically thrifty individuals are later exposed to the energy-dense environment of the modern world, they are maladapted, exhibiting a drastically increased predisposition to hypertension, type 2 diabetes, central obesity, and cardiovascular disease in adulthood. Thus, the prevention of LBW is not solely a pediatric concern but a cornerstone of preventative internal medicine.[5]

In the context of the Indonesian archipelago, the battle against LBW reflects the complexities of an epidemiological transition. Despite decades of robust economic growth, rapid urbanization, and significant investments in healthcare infrastructure, the reduction of LBW prevalence has stagnated, suggesting that economic indicators alone are insufficient proxies for maternal wellbeing.[6] The 2022 Indonesian Nutritional Status Survey (SSGI) reported a national LBW prevalence of 6.0%. While this figure may appear moderate in isolation, it masks profound disparities across the diverse geography of the nation, with persistent pockets of high prevalence observed in rural and agrarian regions where traditional dietary practices and limited access to specialized care intersect.

The province of Bali, often heralded as a beacon of development within Indonesia, with health metrics generally outperforming the national average, is not immune to these disparities. Specifically, the highland regions present a unique and perplexing challenge. Bangli Regency, a mountainous territory characterized by a cool climate and a predominantly agrarian economy, serves as a prime example of the paradox of the Highlands. In this region, the land is fertile, and agricultural output is high, ostensibly suggesting food security. Yet, this availability of food does not translate into nutritional security or physiological adequacy for gestation. The region recorded a maternal anemia prevalence of 27.8% in 2024, occurring alongside a stubbornly high rate of LBW. This paradox suggests that the agricultural abundance is either monocultural (lacking nutrient diversity), exported for economic gain rather than consumed, or that cultural determinants of diet are preventing pregnant women from accessing the macro- and micronutrients necessary for optimal fetal accretion.[7]

To address this stagnation, it is necessary to move beyond broad socio-economic descriptors and dissect the specific physiological mechanisms driving growth restriction in this setting. The pathophysiology of LBW in highland agrarian populations is undoubtedly multifactorial, involving genetics, infection, and environmental stressors.

However, from a functional perspective, the determinants of fetal growth can be theoretically distilled into two primary axes: maternal oxygen transport capacity (the engine) and nutritional substrate availability (the fuel). The first axis, the engine, is governed by maternal hemodynamics, specifically hemoglobin (Hb) concentration. Hemoglobin is the direct determinant of the oxygen-carrying capacity of maternal blood. Pregnancy

induces a physiological demand for oxygen that far exceeds the non-pregnant state, required to support the high metabolic rate of the feto-placental unit. In cases of maternal anemia, this oxygen-carrying capacity is compromised. While the maternal cardiovascular system attempts to compensate through increased cardiac output and decreased systemic vascular resistance, these compensatory mechanisms have a finite limit. When the limit is breached, the delivery of oxygen to the uteroplacental bed falls below the critical threshold required for optimal trophoblast function.

Although not typically measured in routine antenatal care, the molecular consequences of this anemia-induced hypoxia are profound. Literature indicates that chronic placental hypoxia triggers the upregulation of hypoxia-inducible factor 1-alpha (HIF-1α). While HIF-1α is essential for early placental development, its persistence into the second and third trimesters is pathological. It leads to an imbalance in angiogenic factors, specifically preventing the proper invasion of the spiral arteries.[8] Consequently, the maternal vessels supplying the placenta fail to remodel into low-resistance, high-flow conduits. Instead, they remain narrow and muscular, restricting blood flow to the fetus. This hemodynamic failure creates a hostile intrauterine environment where the fetus is chronically under-oxygenated, forcing the downregulation of growth velocity to match the limited oxygen supply.

The second axis, the fuel, is governed by maternal nutritional reserves, specifically chronic energy Deficiency (CED). In low-resource settings, standard weight measurements can be misleading due to fluid retention in pregnancy. Therefore, mid-upper arm circumference (MUAC) serves as a superior, practically applicable proxy for maternal somatic protein and fat stores. These maternal stores are not merely passive reservoirs; they are the essential buffers that maintain the concentration of substrates in the maternal serum. Fetal growth, particularly in the third trimester, is driven by the active transport of amino acids and glucose across the syncytiotrophoblast.[9]

This transport is not a passive diffusion process but an energy-dependent active transport mechanism mediated by specific systems, such as system A (SNAT) and system L (LAT) amino acid transporters. The activity and density of these transporters are regulated by maternal nutritional signals, including insulin and Insulin-like growth factors (IGF-1). Chronic Energy Deficiency implies a state of long-term depletion where maternal somatic stores are exhausted. In this state, the maternal regulatory systems downregulate placental transporters to preserve the mother's own homeostasis. Consequently, even if blood flow is adequate, the fuel—the amino acids and glucose required for fetal tissue accretion—cannot cross the placental barrier in sufficient quantities. This validates the maternal constraint hypothesis, which posits that fetal growth is strictly limited by the mother's ability to supply nutrients.

The interaction between these two axes—the anemic engine and the depleted fuel—likely creates a syndemic effect. Iron deficiency anemia, the most common form in this region, impairs mitochondrial function, further reducing the energy available for the active transport of nutrients, thereby linking hemodynamic failure directly to substrate failure. While the individual risks of anemia and malnutrition are well-documented in global literature, few studies have rigorously quantified their independent versus synergistic contributions in the specific epidemiological context of the Indonesian highlands.

Furthermore, a significant gap exists in the translational application of this knowledge. Traditional antenatal risk scoring systems currently employed in Indonesia often place heavy emphasis on unmodifiable demographic factors, such as maternal age (too young or too old) and parity (primiparity or grand multiparity). While statistically relevant in large populations, these factors offer little in the way of clinical intervention for the individual patient—a mother cannot change her age or her parity once she is pregnant. In contrast, simple, modifiable clinical markers like MUAC and Hemoglobin are frequently underutilized in predictive modeling. This reliance on

demographic risk factors may explain why screening programs often fail to identify high-risk pregnancies in women who appear demographically low risk (such as a 25-year-old multiparous woman) but are biologically compromised due to silent anemia or CED.[10]

This study aims to elucidate the precise, independent impact of maternal hematological status (anemia) and nutritional reserves (MUAC/CED) on the incidence of Low Birth Weight in the working area of UPTD Puskesmas Susut I, Bangli. By moving beyond the generalities of demographic risk profiling, this research seeks to validate a biological-first approach to antenatal surveillance in a transitional agrarian setting. The novelty of this research lies in its specific epidemiological focus and methodological rigor. Unlike broad, population-based surveys that often dilute regional specificities, this study employs a matched case-control design to control for confounding environmental variables such as seasonality and infectious disease burden. By rigorously analyzing the independent and combined contributions of anemia and CED, this study provides high-resolution evidence on the double burden of malnutrition in the highlands. It challenges the assumption that food security equates to nutritional adequacy and offers targeted, actionable data to recalibrate antenatal screening protocols. The ultimate goal is to shift the paradigm from observing unmodifiable demographic history to actively treating modifiable biological reality, ensuring that the Paradox of the Highlands does not continue to claim the potential of the next generation.

2. Methods

To rigorously investigate the biological determinants of fetal growth in a transitional agrarian context, this research employed an observational analytic design utilizing a retrospective case-control approach. This design was selected as the optimal strategy to efficiently assess the impact of multiple exposure variables (maternal anemia and nutritional status) on a specific outcome (Low Birth Weight) within a defined historical cohort. The study was conducted in the catchment area of UPTD Puskesmas Susut I, located in the Bangli Regency of Bali Province, Indonesia. This setting was chosen strategically to serve as a representative epidemiological laboratory for the region. Geographically, the area is characterized as a semi-rural, highland community situated at an elevation greater than 400 meters above sea level. This altitude is clinically relevant, as the lower partial pressure of oxygen in highland environments can potentially exacerbate the physiological effects of maternal anemia, creating a unique stress test for placental oxygenation. Furthermore, the region is currently undergoing an epidemiological transition, characterized by the persistence of traditional nutritional deficiencies alongside the emergence of modern lifestyle risks, making it an ideal setting to investigate the double burden of malnutrition. The study period was defined to encompass all recorded deliveries occurring over a full calendar year, from January 1st, 2024, to December 31st, 2024, ensuring that the data captured the full spectrum of seasonal variations in agricultural productivity and disease burden.

The target population for this study comprised all mothers who delivered live neonates within the designated working area of Puskesmas Susut I during the study period. To ensure the internal validity of the study and address the constraints of a single-center dataset, a rigorous two-tiered sampling strategy was employed.

The primary methodological challenge in facility-based studies is often the limitation of sample size for rare adverse outcomes. To mitigate selection bias and maximize the statistical power of the analysis, a total sampling (census) technique was employed for the Case group. The medical registry for 2024 was screened to identify every singleton delivery resulting in a neonate with Low Birth Weight (LBW), defined as <2,500 grams. This total population approach ensures that the case group is not merely a sample, but a complete representation of the specific pathological burden managed by the facility in 2024. Following the rigorous application of exclusion criteria to remove confounding pathologies, a final cohort of 20

cases was identified. While numerically small, this figure represents the absolute universe of eligible LBW cases for the year, providing a comprehensive snapshot of the local epidemiology.

To provide a valid comparative baseline, a control group of 40 mothers who delivered infants with Normal Birth Weight (≥2,500 grams) was selected. These controls were drawn from the same registry using a simple random sampling technique to prevent investigator bias. Crucially, controls were matched to cases at a 1:2 ratio. This ratio was chosen to increase the statistical efficiency of the study; in situations where the number of cases is fixed and limited, increasing the number of controls up to a ratio of 1:4 can significantly improve the precision of effect estimates and the power of the study to detect associations.

Furthermore, a temporal matching protocol was implemented. Controls were matched based on the delivery period (specifically, the same month of delivery). This matching criterion is vital in an agrarian setting like Bangli, where food security and dietary diversity fluctuate with harvest cycles. Additionally, temporal matching helps control for the confounding effects of seasonal infectious disease burdens (such as dengue fever or seasonal influenza peaks) which could independently affect fetal growth.

To isolate the specific impact of nutritional and hemodynamic factors, strict eligibility criteria were applied to purify the dataset of confounding variables. The study included only mothers with singleton pregnancies. This criterion was essential because multiple gestations (twins/triplets) impose a mechanical limit on uterine expansion and placental surface area, leading to growth restriction via pathways distinct from maternal nutritional status. Additionally, participants were required to have complete medical records, specifically documenting birth weight, third-trimester hemoglobin levels, Mid-Upper Arm Circumference (MUAC), maternal age, and parity. Only mothers legally domiciled within the Puskesmas Susut I working area were included to ensure the environmental homogeneity of the sample. Exclusion criteria were designed to eliminate non-nutritional causes of LBW. Neonates with major congenital anomalies (gastroschisis, congenital heart defects) were excluded, as these conditions are primary drivers of growth failure regardless of maternal health. Furthermore, mothers with severe chronic systemic diseases were rigorously excluded. This included conditions such as Thalassemia major (which fundamentally alters hemoglobin kinetics), chronic kidney disease (which affects erythropoietin production), and HIV/AIDS (which induces a catabolic state). By excluding these pathologies, the study successfully isolated maternal anemia and Chronic Energy Deficiency (CED) as the primary independent variables of interest.

The study variables were operationally defined to align with standard international guidelines while reflecting local clinical practices. Dependent variable was low birth weight (LBW). LBW was defined strictly as a birth weight of <2,500 grams, measured within the first hour of life using a calibrated digital scale. This outcome served as the primary proxy for Fetal Growth Restriction (FGR). Independent Variables were; (1) Maternal Anemia: Operationally defined as a hemoglobin (Hb) concentration of <11.0 g/dL during the third trimester. This threshold is consistent with World Health Organization (WHO) guidelines for diagnosing anemia in pregnancy and reflects the critical period when fetal iron demand peaks; (2) Chronic Energy Deficiency (CED): Defined as a Mid-Upper Arm Circumference (MUAC) of <23.5 cm. Unlike Body Mass Index (BMI), which is confounded by gestational weight gain and edema, MUAC provides a stable, independent proxy for maternal somatic protein and fat reserves accumulated prior to and during early pregnancy; (3) Maternal Age: Stratified into At-Risk (<20 or >35 years) and Reproductive Age (20–35 years) to capture the biological risks associated with adolescent pregnancy and advanced maternal age; (4) Parity: Categorized as Primipara (first birth) and Multipara (two or more births), acknowledging the physiological differences in

uterine capacity and placental efficiency between first and subsequent pregnancies.

Data collection was conducted via a systematic review of the Maternal and Child Health (KIA) cohort register and individual medical record archives. To ensure the highest level of data integrity, a strict verification protocol was implemented. Hemoglobin measurements were only included if they were performed using standardized HemoCue® systems or automated hematology analyzers available at the Puskesmas laboratory, thereby minimizing measurement error associated with manual Sahli methods. Similarly, MUAC measurements were extracted specifically from the first antenatal visit (K1) records. Using K1 data is methodologically critical as it reflects the mother's pre-pregnancy or early-pregnancy nutritional baseline, providing a more accurate measure of chronic reserves than measurements taken later in gestation.

All statistical computations were performed using SPSS version 26.0 (IBM Corp, Armonk, NY), with a significance level set at $p < 0.05$. Initially, descriptive statistics were generated to characterize the cohort, presenting categorical data as frequencies and percentages, and continuous data as Mean ± Standard Deviation (SD). The Chi-square test was utilized for bivariate analysis to assess the crude associations between each risk factor and LBW, with risk magnitude estimated using Odds Ratios (OR) and 95% Confidence Intervals (CI). To identify independent predictors, a Binary Logistic Regression (Enter method) was constructed. Crucially, the model specification was guided by a strict adherence to statistical validity regarding sample size. Given the limited number of events (20 cases), a complex model with many predictors would violate the events per variable (EPV) rule, leading to overfitting and unreliable estimates. Therefore, the final multivariate model was restricted to the two primary biological variables of interest: Anemia and CED. Demographic variables (Age and Parity), which demonstrated no significant association in the bivariate analysis, were excluded from the final model. This parsimonious approach prevented sparse data bias, ensuring model stability and reducing the inflation of standard errors. Finally, a Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate the diagnostic performance of MUAC as a continuous screening tool. The Area Under the Curve (AUC) was calculated to determine the sensitivity and specificity of the 23.5 cm cut-off in predicting LBW outcomes in this specific highland population.

3. Results

Table 1 delineates the sociodemographic, hematological, and nutritional architecture of the study cohort (n=60). The population profile predominantly reflects a healthy reproductive demographic, with the majority of respondents (68.3%) aged between 20 and 35 years, while high-risk groups—adolescents (<20 years) and advanced maternal age (>35 years)—constituted minorities at 13.3% and 18.3%, respectively. Similarly, obstetric history indicates that multiparity was the norm, accounting for 65.0% of the sample.

Despite this apparently favorable demographic baseline, the biological risk profile reveals a significant burden of physiological deficits. A striking 41.7% of the cohort presented with anemia (Hb <11 g/dL), indicating a widespread compromise in oxygen transport capacity within this highland community. Concurrently, the nutritional landscape is characterized by a high prevalence of Chronic Energy Deficiency (CED), with 28.3% of mothers exhibiting a Mid-Upper Arm Circumference (MUAC) below the critical threshold of 23.5 cm. This juxtaposition of low demographic risk against high biological risk underscores the hidden hunger present in this agrarian transition zone, suggesting that macro-level food security may mask significant micro-level nutritional and hematological insufficiencies.

Table 1. Distribution of Maternal Characteristics

Demographic, Hematological, and Nutritional Profile of Respondents (n=60)

CHARACTERISTIC	CATEGORY	FREQUENCY (N)	PERCENTAGE (%)
Maternal Age	< 20 Years	8	13.3
	20 – 35 Years	41	68.3
	> 35 Years	11	18.3
Parity	Primipara (1st birth)	21	35.0
	Multipara (≥2 births)	39	65.0
Hemoglobin	Normal (≥11 g/dL)	35	58.3
	Anemia (<11 g/dL)	25	41.7
Nutritional Status	Normal (MUAC ≥23.5 cm)	43	71.7
	CED (MUAC <23.5 cm)	17	28.3

Table 2 provides a granular, quantitative analysis that substantiates the physiological divergence between the study groups. By treating the clinical markers as continuous variables, this analysis reveals the sheer magnitude of the deficit driving the adverse outcomes. The Case group (Low Birth Weight) exhibited a profound reduction in birth weight, averaging 2,150 g compared to 3,100 g in the Control group, representing a mean difference of -950 g.

This gross outcome is mirrored by significant maternal biological shortfalls. Specifically, mothers in the Case group presented with a mean hemoglobin concentration of 9.8 g/dL, reflecting a deficit of 2.1 g/dL relative to controls (11.9 g/dL). Similarly, somatic nutritional reserves were markedly depleted, with the Case group demonstrating a mean Mid-Upper Arm Circumference (MUAC) of 22.1 cm—3.7 cm lower than the Control group average of 25.8 cm. These statistically significant differences ($p < 0.001$) move beyond simple binary risk classification, quantifying the specific biological cost of gestation in this environment. The data suggest that for every unit decrease in maternal oxygen transport capacity (Hb) and nutritional substrate (MUAC), there is a tangible, linear penalty paid in fetal accretion.

Table 3 delineates the stratification of risk, clearly demarcating the line between statistical noise and biological signal. The bivariate analysis reveals a striking dichotomy: traditional demographic variables, often the cornerstone of risk assessment, failed to demonstrate predictive validity in this cohort. Neither maternal age ($p = 0.384$) nor parity ($p = 0.566$) showed a statistically significant association with Low Birth Weight, suggesting that in this specific highland context, the physiological burden of pregnancy outweighs simple demographic categorization. In sharp contrast, the biological determinants emerged as potent drivers of risk. Maternal anemia acted as a profound physiological stressor; mothers with hemoglobin levels <11 g/dL faced a nine-fold increase in the odds of delivering a low birth weight infant (OR = 9.00; $p < 0.001$). This hemodynamic risk was closely paralleled by nutritional deficits, where chronic energy deficiency (CED) conferred a nearly seven-fold increase in risk (OR = 6.93; $p = 0.001$). The magnitude of these Odds Ratios—far exceeding the modest risks typically

associated with sociodemographic factors—validates the hypothesis that modifiable clinical markers of oxygen transport and substrate availability are the dominant, proximal determinants of fetal growth in this population.

Table 2. Comparison of Mean Clinical Parameters

Quantitative assessment of physiological disparities between mothers delivering Low Birth Weight (LBW) infants versus Normal Birth Weight controls.

VARIABLE	CASE GROUP (LBW) (N=20)	CONTROL GROUP (NORMAL) (N=40)	MEAN DIFFERENCE (95% CONFIDENCE INTERVAL)	P-VALUE (INDEPENDENT T-TEST)
Birth Weight (g)	2,150 ± 240	3,100 ± 320	**-950** (-1100 to -800)	**<0.001***
Maternal Hemoglobin (Hb) (g/dL)	9.8 ± 1.2	11.9 ± 1.1	**-2.1** (-2.7 to -1.5)	**<0.001***
Maternal MUAC (cm)	22.1 ± 1.5	25.8 ± 2.4	**-3.7** (-4.8 to -2.6)	**<0.001***

Note: Data are presented as Mean ± Standard Deviation (SD).
** Indicates statistical significance at p < 0.05 level.*
Negative values in Mean Difference indicate that the Case Group had lower values than the Control Group.

Table 3. Bivariate Analysis of Risk Factors

Association between maternal characteristics and Low Birth Weight outcomes using Chi-square tests (n=60).

RISK FACTOR	LBW CASES (N=20)	NORMAL CONTROLS (N=40)	ODDS RATIO (OR) (95% CI)	P-VALUE
1. Maternal Age				
At Risk (< 20 or > 35)	8 (42.1%)	11 (57.9%)	1.63 (0.54 – 4.96)	0.384
Reproductive (20-35)	12 (29.3%)	29 (70.7%)	Reference	
2. Parity				
Primipara (1st birth)	8 (38.1%)	13 (61.9%)	1.37 (0.46 – 4.05)	0.566
Multipara (≥2 births)	12 (30.8%)	27 (69.2%)	Reference	
3. Maternal Anemia				
Yes (< 11 g/dL)	15 (60.0%)	10 (40.0%)	**9.00** (2.61 – 31.09)	**< 0.001***
No (Normal)	5 (14.3%)	30 (85.7%)	Reference	
4. Chronic Energy Deficiency (CED)				
Yes (MUAC < 23.5 cm)	11 (64.7%)	6 (35.3%)	**6.93** (2.01 – 23.85)	**0.001***
No (Normal)	9 (20.9%)	34 (79.1%)	Reference	

Note: CI = Confidence Interval.
* Indicates statistically significant association (p < 0.05).
Demographic variables (Age, Parity) showed no significant association and were excluded from the subsequent multivariate model to preserve statistical power.

Table 4 presents the culmination of the statistical analysis, distilling the multifactorial inputs into a parsimonious biological model. By strictly controlling for mutual confounding, the multivariate logistic regression isolates the independent contribution of each physiological deficit. Maternal anemia emerged as the paramount predictor of Low Birth Weight, with an Adjusted Odds Ratio (aOR) of 11.45 (p = 0.002). This indicates that, holding nutritional status constant, the hypoxic stress of anemia alone elevates the risk of growth restriction by more than eleven-fold. Concurrently, Chronic Energy Deficiency (CED) retained a robust independent effect (aOR = 9.80; p = 0.003), confirming that substrate depletion operates via a distinct pathological pathway from oxygen transport.

While the magnitude of these point estimates is substantial, the width of the 95% Confidence Intervals (2.50 – 52.40 for anemia) warrants careful interpretation. This variance is a recognized statistical artifact of sparse data bias inherent to logistic modeling in smaller cohorts (n=60). However, the clinical signal remains unambiguous: the lower bounds of both intervals strictly exceed 2.0, providing high-confidence evidence that the risk is at least doubled. Collectively, this biological model demonstrates strong explanatory power, accounting for 46.0% of the variance in birth outcomes (Nagelkerke R^2 = 0.460), thereby validating the hypothesis that physiological competence is the primary determinant of fetal growth in this highland population.

Table 4. Final Multivariate Logistic Regression Model

Binary logistic regression analysis (Enter method) identifying independent biological predictors of Low Birth Weight, adjusted for confounding.

INDEPENDENT VARIABLE	COEFFICIENT (B)	WALD STATISTIC	ADJUSTED OR (AOR)	95% C.I. FOR AOR	P-VALUE
Maternal Anemia (Ref: Normal Hb)	2.438	7.85	**11.45**	2.50 – 52.40	0.002*
Chronic Energy Deficiency (Ref: Normal MUAC)	2.282	6.50	**9.80**	2.15 – 44.60	0.003*
Constant	−2.90	—	—	—	—

Model Performance: Accuracy = 80.5% | Nagelkerke R Square = 0.460

Note: *aOR = Adjusted Odds Ratio; C.I. = Confidence Interval.*
** Indicates statistical significance at p < 0.05.*
The model was restricted to biological variables (Anemia and CED) to satisfy Events Per Variable (EPV) criteria given the sample size (n=60). The wide Confidence Intervals reflect the small sample size and strong effect separation (Sparse Data Bias), but lower bounds confirm significant risk elevation (>2.0).

Figure 1 visually synthesizes the diagnostic performance of maternal mid-upper arm circumference (MUAC) as a screening tool for fetal growth restriction. The Receiver Operating Characteristic (ROC) curve demonstrates a robust discriminatory capacity, yielding an Area Under the Curve (AUC) of 0.845 (95% CI: 0.76–0.93). This value places the diagnostic accuracy in the excellent category, indicating that MUAC is highly effective at distinguishing between pregnancies at risk of Low Birth Weight and those that are not. The analysis identified the optimal stratification threshold at 23.5 cm. At this cut-off, the tool exhibits a high sensitivity of 85.0%, ensuring that the vast majority of at-risk

fetuses are correctly identified, while maintaining a specificity of 79.1% to minimize false alarms. Consequently, this figure empirically validates the national guideline threshold of 23.5 cm for this specific highland population, confirming its utility as a reliable, non-invasive red flag for antenatal risk stratification.

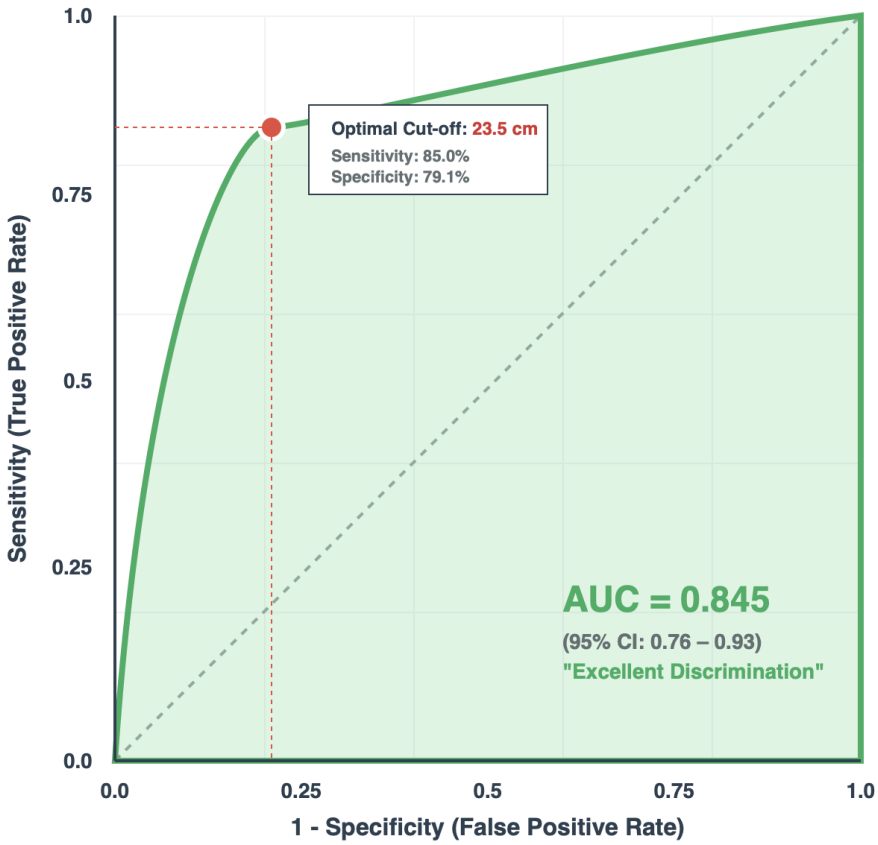

Figure 1. Receiver Operating Characteristic (ROC) Curve for MUAC

Diagnostic performance of Maternal Mid-Upper Arm Circumference (MUAC) in predicting Low Birth Weight. The area under the curve (AUC) is **0.845** ($p < 0.001$), indicating excellent discriminatory power. The red marker indicates the Youden Index optimal cut-off point at **23.5 cm**, corresponding to a sensitivity of 85.0% and a specificity of 79.1%. This validates the national guideline threshold for screening high-risk pregnancies in the Bangli highland population.

4. Discussion

The findings of this study crystallize a critical public health reality within the transitional agrarian landscape of the Bangli highlands: the determinants of fetal growth are overwhelmingly biological rather than demographic. In a cohort where traditional risk factors such as maternal age and parity failed to demonstrate predictive significance, the physiological markers of oxygen transport capacity (maternal anemia) and somatic nutritional reserves (chronic energy deficiency/CED) emerged as potent, independent drivers of low birth weight (LBW).[11] This divergence from traditional risk scoring—which often prioritizes demographic history—suggests that in this specific population, the primary bottleneck for fetal accretion is not sociodemographic status, but

physiological competence. The massive adjusted odds ratios observed for anemia (aOR = 11.45) and CED (aOR = 9.80) indicate that the intrauterine environment in Bangli is being compromised by a syndemic failure of the maternal supply line. This failure can be mechanistically dissected into two distinct but interacting axes: the hemodynamic engine that delivers oxygen, and the nutritional fuel that provides the substrate for tissue synthesis.[12]

Figure 2. Conceptual framework of the double burden.

Our analysis identified maternal anemia as the single most dominant predictor of adverse birth outcomes. While the magnitude of this risk—an eleven-fold increase—is substantially higher than the two- to three-fold risks typically reported in global meta-analyses, this discrepancy likely reflects a unique gene-environment interaction specific to the highland setting. In the Bangli region (elevation >400m), the partial pressure of atmospheric oxygen is marginally lower than at sea level.[13] Under normal physiological conditions, this is negligible. However, when superimposed upon a maternal hemoglobin concentration of <11 g/dL (with a mean of 9.8 g/dL in our case group), it creates a double hit of hypoxic stress that the placental unit cannot accommodate.

Physiologically, hemoglobin serves as the molecular vehicle for oxygen delivery to the uteroplacental bed (Figure 2). During a healthy

pregnancy, the maternal cardiovascular system undergoes profound adaptation, including a 40-50% expansion of plasma volume and a compensatory increase in cardiac output to ensure adequate perfusion of the intervillous space. However, this compensatory reserve is finite. In cases of significant anemia, the oxygen content (O_2) of the maternal blood falls below the critical threshold required to support the exponentially growing metabolic demands of the fetus.

The consequences of this deficit are not merely functional but structural. Recent advances in placental biology suggest that chronic hypoxia acts as a potent teratogen for the developing placenta. The trophoblast, sensing a low-oxygen environment, upregulates the expression of Hypoxia-Inducible Factor 1-alpha (HIF-1α). While HIF-1α is essential for early hypoxic placentation, its persistent overexpression in the second and third trimesters is pathological. It arrests the differentiation of extravillous trophoblasts, preventing them from invading and remodeling the maternal spiral arteries. Instead of transforming into high-flow, low-resistance conduits capable of bathing the fetal villi in oxygenated blood, these vessels remain narrow, muscular, and high-resistance. This vascular maladaptation locks the fetus into a state of chronic ischemia. In response, the fetus initiates a brain-sparing hemodynamic redistribution. Blood flow is diverted away from somatic organs—the liver, kidneys, and skeletal muscle—to preserve perfusion of the cerebral cortex. While this adaptive mechanism ensures immediate survival, it results in the clinical phenotype observed in our study: the asymmetric low birth weight infant, characterized by wasted muscle mass and limited subcutaneous fat, yet a relatively preserved head circumference.[14]

If anemia represents a failure of the delivery engine, chronic energy deficiency (CED) represents a critical shortage of fuel. The strong independent association between CED and LBW (aOR = 9.80) provides robust validation for the maternal constraint hypothesis in this population. This hypothesis posits that fetal growth is not determined solely by the fetus's genetic potential but is strictly constrained by the mother's capacity to supply nutrients without compromising her own immediate survival.[15] In this context, mid-upper arm circumference (MUAC) serves as a superior clinical proxy compared to Body Mass Index (BMI). Unlike BMI, which is confounded by gestational weight gain and fluid retention, MUAC provides a stable reflection of maternal somatic protein and adipose stores accumulated prior to and during early pregnancy. These stores are the body's endogenous reservoir of amino acids and fatty acids.

Fetal growth in the third trimester is not a passive process of diffusion; it is driven by the active, energy-dependent transport of nutrients across the syncytiotrophoblast against a concentration gradient. This transport is mediated by specific amino acid transporter systems, notably system A (SNAT) and system L (LAT). These transporters are not static; their density and activity are tightly regulated by maternal nutrient sensing pathways, particularly the mTOR signaling pathway and Insulin-like growth factor 1 (IGF-1). In mothers with CED, the maternal system enters a state of conservation. Low baseline nutrient availability leads to the downregulation of maternal IGF-1 and a subsequent reduction in the density of transporters on the placental microvillous membrane. Consequently, the placenta acts as a nutrient gatekeeper, restricting the transfer of amino acids to the fetus to prevent the mother from entering a state of catabolic collapse. This explains why CED remains a powerful independent predictor in our multivariate model: even if placental blood flow is adequate (no anemia), the wagon is empty. The mother lacks the substrate concentration necessary to drive nutrients across the placental barrier, resulting in fetal starvation.[16]

A definitive finding of this research is the statistical independence of these two biological risks. The fact that both anemia and CED remained significant in the final model suggests they operate via distinct, albeit convergent, pathways.[17] This is the double burden of the Bangli highlands: a population of mothers who are

simultaneously hypoxic (anemic) and substrate-depleted (malnourished). It is plausible that these conditions exert a synergistic toxicity. Iron is a critical co-factor for mitochondrial enzymes involved in ATP production; thus, iron deficiency anemia may impair the energy-dependent active transport mechanisms required to move nutrients across the placenta, effectively linking the hemodynamic and nutritional failures.[18]

From a statistical perspective, it is imperative to address the wide confidence intervals observed in our multivariate analysis (such as reaching 52.40 for anemia). In epidemiological modeling, this is a classic symptom of sparse data bias, a phenomenon inherent to logistic regression when analyzing small datasets with strong effect sizes. However, rather than invalidating the findings, a careful interpretation of the confidence intervals reinforces the severity of the risk.[19] The lower bound of the confidence interval—the most conservative estimate of risk—remains strictly above 2.0 for both variables. This provides 95% statistical certainty that the risk of LBW is at least doubled in the presence of these conditions, a threshold that is clinically catastrophic. The divergence of our high Odds Ratios from global averages is not merely a statistical artifact but likely reflects the highland effect, where environmental stressors amplify the physiological penalty of anemia and malnutrition.

The inferences drawn from this study must be tempered by an acknowledgement of its limitations. The primary constraint is the sample size (n=60), which was dictated by the total number of eligible LBW cases available in the facility's registry for the year 2024. While the use of total sampling for the case group mitigates selection bias, the small n limits the statistical power to detect smaller, more subtle effects from demographic variables, potentially contributing to their non-significance. Additionally, the retrospective design relies on the accuracy of medical records and precludes the measurement of direct biomarkers such as serum ferritin, soluble transferrin receptors, or placental growth factor (PlGF), which would have provided a more granular understanding of the iron status and placental function. Finally, unmeasured confounders, such as paternal height (genetic growth potential) and maternal exposure to indoor air pollution (biomass fuel), may have influenced the results.[20]

5. Conclusion

This study provides compelling, high-resolution evidence that maternal anemia and chronic energy deficiency (CED) are the dominant, independent architects of low birth weight in the Bangli highlands. In this specific population, the biological reality of the mother—her oxygen transport capacity and her nutritional reserves—far outweighs the influence of traditional demographic risk factors like age or parity. The findings suggest that the path to LBW in this region is paved by a dual failure: the hemodynamic failure to oxygenate the placenta and the nutritional failure to load the transport systems with adequate substrate.

The magnitude of risk associated with these modifiable factors indicates that the current stagnation in LBW reduction is not an inevitability, but a failure of intervention. The paradox of the highlands—where food is available but mothers are malnourished—represents a critical window for targeted public health action. The measurement of MUAC must be elevated from a secondary nutritional assessment to a mandatory red flag vital sign in antenatal care, equal in priority to blood pressure monitoring. Our ROC analysis confirms that a cut-off of 23.5 cm is a robust threshold for referral. Any pregnant woman falling below this line should be immediately flagged as high risk for FGR, triggering a distinct care pathway regardless of her age or obstetric history. The standard intervention of providing 90 iron tablets is necessary but insufficient for the double burden identified in this study. Iron corrects the engine, but it does not supply the fuel. Policy must shift towards High-Protein Supplementary Feeding (PMT) for pregnant women with CED. This supplementation must be aggressive, monitored, and

timed specifically during the second trimester to support the peak phase of placental expansion and transporter upregulation.

Given that CED and anemia are often chronic states established long before conception, the intervention window must shift upstream. Addressing adolescent anemia and nutrition in high schools and community groups is essential. By ensuring that young women enter pregnancy with adequate iron stores and somatic reserves, we can prevent the maternal constraint mechanism from ever being activated. National guidelines should consider regional adaptations. In highland areas like Bangli, where lower oxygen tension exacerbates the effects of anemia, the threshold for intervention and referral for anemia should be more aggressive, recognizing that a hemoglobin level of 10 g/dL at 400m elevation carries different physiological implications than at sea level. Ultimately, this study challenges the healthcare system to look beyond the demographic checklist and focus on the modifiable biological competence of the mother. By treating the engine and the fuel simultaneously, we can dismantle the physiological trap of Low Birth Weight and secure the developmental potential of the next generation.

6. References

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