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Associations between undernutrition and malaria infection: a case–control study from Rwanda

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Abstract

Background Undernutrition and malaria remain major global public health challenges. The relationship between nutritional status and malaria infection is complex. Better understanding of their association is needed to improve prevention and control of these health conditions. Undernutrition can be assessed by evaluating nutrient intake (macronutrient and micronutrient intake) measured through Food Frequency Questionnaire or by using indicators for chronic undernutrition, including the stunting parameter defined by the World Health Organization as child being too short for age. This study aims to investigate associations between inadequate nutrient intake or indicators for undernutrition and malaria infection.

Methods The analysis compares malaria cases diagnosed by a positive blood smear against controls composed of other malaria free people living in the same households with the cases (same household grouping). Data collection was conducted between November 2021 and December 2023 across 9 endemic districts located in all four provinces and Kigali City. Regression models were developed to investigate the association between undernutrition (i.e. inadequate nutrient intake or stunting) and malaria infection.

Results Despite numerous nutrition interventions aimed at reducing the burden of undernutrition, the dietary patterns observed in this study remain predominantly imbalanced. The food composition was predominantly made up of starchy staples, accounting for 56.7% of total energy intake. Such foods are typically rich in macronutrients but low in essential micronutrients. The findings revealed a high prevalence of micronutrient deficiency risk, with a reported risk of vitamin A, B2, B12, calcium, zinc, and selenium deficiency between 50 and 80% in the studied population. Regarding stunting, even if the percentage of severe chronic stunting was higher in malaria cases (17%) compared to controls (10,6%), the association between stunting and malaria infection was not statistically significant.

After adjusting for covariates, risk of vitamin E deficiency and risk of iron deficiency were positively associated with malaria (aOR = 7.46; 95% CI 4.43–12.58; $p < 0.001$ and aOR = 1.80; 95% CI 1.11–2.93; $p = 0.017$, respectively). Conversely, age, sex, and risk of selenium deficiency intake were inversely associated with malaria. Increasing age

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(aOR = 0.58; 95% CI 0.36–0.95; $p < 0.04$), female sex (aOR = 0.67; 95% CI 0.46–0.97; $p < 0.001$), and selenium deficiency (aOR = 0.62; 95% CI 0.43–0.91; $p = 0.013$) were all linked to lower odds of malaria infection.

Conclusions These findings highlight the critical role of nutrient imbalances in influencing malaria infections. Therefore tackling these preventable deficiencies is required through targeted strategies as guided by UNICEF conceptual framework 2020–2030. For instance, improving dietary diversity, regularly monitoring nutritional status, and establishing a comprehensive national food composition database could support such strategies. These approaches will support effective nutrition policies and interventions.

Background

Undernutrition and malaria remain major global public health concerns, particularly in low- and middle-income countries [1]. Although global undernutrition has declined by 4% over the past decade, it still contributes to half of all deaths in children under five [2–4]. Sub-Saharan Africa and South Asia bear over 90% of the burden, with East Africa showing particularly high rates of undernutrition [2, 3], ranking above the World Health Organization (WHO) cut-off of > 30% [5, 6]. Undernutrition weakens immunity and increases vulnerability to diseases such as malaria [7–9].

Indicators for chronic undernutrition include the stunting parameter, defined by the WHO as 'child being too short for age'. In Rwanda, childhood stunting has decreased from 42% in 2000 to 33% in 2020 [10, 11], yet malnutrition is a critical public health issue [9]. Contributing factors to undernutrition include maternal education, household wealth, child age, low birth weight, limited access to health services [9, 12–14], and food insecurity [15]. Despite agriculture being the main livelihood, food insecurity affects up to 35% of households in some areas, especially in the Western Province [16], due to recurrent flooding and limited dietary diversity [15]. Globally, food security access to safe nutritious food remains a challenge, with over 820 million people affected by food insecurity in 2018 [17, 18]. Climate change, conflict, and economic instability are primary drivers [2, 19, 20]. Food insecurity affects human and planetary health and must be tackle through better food system governance to meet sustainable developments goals [17, 21]. While interventions, such as increasing education, women's empowerment, and home gardening, have shown some improvements, rural diets remain heavily reliant on nutrient poor staples [22].

In addition to food access, dietary diversity plays a vital role in nutrient adequacy. Micronutrient deficiencies remain widespread, highlighting the need for stronger food policies and diversified agriculture to improve nutrition outcomes [23]. A study found that 81.8% of women in agriculture had low dietary diversity, with 22.1% affected by anaemia [23]. Interestingly, recent analysis of Rwandan staple foods such as red kidney beans, amaranth leaves, sweet potatoes, and carrots shows that they are rich in nutrients. However, the absence of comprehensive food composition table limits the development of diverse and nutritious diets [24–26].

Micronutrient deficiencies, particularly iron, vitamin A, and zinc, are common probably due to plant-based diets and are linked with poor immunity [23, 27, 28]. Although Rwanda has implemented interventions like vitamin A supplementation and micronutrient powder distribution covering 87% of children aged 6–23 months, gaps are remaining in some districts [29, 30].

Socioeconomic disparities and limited data on micronutrient intakes hinder progress toward the 2025 nutrition targets set by the World Health Assembly and Sustainable Development Goals [13, 14, 31–33]. Studies in East Africa, including Rwanda, reveal poor dietary habits among children between 6 and 23 months. Only 22% of children meet the minimum acceptable diet (MAD), and just 8.4% consume eggs regularly [32–35], despite eggs being rich in protein, energy and essential nutrient like vitamin B12, choline, selenium, and zinc [36]. Anaemia affects 36.6% of children, due to essential micronutrient deficiencies [33]. Minimum dietary diversity (MDD) is also low at 10.47% across East Africa, though Rwanda shows relatively better rates [14]. These findings highlight the urgent need for targeted nutritional interventions based on studies investigating population's micronutrient deficiencies [32, 33].

Malaria continues to be a major health threat, with 263 million cases and 597,000 deaths globally in 2023, 94% occurring in the Africa region [20, 37]. Children under five and pregnant women are most vulnerable due to weak immunity [38, 39].

Malnutrition and malaria are closely linked, with undernutrition, especially deficiencies in iron, vitamin A, and zinc, heightening the severe malaria and complications [27].

Food insecurity contributes to this vulnerability, as shown in studies from Haiti and Uganda, where it correlated with increased malaria incidence. Malnutrition weakens immune function, increasing malaria-related morbidity and mortality [40–42], while malaria can worsen nutritional deficiencies, creating a vicious cycle

[43–48]. This bidirectional relationship is particularly concerning in children, where chronic undernutrition leads to severe malaria outcomes, such as anaemia and high parasitaemia [49]. Addressing food insecurity and nutritional deficiencies may reduce malaria risk and improve child health in resource limited settings [29, 49]. Integrating culturally appropriate nutrition programs into malaria interventions is recommended [45]. While Rwanda has studied dietary habits to inform policy, no research has explored the relationship between dietary nutrient intake, nutritional status, and malaria. This study addresses that gap by examining how macronutrient intake, micronutrient intake and undernutrition indicators like stunting are related to malaria outcomes.

Methods

Study design

This case–control study was conducted in the Republic of Rwanda. The study was implemented by identifying malaria cases from the immediate notification by the case management at healthcare facilities. Then, cases were invited to voluntary participate in the study, and following their consent, the research team visit their household to collect demographic and nutrition status data of the case and their household companions. This convenience sampling strategy was employed due to the declining national incidence of malaria.

The cohort was analysed to estimate whether it is representative of the Rwandan population. Rwanda has a predominantly young demographic population, with 70.3% of its population under the age of 30, according to the Fifth Rwanda Population and Housing Census of 2022 [16, 50]. In comparison, the 2012 census reported that 78.7% of the population was under the age of 30 [51]. In the present cohort, 67.02% were under the age of 30. In this study, the age distribution is slightly lower to that observed in the general population in census 2022, 67.3% versus 70.3% for the population aged below 30 years old. This difference may be caused by the period of data collection, the recruitment method, as in the census, is the general population, while in the study, the index case is positive malaria cases. Moreover, out of the 1025 participants, only 15 were children below the age of 3 (1.5%), suggesting that this category of age was underrepresented in the present cohort and was excluded to avoid misinterpretation of the data (Fig. 1).

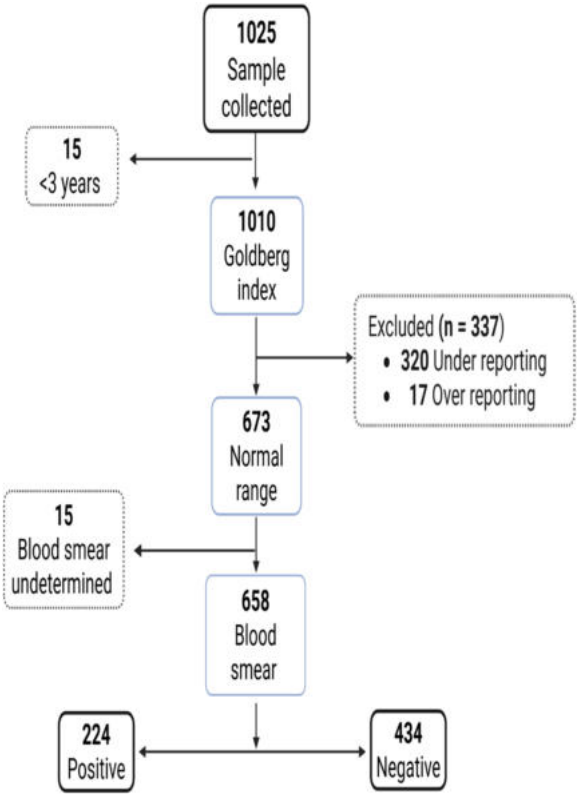

Fig. 1 Study flowchart. Participant data collection flowchart based on energy intake and malaria diagnosis validation

Study sites

Administratively, Rwanda is divided into four provinces and the City of Kigali, comprising a total of 30 districts. The majority of the population (72.1%) resides in rural areas, while nearly half of the urban population is concentrated in Kigali, the capital city. The country topography and climate change increase environmental suitability and favourable condition for the breeding and population growth of the disease vectors (mosquitoes). In Rwanda, malaria is high endemic in 11 out of 30 districts and the remaining 19 districts are prone to epidemics [52]. These areas, located in altitudes generally below 1500 m above sea level, are marked by warmer climate and are characterised by vast marshy plains [53]. Generally varying between 980 m up and 2800 m in the highland of Nyamagabe and Gicumbi. This study was conducted in nine districts of Rwanda namely Rusizi, Nyamasheke, Nyamagabe, Ruhango, Kamonyi, Bugesera, Gicumbi, Rulindo, and Gasabo spanning both urban and rural environments. The area experiences two high malaria transmission peaks associated with the dry seasons, typically observed after the rainy seasons, from November to December and May to July [54].

Participants, and samples

This study involved Western, Southern, Northern, Eastern provinces and Kigali of Rwanda, which are classified as malaria-endemic with stable transmission. A total of 1025 participants were voluntary enrolled in the study. Data collection was performed between

1st of November 2021 until December 2023, also the period encompasses three malaria peak season. Study participant recruitment took place at either a health facility (cases) or within their household (controls). This convenience sampling strategy was adopted to ensure enrolment of sufficient malaria positive participants in view of the reduction in malaria cases, thanks to robust interventions (e.g., indoor residual spraying) deployed by the government of Rwanda in targeted areas at the time of the study. Cases of malaria-infected participants were identified at district hospitals or health centres in their respective catchment areas. Control participants were selected from the same households as the cases, and were visited at their houses on the same day as cases. Case were defined as individuals who tested positive for malaria and controls were those tested negative for malaria. There were no age or gender restrictions for each group. However, to exclude participants with antimalarial, antibiotic or deworming treatments, both case and control were asked to respond either they have been given or not antimalarials, antibiotics, and/or deworming in the past 2 weeks before sample collection.

No other restrictions were considered during the period of recruitment. Upon receiving their signed consent forms, a demographic questionnaire was filled out for each participant. On the same day, for each participant, a confirmatory (for cases met in health facilities) or screening (for controls met in households) rapid diagnostic test (RDT) was performed, and blood smears were prepared for final malaria diagnosis. 1025 subjects were recruited, and the flow of study participants is displayed in Fig. 1. Children under 3 years old were excluded due to underrepresentation. After analysis of reported dietary habits to detect under reporters and over reporters using the Goldberg index, 337 participants were excluded. Then participants with adequacy between energy expenditure (EE) and energy intake (EI) were retained. Finally underdetermined blood smear analysis were excluded from the cohort and 658 participants were remaining with 224 positive as cases and 434 negative as controls (Fig. 1). All malaria positive cases were confirmed by RDT at health facilities or households and were treated in accordance with national malaria treatment guidelines by a trained surveyor. All samples were collected prior to antimalarial drugs administration.

Nutritional questionnaires and anthropometric measurements

Food intake was evaluated using a 7-day Food Frequency Questionnaire (FFQ) and a 24-h recall questionnaire. FFQ and 24 h recall questionnaires were combined to minimize error in recording data related to food items consumed and to enhance complete and accurate food recall [55]. Study participants (both cases and controls) were challenged to report their dietary habits (FFQ) as well as to recall and list all the foods and drinks they had consumed the day before (24-h recall questionnaire). Participants used visual aids provided to support recall of the portion of food consumed from "Photographic Food Atlas for Kenyan adolescents (9–14 years)" to evaluate the serving sizes of various foods, both for the FFQ and 24 h recall. For the FFQ, four categories of consumption frequency were checked for each food item: never or rarely, 1–3 times per week, 4–7 times per week. Information related to the frequency of the food consumed per day was noted either once or twice per day, and 3 times per day. The total quantities of items consumed by study participants were recorded per 7 days. To obtain daily quantities, recorded amounts were divided by 7 before multiplying the result by the number of times the food item was consumed during the week. FFQ was used to estimate energy intake as well as macronutrients and micronutrients consumption. To convert the quantities of each food consumed in nutrients (macronutrients and micronutrients), a Rwanda Food Composition Table (FCT) was established based on the West Africa FCT 2019 and supplemented with the Kenya FCT 2018. Finally, the 7th edition of the Belgian FCT 2022 was used to complete the Rwanda FCT with a few items that were not present in the two previously mentioned tables. The West Africa FCT 2019 and Kenya FCT 2018 were chosen based on the closest proximate in food items and preparation for any given food composition. Thereafter, the Rwanda FCT generated was used to assess the macronutrients content of each food (protein (g), lipids (g), carbohydrates (g) and fibers (g)) that allowed to calculate energy intake (kcal). Micronutrients minerals intake (calcium, copper, iron, phosphorus, selenium, zinc) and vitamins intake (vitamin A, vitamin B2, vitamin B6, vitamin B9, vitamin B12, vitamin C, vitamin D, vitamin E) were also evaluated from the FFQ data using the Rwanda FCT.

To estimate the energy requirements of the participants, Basal Metabolic Rate (BMR) defined as the energy expended at rest based on weight, height, age, and sex, was calculated using Henry formulas [56]. This equation encompasses energy expenditure due to body maintenance for essential physiological functions at rest [57]. In addition, Physical Activity Level (PAL) was attributed to each participant based on age, and activity categories using estimation based on high activity level related to farming, walking long distance since over 70% of the population lives in rural areas. Therefore these PAL values were used: 1,4 from 1 to 3 years old; 1,6 from 4 to 9 years; 1,8 from 10 to 17 years old, 1.8 for adult above 18 years old up to 64 years; and 1.4 above 65 years as the

retirement age is at 65 years old where activity level is considered as reduced. All those PALs were attributed to the different age categories based on criteria mentioned above. Then, the total energy requirement was estimated considering both BMR and physical activity level (PAL) by multiplying the participant's basal metabolic rate by their level of physical activity.

Then, Goldberg index cut-offs were used to identify under-reporters and over-reporters of energy intake by considering BMR and PAL. This validation using the Goldberg index is based on the fundamental principle that, energy intake matches energy expenditure when body weight is maintained stable [58].

The BMI was calculated by dividing the participant's weight (in kg) by the square of their height (in meters) and was expressed in kg/m^2 for adults aged above 18 years old. From the two key anthropometric measurements weight and height recorded for each person, the WHO instruments were used to assess the nutritional status, classifying them as underweight, eutrophic, overweight, and obese [6]. Following WHO recommendations, sex- and age-specific BMI-for-age Z-scores were used for participants aged 2–19, where the observed BMI were compared with the WHO growth reference for the same age and sex [59, 60]. Stunting was defined as a length- or height-for-age Z-score below -2.0, with moderate stunting between -2.0 and -3.0, and severe stunting below -3.0 [61]. The study population was categorized into four age groups (0–2, 3–10, 11–18, and 18 + years old), and those categories were attributed based on nutritional needs corresponding to different growth stages [62].

Ethical considerations

Approval to conduct the study was sought and obtained (reference number 031/CMHS IRB/2021 issued on the 2nd of February 2021, reference number 217/CMHS IRB/2022 issued on the 2nd of February 2022, and reference 257/CMHS IRB/2023 issued on the 2nd of February 2023) from the Institutional Review Board of the University of Rwanda college of Medicine and Health Sciences. Written informed consent was obtained from participants aged 18 years and above, or from parents, relatives, or guardians of younger participants.

Statistical analysis

The nutrition data were analysed for descriptive statistics to perform characterization of the study population. Frequencies and means were calculated with standards deviations for categorical and numerical variables, respectively. Regression logistic analyses were performed where odds ratio with 95% confidence intervals were done to test the association between nutrition parameters in malaria cases versus their control. Case control studies require adjustment for confounding variables to improve comparability. In this study, regression modelling was applied, incorporating age, sex, and sociodemographic covariates into a logistic regression analysis. Adjusted OR were generated from this multivariate logistic regression, including variables with p values < 0.1 from univariate logistic regression in the model. The significance was set at 5% using StataSE 15(64-bit).

Results

Characteristics of study participants

A total of 658 participants were included in the analysis. The participants were categorized into three age groups based on different nutritional needs over the life growth: 197 participants were aged 3–10 years, 129 participants were aged 11–18 years, and 332 participants were over 18 years old.

The characteristics of study participants showed the following gender distribution; for every 1 male, there are approximately 1.22 females (45%/55%) with variations across age groups (Fig. 2A). Nearly equal proportion of males and females were represented in the group of 3–10 years old and 11–18 years old group respectively. A notable difference was observed in the adult group (above 18 years), where 20.8% of males and 29.6% of females were represented, indicating a higher proportion of females in this age category (Fig. 2B).

Characteristics of participants in negative and positive cases are shown in Table 1. Compared to the distribution of negative cases across the different provinces, malaria cases were less likely in Kigali and Northern province while malaria cases were higher in Eastern, Southern, and Western province and the difference is statistically significant ($p < 0.001$) (Table 1).

Dietary patterns influence body composition and associated health risks, contributing to conditions such as underweight, eutrophy, overweight, and obesity. In this dataset, nutritional status varied by age group: the prevalence of underweight increased from 1.5% in children aged 3–10 years to 15.5% in adolescents (11–18 years) and 15.7% in adults (> 18 years) (Fig. 2C). Conversely, eutrophy declined with age, from 89.8% in the youngest group to 79.1% in adolescents and 74.7% in adults.

In this study, overall malaria morbidity was 34.04%; these findings are not comparable to malaria cases observed in the general population due to the participant selection for this study based on malaria cases versus control cases.

Dietary patterns of study participants

Participant's dietary patterns were analysed from the FFQ questionnaires after excluding 337 participants

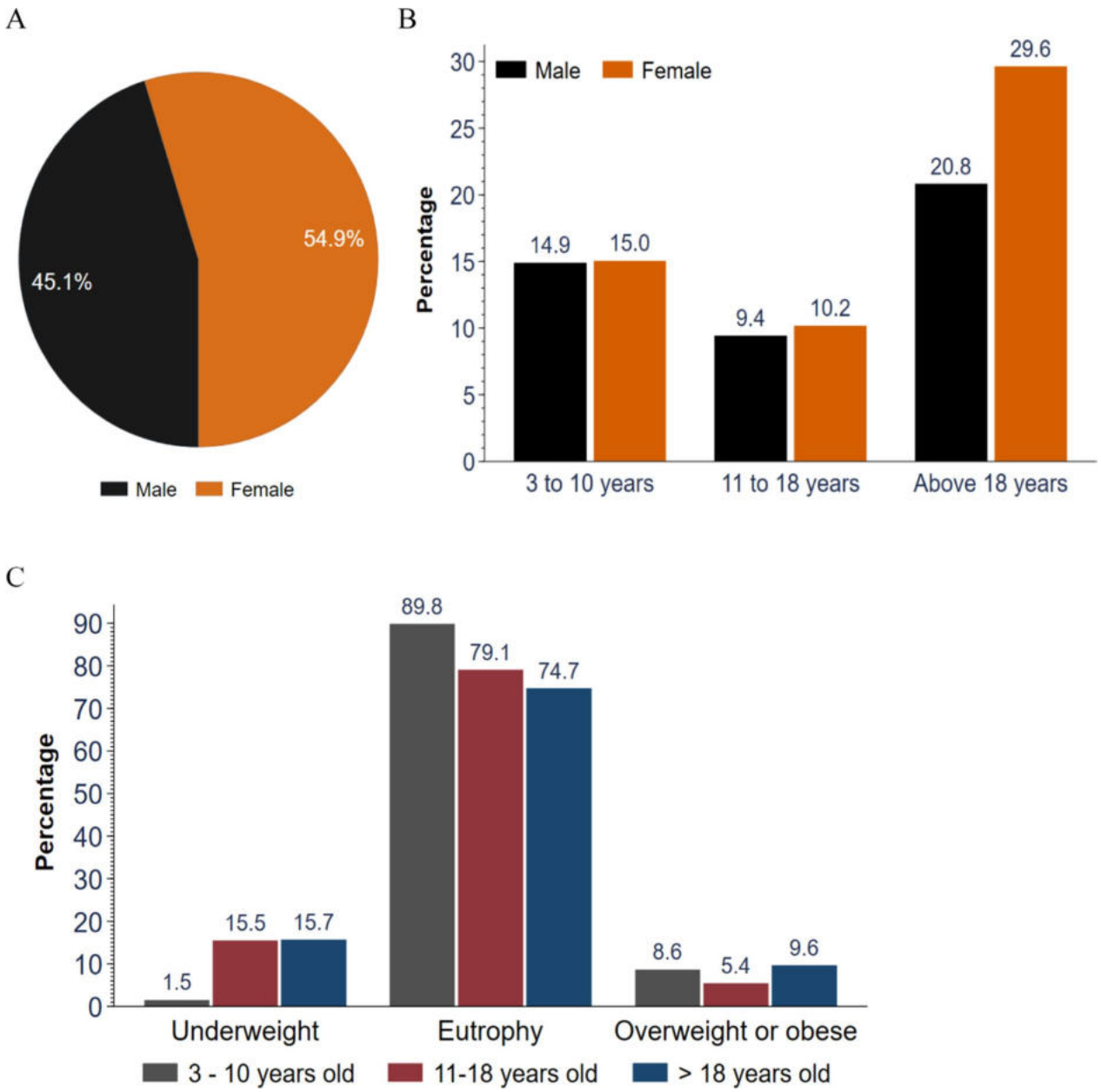

Fig. 2 Characteristic of the cohort population. Sex distribution of the cohort (**A**), Sex distribution in the cohort by Age Group (**B**) and Nutritional status distribution by Age Group 3–10 years old, 11–18 years and above 18 years old in the cohort (**C**)

presenting under-reported or over-reported of their energy intake (Fig. 1).

The dietary habits of the study population were predominantly composed of starchy foods, which accounted for 56.7% of total intake. Fats contributed a moderate 16%, while vegetables and legumes made up 9.4% and 9.3%, respectively. Animal-source proteins were consumed at notably low levels: dairy products at 2.5%, and meat, poultry, fish, and eggs collectively at just 1.1% (Fig. 3).

The coverage between participant's dietary patterns and energy requirements was investigated. For the overall cohort, 58.2% of participants reported caloric intake below 90% of the daily recommended intake (Table 2). A total of 61.5% of female participants versus 54.2% of male participants reported energy intake below 90% of

Table 1 Socio- demographics characteristics of the participants

Demographic & nutrition	Malaria				*p*-value*
	Negative		Positive		
N (%)	n = 434	%	n = 224	%	
Province					
Est	62	14.3	47	21.0	< 0.001
Kigali City	263	60.6	100	44.6	
North	99	22.8	30	13.4	
West	4	0.9	22	9.8	
South	6	1.4	25	11.2	
Age group					
3–10 years	115	26.5	82	36.6	0.024
11–18 years	87	20.1	42	18.8	
Above 18 years	232	53.4	100	44.6	
Sex					
Male	186	42.9	111	49.6	0.102
Female	248	57.1	113	50.4	
Stunting (3–19 years old)					
Normal	91	21.0	52	23.2	0.063
Moderate chronic stunting	65	15.0	34	15.2	
Severe chronic stunting	46	10.6	38	17.0	
Not applicable**	232	53.4	100	44.6	
Body mass (Based on BMI/Z-score)					
Eutrophy	348	80.2	179	79.9	0.934
Obesity	86	19.8	45	20.1	

* Pearson's chi squared. **Not applicable, Stunting calculated up 19 years old as per WHO standards

their estimated daily energy requirements (Table 2). The mean daily caloric intake for females was 1706.6 kcal (SD = 408.1), while for males, it was 1771.8 kcal (SD = 526.8) (Table 2). The proportion of participants with reported intake below 90% increased progressively with advancing age, with the highest prevalence observed among adolescents (11–18 years old) at 76.7% (Table 2). Provincial variation was also noted, with the highest proportion of inadequate energy intake in Kigali (63.4%), followed by the Eastern Province (55%), and the lowest in the Southern Province (45%) (Table 2).

Associations of nutrition characteristics with malaria outcomes

Tables 1, 3, 4, 5 report % of different variable categories across cases compared to % of different variable categories across control subjects whereas Table 6 indicates significant associations between nutrition characteristics and malaria. First, age distribution in malaria cases compared to control cases was investigated: 36.6% of the malaria cases were in the younger age group aged between 3 and 10 years old whereas controls in this age group were at 26.55% (Table 1). In the opposite, the proportion of 11–18 years and above 18 years positive for malaria was lower compared to the proportion of controls negative case in this category. This higher representation of positive cases in 3–10 years old is in accordance higher odds ratio in the 3–10 years old group compared to older groups (Table 6). Indeed, malaria cases decrease with an increase in age (aOR = 0.58; 95% CI 035–0.98

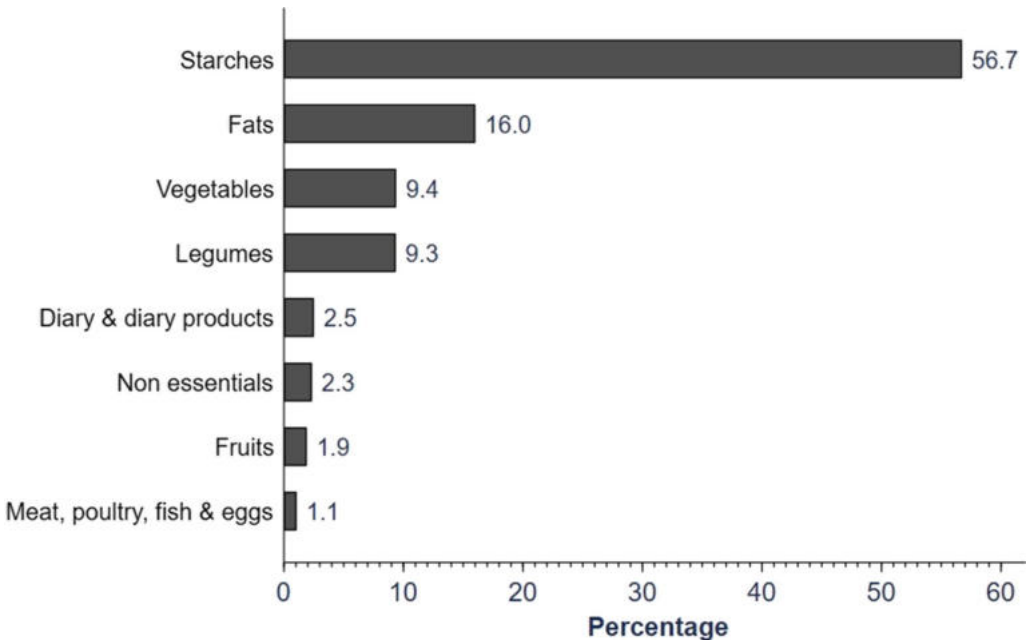

Fig. 3 Distribution of food groups in the cohort: an analysis of dietary sources. Legend: Dietary distribution of starches, fats, vegetables, legumes, and animal protein sources, including meat, poultry, fish, dairy, and eggs

Table 2 Coverage of dietary requirements across the study cohort. Mean values, standard deviations, and percentages per sex, age, and province of the 658 participants classified according to the coverage of energy requirement based on their intake reports

	Average daily caloric intake (kcal/day), mean (sd)	Reported intake as a percentage of actual energy requirements		
		< 90	90–110	> 110
Sex				
Male (n = 297)	1771.8 (526.8)	54.2	26.3	19.5
Female (n = 361)	1706.6 (408.1)	61.5	29.4	9.1
Age				
3 to 10 years (n = 197)	1263.0 (287.3)	36.0	34.5	29.4
11 to 18 years (n = 129)	1810.4 (316.6)	76.7	19.4	3.9
Above 18 years (n = 332)	1987.8 (380.7)	64.2	27.4	8.4
Province				
East (n = 109)	1640.9 (449.4)	55.0	25.7	19.3
Kigali (n = 363)	1703.5 (447.8)	63.4	25.6	11.0
North (n = 129)	1904.1 (478.2)	51.2	30.2	18.6
West (n = 26)	1618.1 (485.5)	50.0	34.6	15.4
South (n = 31)	1850.9 (499.0)	45.2	48.4	6.5
Total (n = 658)	**1736.0 (466.20)**	**58.2**	**28.0**	**13.8**

Table 3 Malaria Proportions according to macronutrient variables

	Malaria				*p*-value
Macronutrient	Negative		Positive		
N(%)	n = 434	%	n = 224	%	
Carbohydrates					
Optimal intake	423	97.5	219	97.8	0.811
Low intake	11	2.5	5	2.2	
Fibers					
Optimal intake	382	88.0	190	84.8	0.249
Low intake	52	12.0	34	15.2	
Proteins					
Optimal intake	356	82.0	186	83.0	0.748
Low intake	78	18.0	38	17.0	
Lipids					
Optimal intake	281	64.7	112	50.0	< 0.001
Low intake	153	35.3	112	50.0	

Table 4 Malaria proportions according to vitamin nutrient variables

Vitamin	Malaria				*p*-value
	Negative (N = 434)		Positive (N = 224)		
Variables	Freq	%	Freq	%	
Vitamin A					
Optimal intake	85	18.6	39	17.4	0.499
Risk of deficiency	349	80.4	185	82.6	
Vitamin B2					
Optimal intake	103	23.7	57	25.5	0.627
Risk of deficiency	331	76.3	167	74.5	
Vitamin B6					
Optimal intake	308	71.0	153	68.3	0.480
Risk of deficiency	126	29.0	71	31.7	
Vitamin B9					
Optimal intake	258	59.5	140	62.5	0.448
Risk of deficiency	176	40.5	84	37.5	
Vitamin B12					
Optimal intake	101	23.3	74	33.0	0.007
Risk of deficiency	333	76.7	150	67.0	
Vitamin C					
Optimal intake	432	99.5	217	96.9	0.005
Risk of deficiency	2	0.5	7	3.1	
Vitamin D					
Optimal intake	5	1.1	4	1.8	0.507
Risk of deficiency	429	98.9	220	98.2	
Vitamin E					
Optimal intake	407	93.8	154	68.7	< 0.001
Risk of deficiency	27	6.2	70	31.3	

for 11–18 years and aOR = 0.58; 95% CI 0.36–0.95 above 18 years; $p < 0.04$) (Table 6). Moreover, being female was negatively associated malaria (aOR = 067; 95% CI 0.46–0.97, $p < 0.001$) (Table 6).

Stunting analysis was conducted up to 19 years since stunting condition is characterizing an impaired growth and is defined as to low height for age. While comparing to controls, severe chronic stunting is higher in positive cases reaching 17% versus 10.6% in control (Table 1). However, moderate chronic malnutrition in

Table 5 Malaria proportions according to minerals nutrient variables

Mineral	Malaria				*p*-value
	Negative		Positive		
Variables	Freq	%	Freq	%	
Calcium					
Optimal intake	76	17.5	46	20.5	0.344
Risk of deficiency	358	82.5	178	79.5	
Iron					
Optimal intake	342	78.8	178	79.5	0.843
Risk of deficiency	92	21.2	46	20.5	
Copper					
Optimal intake	431	99.3	219	97.8	0.087
Risk of deficiency	3	0.7	5	2.2	
Zinc					
Optimal intake	123	28.3	59	26.3	0.586
Risk of deficiency	311	71.7	165	73.7	
Phosphorus					
Optimal intake	338	77.9	168	75.0	0.406
Risk of deficiency	96	22.1	56	25.0	
Selenium					
Optimal intake	198	45.6	128	57.1	0.005
Risk of deficiency	236	54.4	96	42.9	

malaria positive were similar to the proportion observed in negative cases. Besides, in normal stature, a slight increase of 2.2% for positive cases versus negative cases was observed, $p=0.063$ (Table 1). However, even if an increase odds ratio was observed in severe chronic malnutrition (aOR = 1.23; 95% CI 0.67–2.28), the association between malaria and stunting severity was not statistically significant (Table 6).

An association was highlighted between macronutrient intake and malaria, particularly lipid consumption. The proportion of individuals with low lipids intake was higher in malaria cases compared to controls, $p<0.001$ (Table 3). Interestingly, the risk of vitamin B12 deficiency among malaria cases was lower compared to controls (67% versus 76.7%, $p=0.007$) (Table 4). Although, the risk of vitamin C deficiency was low in the study population, it was significantly higher in malaria cases when compared to controls (3.1% versus 0.5%, $p=0.005$) (Table 4).

Moreover, compared to controls, vitamin E insufficient intake was a higher in malaria positive (31.3%) compared to the proportion of vitamin E deficiency in control cases 6.2%, with $p<0.001$ (Table 4). For selenium, the prevalence of risk of deficiency is reduced in malaria cases (42,9%) compared to the risk of deficiency among negative cases (54.4%), $p<0.005$. (Table 5). In the unadjusted univariate analysis, the insufficient intake of selenium and vitamin E were respectively negatively and positively significantly associated with the presence of malaria ($p<0.05$) (Table 6) and this remained significant after adjusting for other covariates using multivariate logistic regression with an aOR at 7.46 (95% CI 4.43–12.58; $p<0,001$) for the risk of vitamin E deficiency and an aOR at 0.62 (95% CI 0.43–0.91; $p=0.013$) for the risk of selenium deficiency (Table 6). In addition, iron deficiency was positively associated with the presence of malaria (aOR = 1.80; 95% CI 1.11–2.93; $p=0.017$) (Table 6).

Discussion

This study aims to investigate the association between nutritional intake and malaria infection in rural areas of Rwanda. These findings indicate that undernutrition, characterised by the risk of macronutrient and micronutrient deficiencies, was common in these rural settings. Moreover, the prevalence of chronic undernutrition evaluated through stunting indicator was important (around 30%, Table 1). This is in agreement with the 2020 Rwanda Demographic and Health Survey that reported stunting prevalence of 33% [63]. The study findings only revealed marginally insignificant association between stunting and malaria in the model. However, the frequencies of severe stunting among malaria positive cases tend to be higher compared to control cases with a $p=0.063$. This is in accordance with the previous study evaluating the relationship between nutritional status and malaria revealing a significant association between malaria and stunting based on DHS data 2010–2020. That said, the relationship between malaria and nutritional status, specifically stunting, remains complex and varies among studies [64–66].

Despite several nutritional interventions to address nutritional burden [15], this study reveals inadequate intake in micronutrients for vitamin A in 81.2%, vitamin B2 in 75.7%, vitamin B12 in 73.4%, calcium in 81.5%, zinc in 72.3%, and selenium in 50.5% of the participants (Tables 4 and 5). These findings corroborate with Arsenault et al. [27], reporting risk of deficiencies in calcium at 75%, vitamin A at 60%, vitamin B12 at 55% and vitamin B2 at 33% in Rwanda. Additionally, inadequate intake of micronutrients in the study population is in accordance with Goto et al. [67] reporting inadequate intake up to 90% in mainland of Zanzibar in the absence of food fortification, whereas a slight decrease in insufficient vitamin A intake from 88 to 66% was observed after fortification. Finally, Mbunga et al. [68] study analysed the levels of minerals in serum and reported relatively high selenium deficiency 84.1% [95% CI 81.4–87], indicating low intake of selenium-containing food products and/or low selenium

Table 6 Regression pooled analysis of the association between malaria infection and nutritional status micronutrient and macronutrient

Malaria (n = 224)	Positive		Odds ratio	[95% conf interval]	*p*-value	Adjusted odds ratio	[95% conf interval]	*p*-value
	Freq	%						
Age group								
3–10 years	82	41.6	1		0.025*	1		0.041
11–18 years	42	32.6	0.68	0.425–1.077		0.58	0.347–0.979	
Above 18 years	100	30.1	0.60	0.418–0.873		0.58	0.355–0.954	
Sex								
Male	111	37.4	1		0.102	1		0.036
Female	113	31.3	0.76	0.552–1.055		0.67	0.455–0.973	
Vitamin E								
Optimal intake	154	27.5	1		< 0.001	1		< 0.001
Risk of deficiency	70	72.2	6.85	4.235–11.086		7.46	4.426–12.581	
Vitamin B9								
Optimal intake	140	35.2	1		0.448	1		0.083
Risk of deficiency	84	32.3	0.88	0.631–1.225		1.42	0.956–2.103	
Stunting (3–19 years)*								
Normal	52	36.4	1		0.170	1		0.552
Moderate chronic stunting	34	34.3	0.92	0.535–1.566		1.02	0.571–1.813	
Severe chronic stunting	38	45.2	1.45	0.835–2.501		1.23	0.667–2.284	
Selenium								
Optimal intake	128	39.3	1		0.005	1		0.013
Risk of deficiency	96	28.9	0.63	0.455–0.871		0.62	0.427–0.905	
Iron								
Optimal intake	178	34.2	1		0.843	1		0.017
Risk of deficiency	46	33.3	0.96	0.646–1.430		1.80	1.111–2.930	

absorption in the region. Possible explanations resulting in these deficiencies include food insecurity and lack of diversified food [29, 69]. This evidence suggest the need for upscaling and improving the implementation of currently ongoing strategies to prevent and control undernutrition in the country including biannual micronutrient powder supplementation [27, 70], vitamin A distribution for children under five, and deworming (Albendazole, Mebendazole) for children under 15 years through Maternal and Child Health Week [27].

This study also reported that composition of foods consumed are mainly based on starches (56.7% of total food intake) which are rich in macronutrients but low in micronutrients [24]. Evidence from the current study indicates that fruits and animal source product consumption were extremely low accounting for 1.9% and 1.1% of total food intake, respectively. This dietary pattern may contribute to the micronutrient deficiency. Al-Bayyari et al. [71] observed that anaemia and micronutrient deficiencies in pregnant women were linked to low intake of animal products, starchy diets, and limited seasonal consumption of fruits and vegetables.

Based on multivariate analysis, this study found that the proportion of the population at risk of selenium deficiency was significantly higher in malaria negative individuals compared to malaria positive individuals. This suggests that selenium deficiency is inversely associated with malaria, as indicated by the adjusted odds ratio (aOR = 0.62; 95% CI 0.43–0.91; $P < 0.013$) (Table 6). One hypothesis supporting this surprising result could be that selenium deficiency induced oxidative stress, which reduced the parasite *Plasmodium falciparum* multiplication in the host. Supporting this hypothesis, the antimalarial drugs also contribute to the oxidative stress as an effective way of parasite clearance within the red blood cell [72]. However, this hypothesis is totally speculative and remains to be investigated.

In Rwanda, the consumption of iron bean biofortified has been shown to improve iron intake [73], which is also seen in this study reporting appropriate iron intake in almost 80% of the study population. However, even if the risk of iron deficiency remains low it was positively associated with malaria in adjusted odds supporting a positive link between malaria and insufficient iron intake. Importantly, these findings suggest that inadequate iron

intake may contribute to anaemia in individuals with malaria in addition to the direct effect of parasite on anaemia [61].

Finally, the regression model revealed that the risk vitamin E deficiency was associated with malaria as indicated by the adjusted odds ratio (aOR = 7.46; 95% CI 4.43–12.58; $p < 0{,}001$). Similarly, in the systematic review and meta-analysis conducted by Kotepui et al. [74], insufficient vitamin E intake were also significantly associated with an increased likelihood of malaria.

Strengths and limitations

Major strengths of this study comprised the highlighting of nutritional determinants including selenium, iron, and vitamin E intake that are associated with the risk of malaria infection. These results will contribute to develop targeted nutrition strategies to improve public health practice which is in alignment with public health programs in Rwanda. Therefore, integration of both dietary intake and infection data is also an important strength of this study. Additionally, including the household companions of the cases as control, reduced the risk of participant selection and reporting bias as well as limited the risk of potential unforeseen lifestyle confounding factors. Furthermore, the use of adjusted odds ratios to control for confounding empowered this study contributing to the limited literature on micronutrient–malaria associations in low-transmission settings. That said, this study also presents some limitations. A limitation of this study was the small number of malaria cases in children under 3 years of age, primarily due to significant changes in malaria epidemiology in Rwanda resulting from successful malaria control interventions. This low number of malaria cases led to a small sample size in this subgroup, limiting the statistical power to detect meaningful associations, therefore children under 3 years old subgroup was excluded from the final analysis. Moreover, it is also important to keep in mind that this study is a case control study which limits the causality of the effect between nutritional intake and malaria. Additional studies such as intervention studies are required to address this causality aspect. Finally, a recall bias due to the retrospective information related to nutrition intake cannot be excluded and could lead to potential risk of error from participants in reporting their dietary habits. Nevertheless, these findings underscore the potential role of nutrient imbalances in influencing malaria infections.

Conclusion

These results emphasize the association between nutrient intake particularly vitamin E, selenium, and iron, and the susceptibility to malaria infection. This suggests that addressing micronutrient deficiencies may be a valuable strategy in malaria control efforts. Improving nutrition status, with an emphasis on food composition and a balanced diet, could further strengthen immunity for the control of infectious diseases including malaria. Therefore, integration or close collaboration between national programmes for nutrition and infectious diseases control are highly recommended.

In perspective, a comprehensive understanding of *Plasmodium* pathogenesis, and particularly the impact of specific micronutrient levels in the host on this pathogenesis, is essential to improving disease prevention and control. Such insights are critical not only for elucidating the parasite's survival and reproduction strategies but also for guiding effective interventions aimed at its elimination.

Author contributions

Conceptualization: A.E, L.M., J.P.C., P.D.C. and N.R.; methodology, A.U., H.A., A.R., L.M. and A.E.; investigation and interpretation: A.U., H.A., J.A.M., J.P.C., L.M. and A.E.; writing—original draft: A.U., L.M. and A.E.; writing—review & editing: A.U., H.A., J.A.M., A.R., N.R., P.D.C., J.P.C., L.M. and A.E.; supervision: L.M. and A.E.; funding acquisition: N.R., P.D.C., J.P.C., L.M. and A.E.

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Data availability

Data will be provided upon request.

Declarations

Competing interests

A.E. and P.D.C. are inventors on patent applications dealing with the use of Akkermansia muciniphila and its components in the treatment of metabolic disorders. A. E. and P.D.C. are inventors on patent applications dealing with gut microbes in food reward dysregulations. A.E. is inventor on patent applications dealing with the use of bacteria metabolites in the prevention or treatment of respiratory viral infections P.D.C. was cofounder of Enterosys. All other authors declare they have no competing interests.

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