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Folate and vitamin B_{12} status and predicted neural tube defects risk among nonpregnant women of reproductive age from the Malawi National Micronutrient Survey, 2015–2016

Yan Ping Qi[1], **Krista S. Crider**[1], **Anne M. Williams**[2], **Katie Tripp**[3], **Carine Mapango**[4], **Elizabeth C. Rhodes**[5], **Eunice Nyirenda**[6], **Felix Phiri**[6], **Mindy Zhang**[4], **Shameem Jabbar**[4], **Christine M. Pfeiffer**[4], **Helena Pachón**[5,7], **Sarah Zimmerman**[2,3], **Jennifer L. Williams**[1]

[1]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA

[2]McKing Consulting Corporation, Atlanta, Georgia, USA

[3]National Center for Chronic Disease Prevention and Health Promotion, CDC, Atlanta, Georgia, USA

[4]National Center for Environmental Health, CDC, Atlanta, Georgia, USA

[5]Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA

[6]Department of Nutrition, HIV and AIDS, Ministry of Health, Lilongwe, Malawi

[7]Food Fortification Initiative, Atlanta, Georgia, USA

Abstract

Background: Maternal folate and vitamin B_{12} deficiency can lead to serious adverse pregnancy outcomes. There are no nationally representative estimates on folate and vitamin B_{12} status among women of reproductive age (WRA) in Malawi.

Correspondence: Yan Ping Qi, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (CDC), 4770 Buford Highway, Mailstop S106-3, Atlanta, GA 30341, USA. irv7@cdc.gov.

AUTHOR CONTRIBUTIONS

Yan Ping Qi led the analyses and drafting of the manuscript. Yan Ping Qi, Krista S. Crider, Anne M. Williams, Katie Tripp, Carine Mapango, Elizabeth C. Rhodes, Eunice Nyirenda, Felix Phiri, and Jennifer L. Williams designed and conducted the research. Carine Mapango provided laboratory-based technical assistance and training for the implementation of the Malawi survey. Carine Mapango and Shameem Jabbar conducted the laboratory analyses on the folate microbiologic and vitamin B_{12} assays. Mindy Zhang and Christine M. Pfeiffer managed the laboratory analyses and interpretation of laboratory results. Helena Pachón and Sarah Zimmerman provided expertise on fortification policies and implementation as well as country-specific fortification legislation, standards, coverage. All authors provided substantive contributions to the development of the manuscript and provided final approval of revisions.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

CONFLICT OF INTEREST STATEMENT

At the time of these analyses, Helena Pachón and Sarah Zimmerman were employed with the Food Fortification Initiative that helps country leaders promote, plan, implement, monitor, or evaluate fortification of industrially milled wheat flour, maize flour, and rice. The authors declare no conflicts of interest.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Objective: We assessed folate and vitamin B_{12} status among nonpregnant WRA in Malawi and predicted the risk of folate-sensitive neural tube defects (NTDs) were they to become pregnant.

Methods: Using data from the cross-sectional, nationally representative 2015–2016 Malawi Micronutrient Survey, we calculated the proportion of folate and vitamin B_{12} deficiency and insufficiency by demographic characteristics among 778 nonpregnant WRA (15–49 years). We predicted NTD prevalence using red blood cell (RBC) folate distributions and a published Bayesian model of the association between RBC folate and NTD risk. Analyses accounted for complex survey design.

Results: Among WRA, 8.5% (95% CI: 6.2, 11.6) and 13.3% (10.0, 17.4) had serum (<7 nmol/L) and RBC folate (<305 nmol/L) deficiency, respectively. The proportion of vitamin B_{12} deficiency (<148 pmol/L) and insufficiency (≤221 pmol/L) was 11.8% (8.6, 16.0) and 40.6% (34.1, 47.4), respectively. RBC folate insufficiency (<748 nmol/L, defined as the concentration associated with the threshold for elevated NTD risk: >8 cases per 10,000 births) was widespread: 81.4% (75.0, 86.4). The predicted NTD risk nationally was 24.7 cases per 10,000 live births. RBC folate insufficiency and higher predicted NTD risk were more common among WRA living in urban areas or with higher education.

Conclusions: These findings highlight the importance of nutritional and NTD surveillance in Malawi and the opportunity for improving folate and vitamin B_{12} nutrition among Malawian WRA.

Keywords

folate; Malawi; neural tube defects; nonpregnant women; vitamin B_{12}

1 | INTRODUCTION

Folate and vitamin B_{12} deficiencies are associated with serious adverse health outcomes among women and children (Finkelstein et al., 2015; World Health Organization, 2015a). Inadequate folate and vitamin B_{12} status is linked to adverse pregnancy outcomes including pre-eclampsia, spontaneous abortions, and low birth weight (Bukowski et al., 2009; De-Regil et al., 2015; Hogeveen et al., 2012; Hubner et al., 2008; Muthayya et al., 2006; Patrick et al., 2004; Pepper & Black, 2011; Relton et al., 2005; Reznikoff-Etievant et al., 2002; Rowland et al., 1995; Scholl & Johnson, 2000; Tamura & Picciano, 2006). It is also well established that poor maternal folate status in early pregnancy increases the risk for neural tube defects (NTDs, serious congenital abnormalities of brain and spine), and the use of folic acid supplements during the periconceptional period lowers the risk of NTDs (Berry et al., 1999; Czeizel & Dudas, 1992; MRC Vitamin Study Research Group, 1991; Smithells et al., 1976). Furthermore, observational studies have reported a higher risk of NTDs in connection with maternal vitamin B_{12} deficiency (Finkelstein et al., 2015; Gernand et al., 2016; Molloy, 2018; Molloy et al., 2009; Ray et al., 2007).

Many countries mandate fortification of some foods with folic acid as a strategy for both NTD prevention and to curtail the prevalence of folate deficiency anemia (Crider et al., 2011; Pachón, 2021). In 2015, the WHO established the population-level red blood cell (RBC) folate threshold for the optimal prevention of NTDs among women of reproductive

age (WRA) (World Health Organization, 2015b). However, population-level data on blood folate concentrations are needed in many parts of the world, particularly among low- and middle-income countries to determine the opportunity for improving folate nutrition to prevent adverse pregnancy outcomes. In Africa, one such example is the nation of Malawi, where folate deficiency and insufficiency among WRA were suspected to be an important modifiable public health challenge (Nyirenda, 2017).

The present study is the first to provide estimates on blood folate and vitamin B_{12} status among a nationally representative group of nonpregnant WRA in Malawi. The objectives were to (1) examine the distribution and status of serum and RBC folate and vitamin B_{12} among a nationally representative sample of nonpregnant WRA in Malawi and (2) predict the risk of folate-sensitive NTDs based on RBC folate concentrations among these women were they to become pregnant to help inform program implementation and policy in Malawi.

2 | METHODS

The 2015–2016 Malawi National Micronutrient Survey (MNS) was conducted between mid-December 2015 to February 2016, as part of the Malawi Demographic and Health Survey (MDHS), a nationally representative cross-sectional survey using a two-stage cluster sampling design (National Statistical Office [NSO], 2017). The MNS was designed to provide data on the prevalence of anemia and micronutrient deficiencies, risk factors for anemia, and coverage of nutritional interventions. A sub-sample of MDHS clusters (105 out of a total of 850 clusters) was randomly selected for the MNS to provide representative estimates for the status of micronutrients and other biomarkers at the national and regional levels. Ethical approvals for the MDHS and MNS were obtained from the National Health Sciences Research Committee in Malawi. Informed consent for survey participation was obtained at the community, household, and individual levels. Details of the MDHS and MNS methodology and laboratory testing are described elsewhere (National Statistical Office [NSO, Malawi] and ICF, 2017; National Statistical Office [NSO], 2017).

Field staff collected the data on demographic and health characteristics via in-person interviews among 838 WRA 15–49 years of age from 2114 households. Field phlebotomists collected venous blood samples and field laboratory technicians prepared whole blood hemolysate samples and serum samples in the field within 2 h of collection. Hemolysate and serum samples were frozen in the field and kept in portable freezers before being transported to and temporarily stored (at −20°C) at the nearest district laboratory. From there, samples were sent on for longer-term storage (at −70°C) at the Community Health Services Unit (CHSU) at the Ministry of Health before shipment to the Centers for Disease Control and Prevention (CDC) in Atlanta for analyses. From July 2016 to January 2017, CDC's nutritional biomarkers laboratory staff performed folate and vitamin B_{12} analyses. Serum and RBC folate concentrations were measured using a microbiologic assay, which included chloramphenicol-resistant *Lactobacillus rhamnosus* and was calibrated with 5-methyltetrahydrofolate (Pfeiffer et al., 2011). The RBC folate concentration was calculated using the formula: RBC folate = (whole blood folate – serum folate × (1 – hematocrit))/hematocrit; and the hematocrit was estimated from the hemoglobin measured in the field (hematocrit = hemoglobin/34.5). Serum and RBC folate deficiencies were defined

as <7 and <305 nmol/L, respectively (Pfeiffer et al., 2016). RBC folate insufficiency was defined as <748 nmol/L, an adjusted value based on the 5-methyltetrahydrofolate-calibrated microbiologic assay and associated with the threshold for elevated NTD risk (>8 cases per 10,000 births) (Pfeiffer et al., 2016; Tinker et al., 2015). CDC laboratory staff also measured serum vitamin B_{12} using an automated electro-chemiluminescence immunoassay (Cobas 6000, Roche Diagnostics). Serum vitamin B_{12} deficiency and insufficiency were defined as <148 and ≤221 pmol/L, respectively (Allen, 2009; Allen et al., 2018; National Statistical Office [NSO], 2017). Among the original 838 WRA, 778 were not pregnant. Of the nonpregnant WRA, 753 WRA had complete serum and RBC folate data and 762 WRA had serum vitamin B_{12} data.

We calculated the proportion of women with folate and vitamin B_{12} deficiency and insufficiency by region, age, level of education, wealth index, and body mass index (BMI). Proportions and prevalence ratios (PR) with 95% confidence intervals (CI) were estimated using SAS-callable SUDAAN version 11.0.1 (Research Triangle Park, NC) with sample weights to account for the complex survey design. We also reported the distribution of serum and RBC folate and serum vitamin B_{12} and estimated the geometric means for the overall nonpregnant WRA population as well as by selected subgroups (Proc Regress SUDAAN). Differences in geometric means across sociodemographic characteristics were assessed using ANOVA. Multivariable logistic regression was used to assess the independent predictors of deficiency and insufficiency (Proc Rlogist SUDAAN). Prevalence ratios were adjusted for confounders selected a priori: age and BMI. Additional covariates were selected based on bivariate associations with $p < .1$. We assessed associations between covariates via χ^2 tests and significant associations were further evaluated for potential interaction in the logistic regression model. We defined statistical significance as $\alpha = 0.05$ (two-sided). Using the distribution of RBC folate concentrations and a published Bayesian model of the association between RBC folate and NTD risk (Crider et al., 2014), we predicted the NTD prevalence (per 10,000 births) with 95% uncertainty intervals (UI) among the overall group of WRA were they to become pregnant as well as among sub-populations within this group of women.

3 | RESULTS

3.1 | Demographic characteristics of the study population

Among a nationally representative sample of nonpregnant WRA aged 15–49 years in the MNS, 46.6%, 41.9%, and 11.5% were from the South, Central, and North regions, respectively. Reflective of country demographics, most women (90.8%) lived in rural areas. The mean age of nonpregnant WRA was 28.4 years (95% CI: 27.7, 29.1) with 26.7% between the ages of 25–34 years and 29.6% between 35–49 years. Most women (79.6%) had less than a secondary-level education. Nearly 14% of the women were overweight or had obesity. Characteristics of WRA from the Malawi MNS are presented in Table 1 alongside published characteristics of WRA from the DHS (National Statistical Office [NSO, Malawi] and ICF, 2017).

3.2 | Serum and RBC folate status

The geometric means for serum and RBC folate concentrations among nonpregnant WRA in the MNS were 18.0 nmol/L (95% CI: 16.1, 20.1) and 499 nmol/L (95% CI: 459, 542; Table S1), respectively. Distributions for serum and RBC folate concentrations are presented in Figure 1a,b and Table S2, respectively. The prevalence of serum and RBC folate deficiency was 8.5% (95% CI: 6.2, 11.6) and 13.3% (95% CI: 10.0, 17.4), respectively (Table 2). In adjusted analyses, serum folate deficiency was associated with women who were older (aged 35–49 vs. aged 15–24: adjusted prevalence ratio [aPR]: 2.81; 95% CI: 1.27, 6.19) and more educated (≥secondary vs. ≤primary: aPR: 1.78; 95% CI: 1.01, 3.16). RBC folate deficiency was also more prevalent among women who were more educated than women who were less educated (≥secondary vs. ≤primary: aPR: 2.06; 95% CI: 1.22, 3.46).

Among nonpregnant WRA aged 15–49 years, the national prevalence of RBC folate insufficiency was 81.4% (95% CI: 75.0, 86.4; Table 2). Both urban residence and higher education were independently associated with folate insufficiency (residence cPR: 1.23, 95% CI: 1.14, 1.33; education cPR: 1.17; 95% CI: 1.06, 1.30). Urban versus rural residence was statistically significantly associated with education ($p = .03$) with 66.2% (95% CI: 49.3, 79.8) of urban women having at least a secondary education, while only 16.2% (95% CI: 122.4, 20.9) of rural women had a secondary education or higher. In multivariate analysis, there was no significant interaction effect ($p = .07$) between urban versus rural residence and education on folate insufficiency. To avoid overadjustment with the inclusion of urban versus rural residence and education in the same model, we ran separate models for urban versus rural residence and education to assess the association of these variables with folate insufficiency (Table S3). Women living in urban areas were more likely to have RBC folate insufficiency than women living in rural areas (aPR: 1.23; 95% CI: 1.14, 1.33; Table 2). Women with at least a secondary-level education were more likely to have RBC folate insufficiency than women with lower education (≥secondary vs. ≤primary: aPR: 1.17; 95% CI: 1.06, 1.30; Table S3).

3.3 | Serum vitamin B_{12} status

The geometric mean for serum vitamin B_{12} concentration for all nonpregnant WRA aged 15–49 years in the MNS was 266 pmol/L (95% CI: 247, 285; Table S1). The distribution for serum B_{12} concentrations is presented in Figure 1c. The prevalence of serum vitamin B_{12} deficiency was 11.8% (95% CI: 8.6, 16.0; Table 3). Serum vitamin B_{12} deficiency was associated with region, urban versus rural residence, and wealth index in crude and adjusted analyses. Compared with the Central region of Malawi, serum vitamin B_{12} deficiency was significantly less prevalent in the South (aPR: 0.45; 95% CI: 0.22, 0.94). Urban WRA were less likely to have serum vitamin B_{12} deficiency than rural women (aPR: 0.06; 95% CI: 0.01, 0.34). WRA in the higher wealth index quintiles were also less likely to be serum vitamin B_{12} deficient than WRA in the lower wealth index quintiles (aPR: 0.32; 95% CI: 0.15, 0.70).

The prevalence of serum vitamin B_{12} insufficiency was 40.6% (95% CI: 34.1, 47.4; Table 3). Serum vitamin B_{12} insufficiency was associated with region, urban versus rural residence, and wealth index. Compared with the Central region of Malawi, serum vitamin

B_{12} insufficiency was significantly less prevalent in the South (aPR: 0.57; 95% CI: 0.38, 0.84). Urban WRA were less likely to have serum vitamin B_{12} insufficiency than rural women (aPR: 0.66; 95% CI: 0.44, 0.99). WRA in the higher wealth index quintiles were also less likely to be serum vitamin B_{12} insufficient than WRA in the lower wealth index quintiles (aPR: 0.54; 95% CI: 0.38, 0.77).

3.4 | Predicted NTD risk

Among nonpregnant WRA, the predicted NTD risk were they to become pregnant was 24.7 cases per 10,000 live births (95% UI: 20.1, 30.2; Table S4). Predicted NTD risk was higher among women living in urban areas compared with women living in rural areas (29.9 vs. 24.0 per 10,000; difference: 5.9 per 10,000; 95% UI: 1.3, 10.6; distribution shown in Figure 2a). Predicted NTD risk was higher among WRA with at least a secondary-level education compared with WRA with lower education (28.9 vs. 22.8 per 10,000; difference: 6.0 per 10,000; 95% UI: 1.7, 10.7; distribution shown in Figure 2b). No significant differences in NTD risk were observed by region, age, wealth index, BMI, or serum vitamin B_{12} status (Table S4).

4 | DISCUSSION

The MNS was the first survey to provide estimates on blood folate and vitamin B_{12} status among a nationally representative sample of WRA in Malawi. These data showed that among Malawian WRA, the prevalence of deficiencies in serum and RBC folate and serum vitamin B_{12} are notable (8.5%, 13.3%, and 11.8%, respectively). Serum vitamin B_{12} insufficiency among WRA was widespread (40.6%), and when occurring in pregnant women, can increase the risk for growth failure and abnormal brain and motor development in infants (Black, 2008; Pepper & Black, 2011). Four-fifths (81.4%) of WRA had RBC folate insufficiency with concentrations below the cutoff for optimal NTD prevention. Even though RBC folate insufficiency was high (>75%) across all regions and residential settings, it was significantly higher among urban WRA compared with rural WRA with over 98% insufficiency among urban women. In addition, folate deficiency and insufficiency were higher among WRA with at least a secondary-level education compared with WRA with lower education. Over 90% of women with a secondary-level education or higher had RBC folate insufficiency. Conversely, vitamin B_{12} status deficiency and insufficiency were more prevalent among rural women and women from with lower income households. These findings are consistent with observations from other African countries where higher consumption of animal-sourced protein-rich foods (with higher vitamin B_{12} content) are associated with urban settings and households with higher socioeconomic status, while diets in leafy vegetables (with higher folate content) were more common among poorer populations in rural areas (Becquey & Martin-Prevel, 2010; Rhodes et al., 2020). Furthermore, blood samples were collected during the rainy season, a time during which, typically, there was a greater availability of leafy vegetables in the rural, poorer populations.

Using the distribution of RBC folate concentrations, the predicted prevalence of folate-sensitive NTDs among Malawian WRA were they to become pregnant was almost four times higher than the only published study on NTD surveillance from Malawi, a hospital-

based study from 1998 to 1999 estimating the prevalence of spina bifida (a major form of NTD) at 6.3 per 10,000 live births (Msamati et al., 2000). Other types of NTDs were not included in the hospital-based study. Our estimated predicted NTD prevalence in Malawi varied by urban versus rural residence and education. The predicted NTD prevalence was higher among urban WRA compared with rural WRA and higher among WRA with at least a secondary-level education compared with WRA with lower education. High-quality population-based birth defects surveillance data from Malawi would be needed corroborate the prevalence of NTDs estimated from our model.

Compared with the United States (23%), the proportion of WRA with RBC folate insufficiency (<748 nmol/L) in Malawi was more than three times as high (Tinker et al., 2015). Our predicted prevalence of NTDs among WRA in Malawi was also more than three times as high as the known and predicted prevalence in the United States (~7 per 10,000 live births) (Crider et al., 2018; Mai et al., 2019; Williams et al., 2015). Compared with previously published predicted NTD prevalence estimates using the same modeling methodology, the prevalence in our study was higher than estimates from a South Indian WRA population without exposure to mandatory fortification with folic acid (20.6 per 10,000 live births; 95% UI: 16.5–25.5; proportion of WRA with RBC folate <748 nmol/L: 79%) and higher than estimates from a WRA population in Guatemala, which mandates fortification with folic acid (14 per 10,000 live births; 95% UI: 11.1–18.6; proportion of WRA with RBC folate <748 nmol/L: 47%) (Finkelstein et al., 2021; Rosenthal et al., 2016).

At the time the MNS was conducted, national policies for fortification and supplementation with folic acid were in place but their impact was limited. In May 2015, Malawi enacted legislation for the mandatory fortification of wheat and maize flour with iron, folic acid, vitamin B_{12}, niacin, riboflavin, thiamin, vitamin A (wheat flour only), and zinc (Sanku Project Healthy Children, 2015). While national fortification is a strategy effective at reducing micronutrient deficiencies in a population overall, its impact is affected by the availability of and access to fortified foods in different communities and food preferences that can influence the acceptance and consumption of fortified staples (Global Fortification Data Exchange, 2023; Mildon et al., 2015). Current national standards for the level of folic acid (2 mg/kg) used in wheat flour fortification are 60% lower than WHO recommended level (5 mg/kg); while the national standards for maize flour compared with WHO standards are unknown (Global Fortification Data Exchange, 2023). Additionally, a recent market scan throughout Malawi suggested that foods may be fortified at levels below mandatory national standards (Tang et al., 2022). Aside from these issues of adherence and compliance, access to and preference for fortified products can also pose challenges. For example, in Malawi, maize is the main dietary staple consumed by the population (~90%) and maize flour is available at ~300 g per capita per day (Global Fortification Data Exchange, 2023; Obare et al., 2017). However, because only 15% of the maize flour is industrially milled and only half of the industrially milled flour is fortified (Food Fortification Initiative, 2023), it is likely that most people are not eating fortified maize flour. Wheat flour is not widely consumed in Malawi and is only available at ~30 g per capita per day (Global Fortification Data Exchange, 2023; Obare et al., 2017). Even though nearly 100% of wheat flour is industrially milled, only 20% of milled wheat flour is fortified (Food Fortification Initiative, 2023). Furthermore, wheat flour is typically consumed by those with higher incomes and living in

urban areas (Obare et al., 2017). Given that most of the population (~84%) reside in rural areas and have lower incomes (Obare et al., 2017), consumption of fortified wheat flour is also likely to be low (Tang et al., 2022). A recent hospital-based study conducted in one hospital in the Southern region of Malawi reported a 13.6% increase in the prevalence of spina bifida from 2014 (pre-fortification) to 2018 (post-fortification) (Chapweteka, 2020). While various reasons could have contributed to the change in prevalence in this study including shifting referral patterns, it brought into question the effectiveness of the current fortification program and highlighted the need for further investigation into the reach (including inequities in reach) of fortified products, food preferences of fortified versus unfortified products, and consumption patterns of women in Malawi to know whether they are consuming flour fortified with folic acid. Implementation science research can help understand the barriers to successful implementation of the fortification program and develop strategies for addressing these barriers.

During data collection for this study, the government of Malawi also had a mandate for the universal supplementation of iron (FE: 64 mg/day) and folic acid (FO: 250 μg/day) to all pregnant women starting at 16 weeks of pregnancy to prevent and control iron and folate deficiency (Nyirenda, 2017). In 2015–2016, coverage for FEFO supplementation among pregnant women was 89.4%; however, only 33% of pregnant women took supplements for ≥90 days during pregnancy, as recommended by this program (National Statistical Office [NSO, Malawi] and ICF, 2017; Nyirenda, 2017). Thus, the effectiveness of the supplementation program was limited by adherence issues. In addition, starting women on folic acid supplements at 4 months into pregnancy would not prevent NTDs.

Our study is the first to provide representative estimates on folate and vitamin B_{12} biomarkers among WRA in Malawi at the national and regional levels as well as among various subgroups. It is also the first study to use distributions of RBC folate concentrations as measured by the microbiologic assay among Malawian WRA to estimate the predicted NTD risk in the country. Our study also has several limitations. First, our findings may lead to generalized decision-making at national and regional levels. However, as Malawi moves towards governmental decentralization, additional data from the district level will be required to help inform specific policy decisions. Second, the cross-sectional design of the study did not allow for comparisons before and after fortification. Given the timing of the Malawi MNS (conducted shortly after the passing of the 2015 legislation) and the potential limitations in access to and consumption of fortified products, these data likely serve as modeled population estimates pre-fortification. Future population-level MNS would provide the opportunity to further examine folate and vitamin B12 status among WRA and assess the association between RBC folate and NTD risk in Malawi post-fortification. Third, no dietary intake data were collected on folic acid or vitamin B_{12} among WRA which limited our ability to assess the causes of some disparities in observed deficiency and insufficiency. In addition, NTD prevalence was modeled based on the distribution of RBC folate concentrations (Crider et al., 2014); however, we could not model the impact of folic acid intake on RBC folate concentrations because this information was not collected. Lastly, we assume that the relation between NTD risk and RBC folate concentrations in our population of nonpregnant women behaves similarly as the populations from which

the model was produced (the model was based on Chinese and Irish populations and later validated within a representative US population) (Crider et al., 2014).

In conclusion, the current analyses provide the first evidence and confirm concerns that inadequate folate and vitamin B_{12} status are important problems among WRA in Malawi. This is also the first time that the population-level RBC folate threshold for optimal NTD prevention established by the WHO was applied to an African country's data, and RBC folate concentrations from WRA were used to predict NTD prevalence if these women were to become pregnant. Widespread folate insufficiency among Malawian WRA and the high prevalence of NTDs predicted by our model highlight the need for quality population-based surveillance data to monitor NTD prevalence and evaluate the effectiveness and implementation of mandatory fortification to reduce folate and vitamin B_{12} insufficiency and deficiency. Our findings demonstrate existing gaps in folate and vitamin B_{12} status among women that put their pregnancies at risk for NTDs and underscore the importance of nutritional and NTD surveillance for planning and prevention efforts in Malawi.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Abbreviations:

aPR	adjusted prevalence ratio
CI	confidence interval
MDHS	Malawi Demographic and Health Survey
MNS	Malawi Micronutrient Survey
NTD	neural tube defect
RBC	red blood cell
UI	uncertainty interval

WHO	World Health Organization
WRA	women of reproductive age

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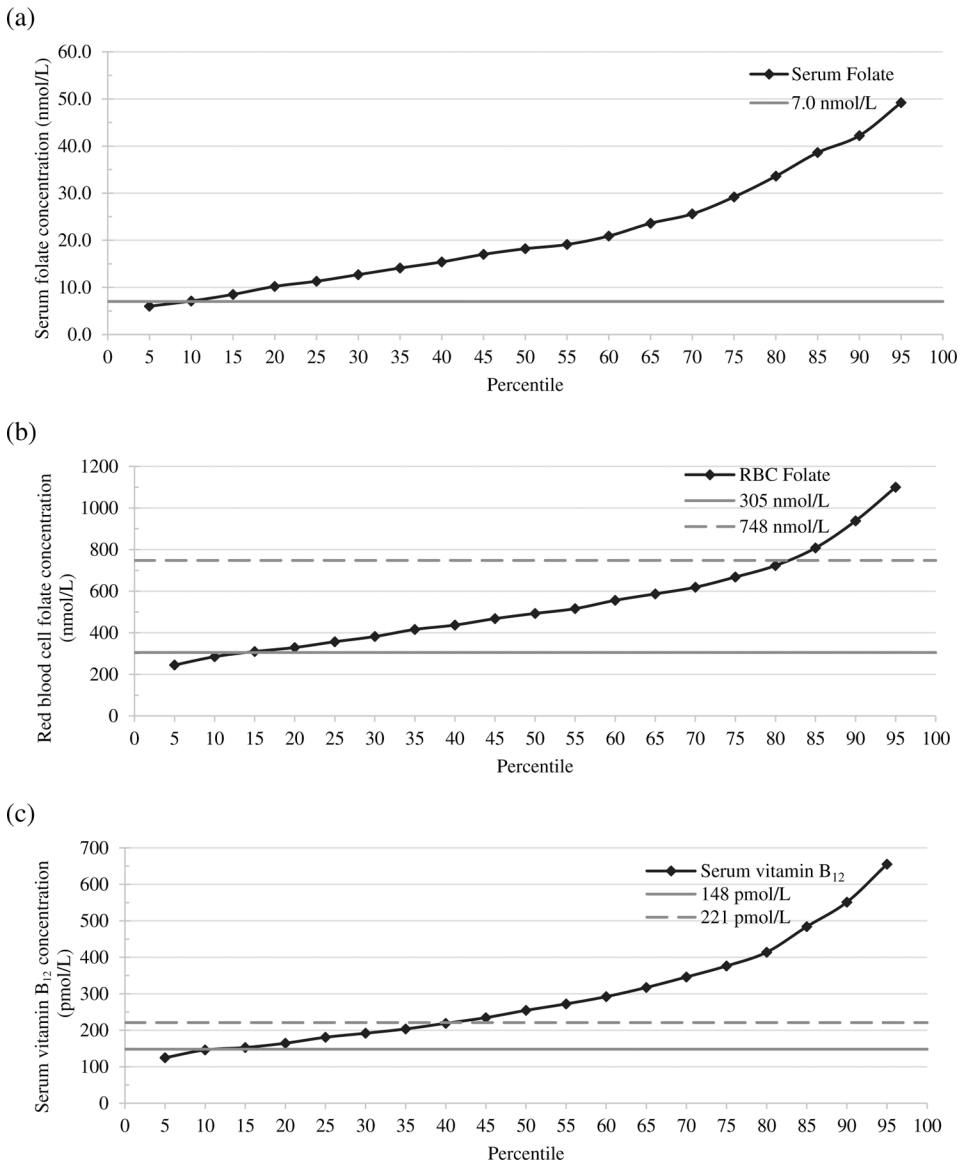

FIGURE 1.

Distributions of serum folate, red blood cell folate, and serum vitamin B_{12} among nonpregnant women of reproductive aged 15–49 years, Malawi Micronutrient Survey, 2015–2016. RBC, red blood cell.

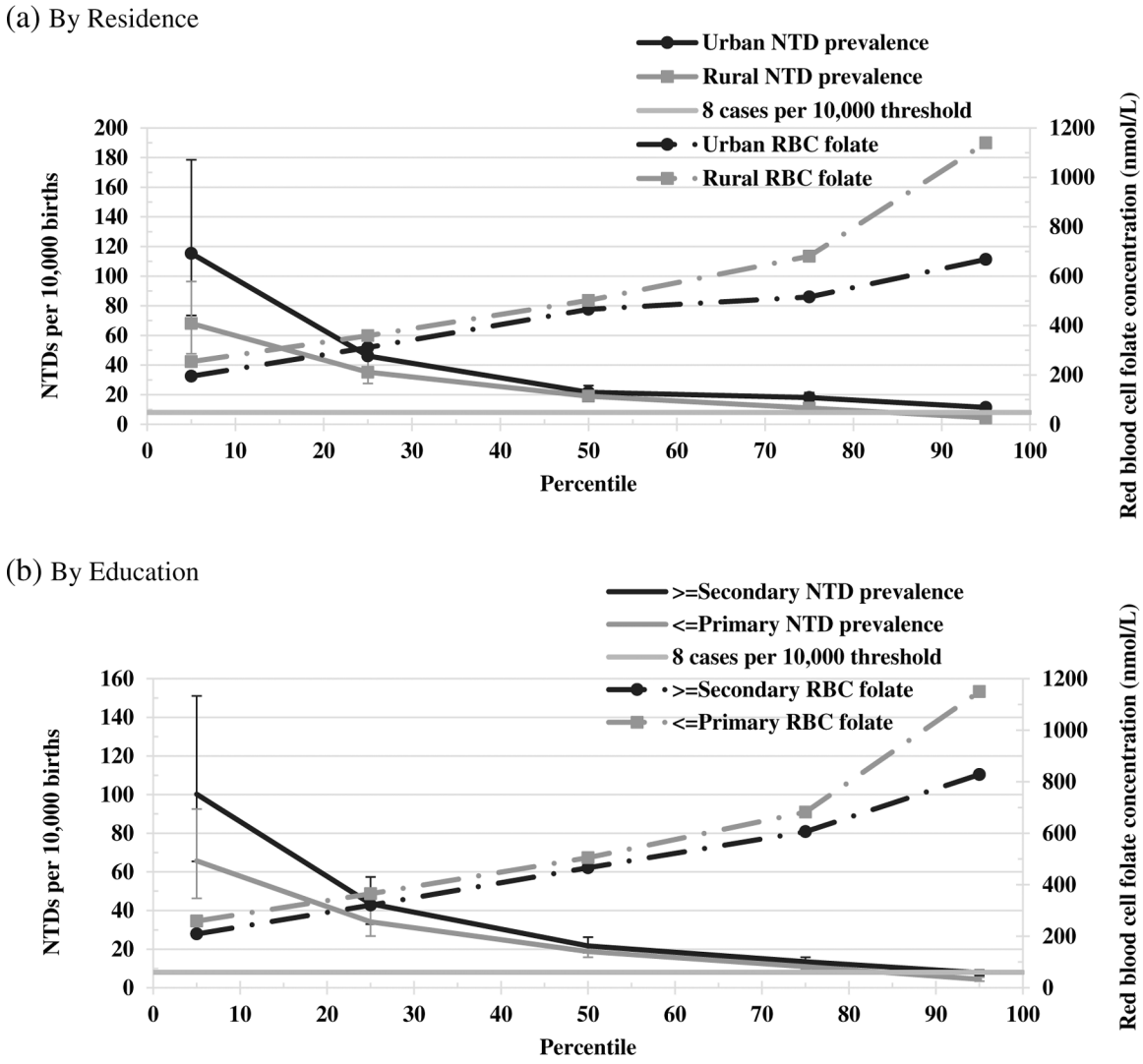

FIGURE 2.

Predicted prevalence of neural tube defects and red blood cell folate distribution among nonpregnant women of reproductive age 15–49 years, Malawi Micronutrient Survey, 2015–2016. (a) By residence. (b) By education. NTD, neural tube defect; RBC, red blood cell.

TABLE 1

Characteristics of women of reproductive aged 15–49 years, Malawi Micronutrient Survey and Malawi Demographic and Health Survey, 2015–2016.

	Malawi MNS 2015–2016[a]		**Malawi DHS 2015–2016[b]**
	***n* (unweighted)**	**Weighted % (95% CI)**	**Weighted %**
Total	778	100	100
Region			
North	244	11.5 (8.1, 15.9)	11.6
Central	270	41.9 (34.2, 50.1)	42.9
South	264	46.6 (38.5, 54.9)	45.6
Residence			
Urban	124	9.2 (3.8, 20.5)	18.3
Rural	654	90.8 (79.5, 96.2)	81.7
Age (years)			
15–24	328	43.7 (39.8, 47.8)	42.4
25–34	215	26.7 (22.6, 31.1)	31.0
35–49	235	29.6 (26.4, 33.0)	26.6
Education			
≤Primary	585	79.6 (73.0, 85.0)	74.2
≥Secondary	192	20.4 (15.0, 27.0)	25.8
Missing	1	-	
Wealth index[c]			
≤Poor	290	42.5 (35.4, 50.0)	38.4
Average	150	20.2 (16.1, 24.5)	18.9
≥Rich	338	37.3 (30.4, 44.7)	42.8
Body mass index			
<18.5 kg/m^2	74	9.8 (7.8, 12.2)	7.2
18.5-<25 kg/m^2	568	76.3 (71.9, 80.2)	72.1
≥25 kg/m^2	133	13.9 (10.8, 17.8)	20.7
Missing	3	-	-

Abbreviations: BMI, body mass index; CI, confidence interval.

[a]Nonpregnant women of reproductive age, 15–49 years, Malawi Micronutrient Survey (MNS) 2015–2016.

[b] All women of reproductive age, 15–49 years, unweighted n=24,562, Malawi Demographic and Health Survey (DHS) 2015–2016 (National Statistical Office [NSO, Malawi] and ICF, 2017). BMI proportions reported (based on n=7,180) excludes pregnant women and women with a birth in the preceding 2 months.

[c] Categorized based on wealth index quintiles from the 2015–2016 Malawi Demographic and Health Survey. Lowest and second quintiles categorized as "≤poor." Middle quintile categorized as "average." Fourth and highest quintiles categorized "≥rich."

TABLE 2

Folate deficiency and insufficiency by demographic characteristics among nonpregnant women of reproductive aged 15–49 years, Malawi Micronutrient Survey, 2015–2016.

	N [a]	Weighted % (95% CI)	Crude prevalence ratio (95% CI)	Adjusted prevalence ratio[b] (95% CI)
Serum folate deficiency (<7 nmol/L)				
Total	753	8.5 (6.2, 11.6)	-	-
Region				
North	238	9.6 (5.7, 15.5)	1.51 (0.69, 3.32)	-
Central	258	6.3 (3.4, 11.5)	Referent	-
South	257	10.1 (6.6, 15.2)	1.60 (0.76, 3.35)	-
Residence				
Urban	118	9.0 (4.9, 16.0)	1.06 (0.53, 2.13)	-
Rural	635	8.4 (5.9, 11.8)	Referent	-
Age (years)				
15–24	321	5.6 (3.0, 10.1)	Referent	Referent
25–34	210	8.3 (4.8, 14.0)	1.50 (0.70, 3.19)	1.61 (0.74, 3.51)
35–49	222	13.2 (8.3, 20.2)	2.36 (1.08, 5.14)	2.81 (1.27, 6.19)
Education				
≤Primary	565	7.8 (5.5, 11.1)	Referent	Referent
≥Secondary	187	11.0 (6.3, 18.5)	1.41 (0.77, 2.58)	1.78 (1.01, 3.16)
Wealth index[c]				
≤Poor	282	6.4 (3.4, 11.8)	Referent	-
Average	143	7.2 (4.1, 12.3)	1.12 (0.52, 2.44)	-
≥Rich	328	11.4 (7.4, 17.2)	1.78 (0.82, 3.88)	-
Body mass index				
<18.5 kg/m^2	68	16.1 (7.4, 31.6)	2.26 (0.95, 5.40)	2.26 (0.94, 5.41)
18.5-<25 kg/m^2	553	7.1 (4.7, 10.6)	Referent	Referent
≥25 kg/m^2	130	10.7 (5.6, 19.6)	1.51 (0.77, 2.95)	1.24 (0.61, 2.54)
RBC folate deficiency (<305 nmol/L)				
Total	753	13.3 (10.0, 17.4)	-	-
Region				

	N [a]	Weighted % (95% CI)	Crude prevalence ratio (95% CI)	Adjusted prevalence ratio[b] (95% CI)
North	240	14.1 (8.5, 22.3)	0.88 (0.48, 1.62)	-
Central	259	15.9 (10.9, 22.6)	Referent	-
South	254	10.8 (6.3, 17.9)	0.68 (0.36, 1.29)	-
Residence				
Urban	119	20.9 (9.1, 41.0)	1.67 (0.74, 3.74)	-
Rural	634	12.5 (9.5, 16.4)	Referent	-
Age (years)				
15–24	315	13.2 (8.5, 20.0)	Referent	Referent
25–34	209	13.8 (8.9, 20.8)	1.05 (0.60, 1.83)	1.14 (0.65, 1.98)
35–49	229	12.9 (8.9, 18.4)	0.97 (0.57, 1.66)	1.21 (0.69, 2.11)
Education				
≤Primary	566	11.1 (8.2, 14.8)	Referent	Referent
≥Secondary	186	21.8 (13.8, 32.5)	1.96 (1.23, 3.14)	2.06 (1.22, 3.46)
Wealth index[c]				
≤Poor	278	11.1 (7.2, 16.7)	Referent	-
Average	146	9.7 (4.8, 18.5)	0.87 (0.36, 2.10)	-
≥Rich	329	17.7 (12.0, 25.3)	1.59 (0.91, 2.80)	-
Body mass index				
<18.5 kg/m^2	71	14.9 (7.3, 28.2)	1.15 (0.50, 2.67)	1.09 (0.46, 2.61)
18.5-<25 kg/m^2	551	13.0 (8.9, 18.5)	Referent	Referent
≥25 kg/m^2	130	14.0 (6.6, 27.3)	1.08 (0.47, 2.48)	0.93 (0.37, 2.35)
RBC folate insufficiency (<748 nmol/L)				
Total	753	81.4 (75.0, 86.4)	-	-
Region				
North	240	87.3 (78.5, 92.9)	1.04 (0.92, 1.18)	-
Central	259	83.8 (74.7, 90.0)	Referent	-
South	254	77.8 (66.9, 85.9)	0.93 (0.80, 1.08)	-
Residence				
Urban	119	98.3 (93.5, 99.5)	1.23 (1.14, 1.33)	1.23 (1.14, 1.33)
Rural	634	79.7 (73.1, 85.0)	Referent	Referent
Age (years)				

	N [a]	Weighted % (95% CI)	Crude prevalence ratio (95% CI)	Adjusted prevalence ratio[b] (95% CI)
15–24	315	80.7 (72.1, 87.2)	Referent	Referent
25–34	209	84.7 (77.0, 90.1)	1.05 (0.94, 1.17)	1.04 (0.93, 1.16)
35–49	229	79.3 (70.1, 86.2)	0.98 (0.88, 1.09)	0.98 (0.89, 1.09)
Education				
≤Primary	566	78.6 (71.1, 84.5)	Referent	-
≥Secondary	186	92.2 (84.9, 96.1)	1.17 (1.06, 1.30)	-
Wealth index[c]				
≤Poor	278	78.6 (69.7, 85.4)	Referent	-
Average	146	80.4 (68.8, 88.4)	1.02 (0.90, 1.16)	-
≥Rich	329	85.0 (77.7, 90.2)	1.08 (0.98, 1.20)	-
Body mass index				
<18.5 kg/m^2	71	82.9 (71.1, 90.5)	1.03 (0.93, 1.15)	1.02 (0.91, 1.14)
18.5-<25 kg/m^2	551	80.2 (7.2, 85.7)	Referent	Referent
≥25 kg/m^2	130	86.3 (75.9, 92.7)	1.08 (0.97, 1.20)	1.04 (0.93, 1.17)

Abbreviations: BMI, body mass index; CI, confidence interval; RBC, red blood cell.

[a] *N*, unweighted.

[b] Analyses for serum and RBC folate deficiency adjusted for age, education level, and BMI. Analyses for RBC folate insufficiency adjusted for residence, age, and BMI.

[c] Categorized based on wealth index quintiles from the 2015–2016 Malawi Demographic and Health Survey. Lowest and second quintiles categorized as "≤poor." Middle quintile categorized as "average." Fourth and highest quintiles categorized "≥rich."

TABLE 3

Serum vitamin B_{12} deficiency and insufficiency by demographic characteristics among nonpregnant women of reproductive age 15–49 years, Malawi Micronutrient Survey, 2015–2016.

	N [a]	Weighted % (95% CI)	Crude prevalence ratio (95% CI)	Adjusted prevalence ratio[b] (95% CI)
Serum vitamin B_{12} deficiency (<148 pmol/L)				
Total	762	11.8 (8.6, 16.0)	-	-
Region				
North	242	12.3 (5.7, 24.6)	0.69 (0.31, 1.56)	0.91 (0.45, 1.81)
Central	262	17.7 (12.1, 24.1)	Referent	Referent
South	258	6.3 (3.1, 12.7)	0.36 (0.16, 0.78)	0.45 (0.22, 0.94)
Residence				
Urban	122	0.4 (0.1, 1.8)	0.03 (0.01, 0.15)	0.06 (0.01, 0.34)
Rural	640	12.9 (9.5, 17.3)	Referent	Referent
Age (years)				
15–24	322	9.5 (5.7, 15.5)	Referent	Referent
25–34	211	10.5 (5.8, 18.1)	1.10 (0.51, 2.39)	1.22 (0.56, 2.67)
35–49	229	16.3 (8.4, 29.4)	1.71 (0.73, 4.02)	1.67 (0.73, 3.80)
Education				
≤Primary	572	13.2 (9.4, 18.3)	Referent	-
≥Secondary	189	6.2 (2.7, 13.4)	0.47 (0.19, 1.14)	-
Wealth index[c]				
≤Poor	283	18.6 (13.9, 24.5)	Referent	Referent
Average	147	11.2 (4.2, 26.6)	0.60 (0.23, 1.54)	0.66 (0.27, 1.63)
≥Rich	332	4.4 (2.3, 8.1)	0.23 (0.11, 0.48)	0.32 (0.15, 0.70)
Body mass index				
<18.5 kg/m^2	70	8.9 (2.1, 31.2)	0.68 (0.19, 2.50)	0.71 (0.21, 2.38)
18.5-<25 kg/m^2	558	13.1 (9.8, 17.2)	Referent	Referent
≥25 kg/m^2	132	6.9 (3.5, 13.0)	0.53 (0.26, 1.08)	0.74 (0.37, 1.47)
Serum vitamin B_{12} insufficiency (≤221 pmol/L)				
Total	762	40.6 (34.1, 47.4)	-	-
Region				

	N [a]	Weighted % (95% CI)	Crude prevalence ratio (95% CI)	Adjusted prevalence ratio[b] (95% CI)
North	242	38.4 (26.5, 51.7)	0.69 (0.48, 0.99)	0.78 (0.58, 1.06)
Central	262	55.6 (48.0, 63.0)	Referent	Referent
South	258	27.7 (18.3, 39.7)	0.50 (0.33, 0.75)	0.57 (0.38, 0.84)
Residence				
Urban	122	17.7 (8.3, 34.0)	0.41 (0.20, 0.87)	0.66 (0.44, 0.99)
Rural	640	42.9 (36.1, 50.1)	Referent	Referent
Age (years)				
15–24	322	40.7 (30.8, 51.4)	Referent	Referent
25–34	211	40.1 (31.8, 49.1)	0.99 (0.74, 1.32)	1.05 (0.80, 1.38)
35–49	229	40.8 (30.9, 51.6)	1.00 (0.73, 1.39)	1.00 (0.74, 1.37)
Education				
≤Primary	572	43.1 (35.7, 50.7)	Referent	-
≥Secondary	189	30.9 (20.3, 43.9)	0.72 (0.47, 1.09)	-
Wealth index[c]				
≤Poor	283	54.6 (44.6, 64.2)	Referent	Referent
Average	147	40.1 (27.5, 54.2)	0.73 (0.50, 1.09)	0.80 (0.55, 1.15)
≥Rich	332	25.1 (18.6, 32.9)	0.46 (0.33, 0.64)	0.54 (0.38, 0.77)
Body mass index				
<18.5 kg/m^2	70	29.5 (17.9, 44.6)	0.68 (0.44, 1.06)	0.72 (0.47, 1.09)
18.5-<25 kg/m^2	558	43.3 (36.4, 50.5)	Referent	Referent
≥25 kg/m^2	132	34.2 (22.4, 48.4)	0.82 (0.55, 1.21)	0.98 (0.69, 1.40)

Abbreviations: BMI, body mass index; CI, confidence interval.

[a] *N*, unweighted.

[b] Adjusted for region, residence, age, wealth index, and BMI.

[c] Categorized based on wealth index quintiles from the 2015–2016 Malawi Demographic and Health Survey. Lowest and second quintiles categorized as "≤poor." Middle quintile categorized as "average." Fourth and highest quintiles categorized "≥rich."