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Adiponectin and Altered Metabolic Signalling in Asymptomatic Malaria: A Community-Based, Cross-Sectional Study of Nigerian Children

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Abstract

Background: Asymptomatic *Plasmodium falciparum* infection is common among school-aged children in endemic communities. Whether a microscopy-detectable infection is accompanied by a clinically important disturbance of adipocytokine signalling in apparently well children remains uncertain.

Objective: To determine whether microscopy-detectable asymptomatic *Plasmodium falciparum* infection is associated with changes in circulating adiponectin, leptin, resistin and the leptin-to-adiponectin ratio among afebrile Nigerian school-aged children.

Methods: A community-based, cross-sectional study was conducted among afebrile, symptom-screen-negative children aged 5-9 years, recruited from 20 public primary schools in Southwest Nigeria between March and June 2024. Malaria status was determined by microscopy of Giemsa-stained thick and thin blood films. Plasma adiponectin, leptin and resistin levels were measured by duplicate enzyme-linked immunosorbent assay, and the leptin-to-adiponectin ratio was calculated. Log-transformed outcomes were analysed using multivariable linear regression with school-level cluster-robust standard errors.

Results: Overall, 106/317 children (33.4%) had microscopy-detectable malaria. Baseline characteristics were broadly comparable, although malaria-positive children had lower mean weight-for-age z-scores. In the fully adjusted model, malaria positivity was not independently associated with adiponectin (-2.4%; 95% CI -10.9 to 6.9), leptin (-2.9%; 95% CI -11.4 to 6.4), resistin (2.1%; 95% CI -13.4 to 20.5) or the leptin-to-adiponectin ratio (-0.5%; 95% CI -11.2 to 11.4). Among malaria-positive children with parasite density data, adiponectin showed a weak positive monotonic association with parasite density (Spearman's rho = 0.31; p = 0.002).

Conclusion: Binary microscopy-defined asymptomatic malaria was not associated with major adipocytokine disruption. Parasite burden may carry a weak adiponectin signal, but the finding is hypothesis-generating and requires longitudinal studies using molecular parasite detection and fuller inflammatory-metabolic phenotyping.

Keywords: Adipocytokines, Adiponectin, Leptin, Laboratory medicine, Plasmodium falciparum.

Introduction

Malaria remains a major cause of preventable morbidity and mortality in children. The World Health Organisation estimated 282 million malaria cases and 610,000 deaths in 2024, with the African Region accounting for most cases and deaths. [1] Although paediatric practice often focuses on febrile malaria, asymptomatic *Plasmodium falciparum* infection is common in malaria-endemic communities. This scenario is epidemiologically important because apparently well children may be parasitaemic for prolonged periods, thus contributing to transmission and remaining outside routine clinical detection. [2-4] School-aged children are particularly relevant because repeated or persistent parasitaemia may coexist with anaemia, impaired growth, school absence and reduced learning. [5,6]

Recent Nigerian school-based studies also support the continuing local relevance of asymptomatic malaria in primary-school populations, with reported burdens varying by ecology, season, diagnostic method and sampling frame. [7,8] The present study was, therefore, positioned within a clinical-laboratory question rather than a purely prevalence question: whether apparently well children with microscopy-detectable malaria parasitaemia have measurable differences in selected adipocytokines, after accounting for age, sex, anthropometric status and haemoglobin concentration.

The absence of fever should not be interpreted as the absence of a biological effect. Asymptomatic infection may reflect a state of host-parasite tolerance in which inflammatory activation is muted rather than absent. [2,4,9] In many African settings, this occurs against a background of undernutrition, micronutrient vulnerability, anaemia and recurrent infectious exposures. For clinicians and laboratory physicians, the important question is not only whether parasites are present, but whether parasite carriage is accompanied by measurable changes in host physiology that could matter for growth or metabolic adaptation.

Adipocytokines provide a useful laboratory window into the interface between infection, nutrition and metabolism. Adiponectin is generally associated with insulin-sensitising and anti-inflammatory signalling. Leptin links adipose stores to appetite, neuroendocrine regulation and immune activation, while resistin has been associated with inflammatory and insulin-resistance pathways. [10-17] These mediators are not diagnostic tests for malaria. Rather, they may help characterise host response when interpreted with parasite burden, nutritional status, anaemia and inflammatory context. Evidence on malaria and adipocytokines remains limited. Available studies have largely involved adults, symptomatic disease or cardiometabolic comorbidity, and adult data suggest that falciparum malaria can alter adiponectin and leptin responses. [18] Much less is known about asymptomatic infection in pre-adolescent children. This study, therefore, compared circulating adiponectin, leptin, resistin and the leptin-to-adiponectin ratio by microscopy-determined malaria status. It also assessed whether observed differences persisted after adjustment and examined whether parasite density among infected children showed a graded relationship with adipocytokine concentrations.

Methods

Study design and setting

This was a community-based, cross-sectional study reported in line with the Strengthening the Reporting of Observational Studies in Epidemiology guidance for cross-sectional studies. [19] The survey was conducted from 10 March to 30 June 2024 among public primary school children in an urbanising local

government area of Southwest Nigeria. The area has perennial malaria transmission with seasonal intensification during and shortly after the rains. Field assessment, specimen processing and laboratory analyses followed a prespecified protocol.

Study population, sampling and eligibility

The source population comprised children aged 5-9 years attending public primary schools in the study area. Twenty public primary schools were visited as field clusters to improve community spread and avoid drawing all participants from a single school. Within each school, age-eligible children who were present on the survey day, with written parental or guardian consent, were screened. The design should therefore be interpreted as a school-based community sample rather than a probability sample of all children in the local government area.

Child assent was obtained where appropriate. Children were excluded if they declined participation, had an axillary temperature of 37.5 °C or higher, or had any symptom suggestive of acute illness during the preceding 48 hours. The symptom screen included fever, headache, malaise, vomiting, chills, body pains, poor appetite and current treatment for illness. The analytic population comprised children who were afebrile, symptom-screen negative and had complete microscopy malaria classification and adipocytokine measurements.

Study Size

The present study used all eligible children with complete malaria microscopy and adipocytokine data. No separate *a priori* power calculation was performed for the adipocytokine comparison; the analysis was, therefore, interpreted with emphasis on effect sizes and confidence intervals rather than statistical significance alone. This limitation has been made explicit because the study may not detect small or modest biomarker differences, particularly within the malaria-positive subgroup.

Ethical considerations

The study was approved by the Oyo State Ministry of Health Research Ethics Committee, Ibadan, Nigeria (Approval certificate number AD13/479/016c;2024). Written informed consent was obtained from parents or legal guardians, while assent was obtained from children aged seven years or older. Children with microscopy-confirmed malaria were referred for standard antimalarial treatment according to national guidance.

Clinical, anthropometric and haematological measurements

Age and sex were recorded using structured study forms. Weight and height were measured using standardised field procedures. Height-for-age and weight-for-age z-scores were generated using the 2007 World Health Organisation Growth References for school-aged children and adolescents and the WHO AnthroPlus software. [20,21] Venous blood was collected into ethylenediaminetetraacetic acid tubes between 7:00 and 8:00 am before the first meal of the day. Samples were transported at 4-8 °C, centrifuged within four hours, aliquoted and stored at -80 °C until assay. Haematocrit, haemoglobin concentration, white blood cell count and platelet count were measured using routine haematology procedures.

Malaria microscopy and biomarker assays

Thick and thin blood films were prepared, stained with Giemsa and examined under light microscopy according to World Health Organisation procedures. [22] Children were classified as malaria-positive if Plasmodium parasites were detected, and malaria-negative if no parasite was detected on microscopy reading. Two trained microscopists, blinded to clinical and biomarker data, read each slide independently;

discrepancies in positivity, species classification or parasite counts were resolved by a senior microscopist. Parasite density was estimated from thick films using an assumed leukocyte count of 8,000 cells/μL. [22]

Plasma adiponectin, leptin and resistin concentrations were measured in duplicate using commercially available human enzyme-linked immunosorbent assay kits from Melsin Medical Co., Limited, Changchun, Jilin Province, China. The catalogue numbers were EKHU-0843 for adiponectin, EKHU-0715 for leptin and EKHU-0845 for resistin. Assays were performed according to the manufacturer's instructions using the quantitative double-antibody sandwich enzyme immunoassay principle, with optical density read at 450 nm and analyte concentrations derived from the corresponding standard curves. The mean duplicate value was used for analysis; samples with a duplicate coefficient of variation above 15% were repeated. Eight samples required a repeat assay. The leptin-to-adiponectin ratio was calculated as a marker of the balance between pro-inflammatory and insulin-sensitising adipocytokine signalling. C-reactive protein was measured only in a limited subset and was not included in the primary analyses. Cortisol, erythrocyte sedimentation rate, interleukin-6, tumour necrosis factor-alpha, ferritin, insulin, fasting glucose and lipid fractions were not measured.

Screening for Other Illnesses

The study screened out clinically apparent acute illness through temperature measurement and a structured 48-hour symptom screen. However, systematic testing for helminth infection, schistosomiasis, occult bacterial or viral infection and subclinical inflammatory states was not performed. This is important for interpretation because such conditions may independently influence adipocytokine concentrations.

Statistical analysis

Continuous variables were summarised as mean and standard deviation when approximately symmetric. Adipocytokines were right-skewed and are presented as geometric means with 95% Confidence Intervals (95% CI). Categorical variables are presented as frequencies and percentages. Baseline comparisons used Welch t tests for continuous variables and Chi-Square or Fisher's Exact tests for categorical variables. Adipocytokine distributions were compared using Wilcoxon rank-sum tests. Associations between malaria status and each log-transformed adipocytokine outcome were examined using linear regression analysis with school-level cluster-robust standard errors. [23,24] Exponentiated coefficients were expressed as percentage differences comparing malaria-positive with malaria-negative children. Model 1 adjusted for age and sex; Model 2 additionally adjusted for height-for-age and weight-for-age z-scores; and Model 3 additionally adjusted for haemoglobin concentration. Socioeconomic status was added in the sensitivity analysis because of incomplete questionnaire data and its role as a distal determinant. Among malaria-positive children, Spearman's correlation assessed relationships between parasite density and adipocytokines; false-discovery-rate adjustment used the Benjamini-Hochberg approach, with bootstrap confidence intervals where appropriate.[25, 26] Analyses were performed using Stata 18. [27] Statistical significance was assessed at a two-sided p-value below 0.05, while interpretation emphasised effect size, precision, temporality and biological plausibility.

Results

A total of 789 age-eligible children were present in the selected schools, of whom 452 had written parental consent. After consent, 135 children were excluded because assent was declined or refused (n = 104) or because at least one symptom was reported during the preceding 48 hours (n =

31). The final analytic sample comprised 317 afebrile, symptom-screen negative children with complete microscopy malaria status and adipocytokine data. Of these, 211 (66.6%) were malaria-negative, and 106 (33.4%) were malaria-positive by microscopy. The participant flow from school screening to final analytic classification is shown in Figure 1.

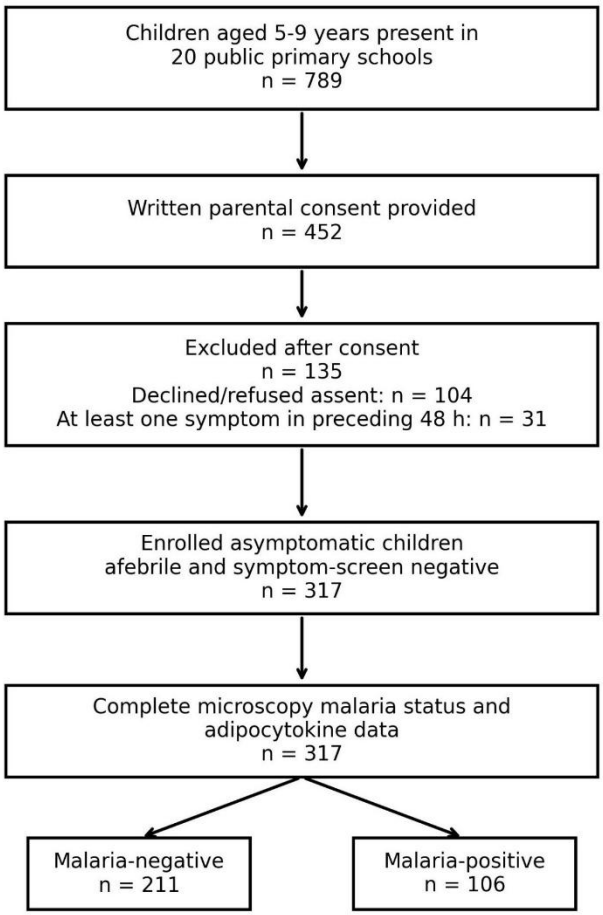

Figure 1: Participant flow from school screening to final analytic classification by microscopy malaria status

Baseline demographic, anthropometric and haematological characteristics are shown in Table I and were broadly similar between malaria-positive and malaria-negative children. Denominators and standardised effect sizes for baseline characteristics and biomarker distributions are provided in Supplementary Table I. The mean age of participants was 7.1 years, and 153 (48.3%) were male. Baseline demographic, anthropometric and haematological characteristics were broadly similar between malaria-positive and malaria-negative children. Malaria-positive children had a modestly lower mean weight-for-age z-score than malaria-negative children (-1.4 versus -1.2; p = 0.024). Mean haemoglobin concentration, white blood cell count, haematocrit and platelet count did not differ materially by microscopy malaria status.

Unadjusted adipocytokine concentrations are summarised in Table II and showed no clear separation between malaria-positive and malaria-negative children. The corresponding distributional plots are shown in Supplementary Figure 1. Unadjusted adipocytokine distributions

showed no clear separation between malaria-positive and malaria-negative children. The geometric mean adiponectin concentration was 67.8 µg/mL in malaria-negative children and 66.5 µg/mL in malaria-positive children (p = 0.890). Geometric mean leptin concentration was 3.0 ng/mL in malaria-negative children and 2.9 ng/mL in malaria-positive children (p = 0.509). Resistin was also comparable between groups, with geometric means of 3.8 ng/mL and 4.0 ng/mL, respectively (p = 0.410). The mean leptin-to-adiponectin ratio was similar in both groups (p = 0.366).

The multivariable regression results are shown in Table III. In regression analyses of log-transformed outcomes, malaria positivity was not independently associated with any measured adipocytokine across the sequential adjustment strategyIn regression analyses of log-transformed outcomes, malaria positivity was not independently associated with any measured adipocytokine across the sequential adjustment strategy. In the fully adjusted model, malaria positivity was associated with a -2.4% difference in adiponectin (95% CI -10.9 to 6.9; p = 0.600), a -2.9% difference in leptin (95% CI -11.4 to 6.4; p = 0.526), a 2.1% difference in resistin (95% CI -13.4 to 20.5; p = 0.802), and a -0.5% difference in the leptin-to-adiponectin ratio (95% CI -11.2 to 11.4; p = 0.927). The fully adjusted percentage differences are displayed in Figure 2. Additional adjustment for socioeconomic status produced no material change.

Table I: Baseline characteristics of the 317 participants by microscopy malaria status

Characteristic	Overall	Malaria-negative	Malaria-positive	p-value
Age (years)	7.1 (1.2)	7.1 (1.2)	7.2 (1.2)	0.949
Male sex, n (%)	153 (48.3)	102 (48.3)	51 (48.1)	1.000
Height (cm)	117.8 (8.1)	118.2 (8.1)	116.9 (7.9)	0.160
Weight (kg)	19.7 (3.5)	19.9 (3.6)	19.2 (3.1)	0.073
Height-for-age z-score	-0.8 (1.1)	-0.7 (1.1)	-0.9 (1.1)	0.059
Weight-for-age z-score	-1.2 (0.9)	-1.2 (0.9)	-1.4 (0.9)	0.024
BMI-for-age z-score	-1.1 (0.9)	-1.1 (0.9)	-1.2 (0.9)	0.252
Haemoglobin (g/dL)	11.0 (2.1)	11.1 (2.1)	10.9 (2.1)	0.480
White blood cell count (×10^9/L)	7.1 (1.9)	7.1 (2.0)	7.0 (1.7)	0.483
Haematocrit (%)	33.8 (5.4)	33.9 (5.3)	33.6 (5.8)	0.624
Platelets (×10^9/L)	254.9 (100.8)	260.3 (106.0)	244.1 (88.9)	0.151
Low socioeconomic status, n (%)	168 (55.6)	113 (53.6)	55 (60.4)	0.104

Values are mean (SD) or n (%). Continuous variables were compared using Welch t tests; categorical variables were compared using Chi-Square or Fisher's Exact tests as appropriate. Socioeconomic status had 15 missing values.

Table II: Adipocytokine concentrations by microscopy malaria status

Biomarker	Overall (95% CI)	Malaria-negative (95% CI)	Malaria-positive (95% CI)	p-value
Adiponectin (µg/mL)	67.3 (65.3-69.4)	67.8 (65.7-69.9)	66.5 (62.2-71.1)	0.890
Leptin (ng/mL)	3.0 (2.9-3.1)	3.0 (2.9-3.2)	2.9 (2.8-3.1)	0.509
Resistin (ng/mL)	3.9 (3.6-4.2)	3.8 (3.5-4.2)	4.0 (3.5-4.6)	0.410
Leptin-to-adiponectin ratio	0.04 (0.04-0.05)	0.04 (0.04-0.05)	0.04 (0.04-0.05)	0.366

Values are geometric means (95% CI). P values compared malaria-positive and malaria-negative groups using Wilcoxon rank-sum tests. CI = confidence interval.

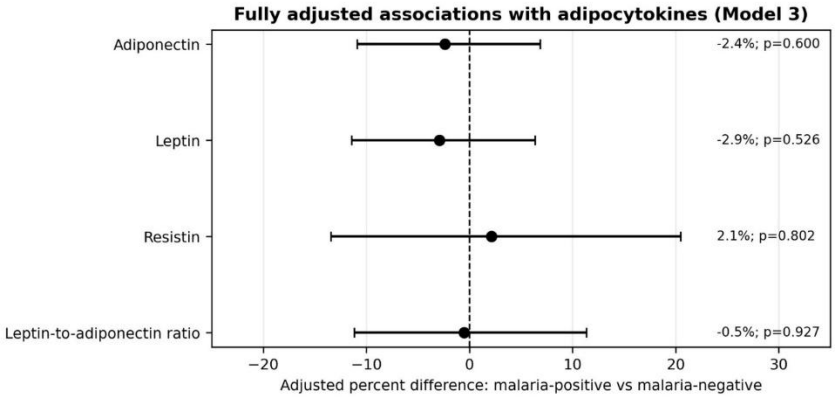

Figure 2: Fully adjusted percentage differences in adipocytokines comparing malaria-positive with malaria-negative children. Model 3 adjusted for age, sex, height-for-age z-score, weight-for-age z-score and haemoglobin concentration.

Table III: Multivariable associations between microscopy malaria status and adipocytokines

Outcome/Model	**N**	Per cent **difference (95% CI)**	p-**value**
Adiponectin			
Model 1 (age, sex)	317	-1.9 (-10.6 to 7.6)	0.682
Model 2 (+ HAZ, WAZ)	317	-2.6 (-11.2 to 6.9)	0.586
Model 3 (+ haemoglobin)	317	-2.4 (-10.9 to 6.9)	0.600
Sensitivity (Model 3 + SES)	302	-4.4 (-14.4 to 6.8)	0.430
Leptin			
Model 1 (age, sex)	317	-2.8 (-11.8 to 7.1)	0.561
Model 2 (+ HAZ, WAZ)	317	-3.2 (-11.9 to 6.5)	0.505
Model 3 (+ haemoglobin)	317	-2.9 (-11.4 to 6.4)	0.526
Sensitivity (Model 3 + SES)	302	-2.6 (-12.0 to 7.7)	0.604
Resistin			
Model 1 (age, sex)	317	4.4 (-11.4 to 22.9)	0.608
Model 2 (+ HAZ, WAZ)	317	2.1 (-13.5 to 20.6)	0.806
Model 3 (+ haemoglobin)	317	2.1 (-13.4 to 20.5)	0.802
Sensitivity (Model 3 + SES)	302	-0.3 (-15.9 to 18.2)	0.974
Leptin-to-adiponectin ratio			
Model 1 (age, sex)	317	-0.9 (-11.4 to 10.7)	0.867
Model 2 (+ HAZ, WAZ)	317	-0.6 (-11.2 to 11.2)	0.911
Model 3 (+ haemoglobin)	317	-0.5 (-11.2 to 11.4)	0.927
Sensitivity (Model 3 + SES)	302	1.8 (-8.6 to 13.4)	0.745

Outcomes were log-transformed. Per cent differences compared malaria-positive with malaria-negative children and were calculated as (exp(beta)-1) x 100. Model 1 adjusted for age and sex; Model 2 added HAZ and WAZ; Model 3 added haemoglobin. SES - Socioeconomic status.

Exploratory age- and sex-stratified adjusted associations are shown in Supplementary Figure 2. Distributions of adiponectin, leptin and the leptin-to-adiponectin ratio by malaria status within sex and age bands are shown in Supplementary Figure 3. Sensitivity distribution checks across analytic subsets are shown in Supplementary Figure 4. Among malaria-positive children with parasite-density data, the adiponectin-parasite density relationship is

displayed in Figure 3, while the corresponding Spearman correlation results are summarised in Table IV. False-discovery-rate-adjusted parasite-density analyses are provided in Supplementary Table II. Among malaria-positive children with parasite-density data (n = 101), adiponectin showed a weak positive monotonic relationship with parasite density (Spearman's rho = 0.31; p = 0.002). This association remained the clearest parasite-density signal after false-discovery-rate adjustment. In contrast, parasite density showed no meaningful correlation with leptin, resistin or the leptin-to-adiponectin ratio. Since this was a secondary subgroup analysis in a cross-sectional dataset, the parasite-density finding was treated as hypothesis-generating. Additional distributional, subgroup and sensitivity analyses are shown in Supplementary Table I, Supplementary Table II and Supplementary Figures 1-4. False-discovery-rate-adjusted parasite-density analyses are provided in Supplementary Table II.

Discussion

This community-based study found that microscopy-detectable asymptomatic malaria was not associated with major differences in circulating adiponectin, leptin, resistin or the leptin-to-adiponectin ratio among apparently healthy Nigerian school-aged children after adjustment for age, sex, anthropometric status and haemoglobin concentration. The principal laboratory signal was not a categorical difference between infected and uninfected children, but a weak positive association between parasite density and adiponectin among microscopy-positive children.

The lack of a strong binary association is plausible. Asymptomatic parasitaemia is not equivalent to acute febrile malaria. Children living in endemic settings may acquire partial clinical immunity that limits fever and severe inflammation despite persistent or recurrent parasitaemia. [2,4,9]

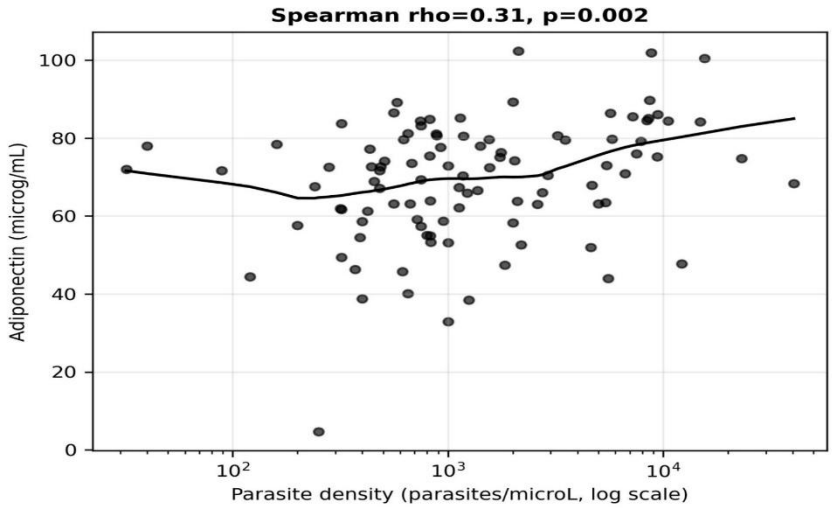

Figure 3: Plasma adiponectin concentration and parasite density among malaria-positive children. The x-axis is logarithmic; the fitted line is a non-parametric smooth. Spearman's rho = 0.31; p = 0.002.

Table IV: Spearman correlations among malaria-positive children

Association	N	Spearman's rho (95% CI)	p-value
Parasite density vs adiponectin	101	0.31 (0.13 to 0.48)	0.002
Parasite density vs leptin	101	0.12 (-0.07 to 0.29)	0.251
Parasite density vs resistin	101	-0.06 (-0.24 to 0.12)	0.532
Parasite density vs leptin-to-adiponectin ratio	101	-0.13 (-0.31 to 0.06)	0.194
Haemoglobin vs adiponectin	106	0.04 (-0.16 to 0.22)	0.715
Haemoglobin vs leptin-to-adiponectin ratio	106	-0.09 (-0.27 to 0.09)	0.347

Parasite density is expressed as parasites/μL. Parasite-density analyses included malaria-positive children with available parasite counts. Confidence intervals for parasite-density correlations are bootstrap 95% Confidence Intervals.

A single positive microscopy result may, therefore, represent diverse host-parasite states, ranging from low-density carriage with minimal systemic response to higher parasite burdens with more active immune-metabolic signalling.

The adiponectin-parasite density association deserves cautious interpretation. Adiponectin is often viewed as anti-inflammatory and insulin-sensitising, but its behaviour during infection may be context-specific. [10-14] A weak positive relationship with parasite density could reflect compensatory anti-inflammatory signalling, altered adipose-tissue response to chronic parasitic exposure, hepatic or endothelial involvement, or residual confounding by nutritional and inflammatory factors not fully captured in this study. It should not be interpreted as diagnostic, prognostic or therapeutic evidence.

The null findings for plasma leptin, resistin and the leptin-to-adiponectin ratio are also informative. Leptin is closely linked to adiposity, appetite regulation and immune activation, while plasma resistin level has been associated with inflammatory pathways and insulin resistance. [15-17] In acute infection or cardiometabolic disease, more pronounced shifts may be expected. Adult data from Ghana suggested that falciparum malaria can raise plasma adiponectin and produce differing leptin responses in diabetic and non-diabetic adults. [18] The present paediatric findings differ in age, symptom status and metabolic background, and suggest that asymptomatic malaria in pre-adolescent schoolchildren may produce subtler laboratory changes than symptomatic disease or infection in metabolically vulnerable adults.

For paediatric practice, the message is proportionate interpretation. School-aged children with asymptomatic malaria remain important for malaria control because they may contribute to transmission and may experience anaemia or educational consequences over time. [5,6] However, these data do not support a claim that microscopy-positive, apparently well children have major disruption of plasma adiponectin, leptin or resistin as a group. For laboratory medicine, the findings highlight the importance of pre-analytical and biological context: fasting morning sampling, nutritional status, haemoglobin concentration, parasite density, assay precision and inflammatory markers all matter when adipocytokine levels are interpreted.

The study also clarifies the limits of what a cross-sectional design can answer. It cannot determine whether plasma adipocytokine patterns preceded infection, resulted from current parasite carriage, represented recovery from a previous infection or reflected stable child-level traits. This limitation is central, not incidental. The analysis, therefore, supports association and description, not causation. A longitudinal cohort with pre-infection baseline sampling, molecular parasite

detection and post-treatment follow-up would be a stronger design for causal inference.

Other limitations should be considered. Microscopy may have missed a sub-microscopic infection detectable by polymerase chain reaction. The study covered one field season only and may not represent other transmission periods. No formal *a priori* sample-size calculation was done for the adipocytokine comparison; consequently, modest differences could have been missed. Systematic testing for helminths, schistosomiasis and occult infections was not performed. C-reactive protein was available only in a small subset, and cortisol, erythrocyte sedimentation rate, interleukin-6, tumour necrosis factor-alpha, ferritin, insulin, glucose, lipid fractions and pubertal staging were not measured. Manufacturer-specific ELISA kit details and reference ranges should be reported in future replication-focused laboratory studies.

The strengths include community-based recruitment across twenty schools, focus on school-aged children, strict symptom screening, fasting morning sampling, duplicate enzyme-linked immunosorbent assays, blinded double microscopy with adjudication, school-level cluster-robust standard errors and transparent presentation of effect sizes with confidence intervals. These features reduce, but do not eliminate, the interpretive constraints of a cross-sectional biomarker study.

Conclusion

Microscopy-detectable asymptomatic malaria was not associated with major adipocytokine differences in the cohort studied, but parasite density showed a weak positive relationship with adiponectin. The finding should be viewed as a signal for future study rather than proof of altered metabolic signalling. Future studies should combine longitudinal follow-up, molecular malaria detection, inflammatory markers and insulin-glucose-lipid phenotyping to clarify whether adiponectin variation is adaptive, compensatory or clinically irrelevant.

References

1. World Health Organisation. World malaria report 2025: addressing the threat of antimalarial drug resistance. Geneva: World Health Organisation; 2025. Available from: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2025.
2. Bousema T, Okell L, Felger I, Drakeley C. Asymptomatic malaria infections: detectability, transmissibility and public health relevance. *Nat Rev Microbiol* 2014;12:833-40. https://doi.org/10.1038/nrmicro3364
3. Lindblade KA, Steinhardt L, Samuels A, Kachur SP, Slutsker L. The silent threat: asymptomatic parasitemia and malaria transmission. *Expert Rev Anti Infect Ther* 2013;11:623-39. https://doi.org/10.1586/eri.13.45
4. Chen I, Clarke SE, Gosling R, Hamainza B, Killeen G, Magill A, *et al.* Asymptomatic malaria: a chronic and debilitating infection that should be treated. *PLoS Med* 2016;13:e1001942.

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https://doi.org/10.1371/journal.pmed.1001942.

5. Brooker SJ, Clarke S, Fernando D, Gitonga CW, Nankabirwa J, Schellenberg D, *et al.* Malaria in school-age children in Africa: An increasingly important challenge. *Trop Med Int Health* 2014;19:1294-309. https://doi.org/10.1111/tmi.12374
6. Nankabirwa JI, Wandera B, Amuge P, Kiwanuka N, Dorsey G, Rosenthal PJ, *et al.* Impact of intermittent preventive treatment with dihydroartemisinin-piperaquine on malaria in Ugandan schoolchildren: A randomised, placebo-controlled trial. *Clin Infect Dis* 2014;58:1404-12. https://doi.org/10.1093/cid/ciu150
7. Oduwole OA, Ale T, Bello S, Shoyinka S, Okebe J. The prevalence and density of asymptomatic Plasmodium infections among children in a rural community of South-Western Nigeria. *Sokoto J Med Lab Sci* 2023;8:33-9. https://doi.org/10.4314/sokjmls.v8i1.4
8. Ayogu EE, Anosike C, Azumara SI, Ani DN. Prevalence of asymptomatic malaria and anemia among primary school children in Enugu State, Nigeria. *Int J Pharm Pharm Sci* 2023;15:14-8. https://doi.org/10.22159/ijpps.2023v15i8.48216
9. Laishram DD, Sutton PL, Nanda N, Sharma VL, Sobti RC, Carlton JM, *et al.* The complexities of malaria disease manifestations with a focus on asymptomatic malaria. *Malar J* 2012;11:29. https://doi.org/10.1186/1475-2875-11-29
10. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. *Nature* 2017;542:177-85. https://doi.org/10.1038/nature21363
11. Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. *Nat Rev Immunol* 2011;11:85-97. https://doi.org/10.1038/nri2921
12. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. *Nat Rev Immunol* 2006;6:772-83. https://doi.org/10.1038/nri1937
13. Yamauchi T, Kamon J, Waki H, Terauchi Y, Kubota N, Hara K, *et al.* The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. *Nat Med* 2001;7:941-6. https://doi.org/10.1038/90984
14. Fantuzzi G. Adiponectin and inflammation: consensus and controversy. *J Allergy Clin Immunol* 2008;121:326-30. https://doi.org/10.1016/j.jaci.2007.10.018
15. Friedman JM, Halaas JL. Leptin and the regulation of body weight in mammals. *Nature* 1998;395:763-70. https://doi.org/10.1038/27376
16. Matarese G, Moschos S, Mantzoros CS. Leptin in Immunology. *J Immunol* 2005;174:3137-42. https://doi.org/10.4049/jimmunol.174.6.3137
17. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, *et al.* The hormone resistin links obesity to diabetes. *Nature* 2001;409:307-12. https://doi.org/10.1038/35053000
18. Acquah S, Boampong JN, Eghan BA Jr, Eriksson M. Elevated adiponectin but varied response in circulating leptin levels to falciparum malaria: results from a prospective study. *Lipids Health Dis* 2016;15:187. https://doi.org/10.1186/s12944-016-0361-z
19. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, for the STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology statement: guidelines for reporting observational studies. *PLoS Med* 2007;4:e296. https://doi.org/10.1371/journal.pmed.0040296
20. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ* 2007;85:660-7. https://doi.org/10.2471/BLT.07.043497
21. World Health Organisation. WHO AnthroPlus for personal computers: software for assessing growth of the world's children

and adolescents. Geneva: World Health Organisation; 2009. Available from: https://www.who.int/tools/growth-reference-data-for-5to19-years/anthroplus-software.

22. World Health Organisation. Basic malaria microscopy. Part I: learner's guide. 2nd ed. Geneva: World Health Organisation; 2010. Available from: https://apps.who.int/iris/handle/10665/44208.
23. Huber PJ. The behaviour of maximum likelihood estimates under nonstandard conditions. In: Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability. Berkeley: University of California Press; 1967. p. 221-33.
24. White H. A heteroskedasticity-consistent covariance matrix estimator and a direct test for heteroskedasticity. *Econometrica* 1980;48:817-38. https://doi.org/10.2307/1912934
25. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc* Series B 1995;57:289-300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x
26. Efron B, Tibshirani RJ. An introduction to the bootstrap. Boca Raton: Chapman & Hall/CRC; 1994.
27. StataCorp. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC; 2023.

Supplementary Materials

Supplementary Table I. Baseline characteristics with denominators and standardised effect sizes.

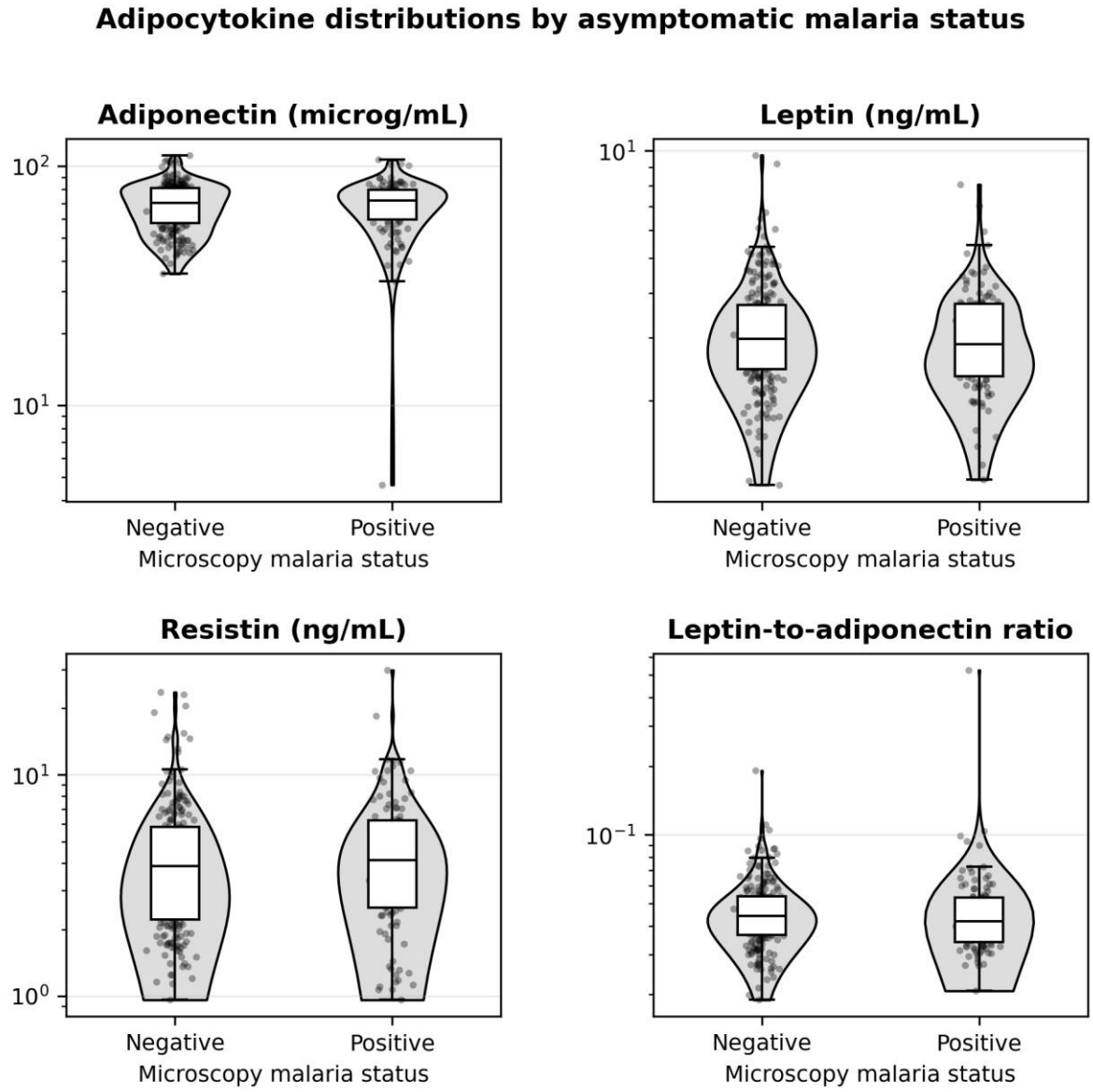
Characteristic	N	Overall	Malaria-negative	Malaria-positive	p-value	Effect size
Age (years)	317	7.1 (1.2)	7.1 (1.2)	7.2 (1.2)	0.949	0.01
Male sex, n (%)	317	153 (48.3)	102 (48.3)	51 (48.1)	1.000	0.00
High socioeconomic status, n (%)	302	9 (3.0)	9 (4.3)	0 (0.0)	0.097	0.12
Middle socioeconomic status, n (%)	302	125 (41.4)	89 (42.2)	36 (39.6)		
Low socioeconomic status, n (%)	302	168 (55.6)	113 (53.6)	55 (60.4)		
Height (cm)	317	117.8 (8.1)	118.2 (8.1)	116.9 (7.9)	0.160	-0.17
Weight (kg)	317	19.7 (3.5)	19.9 (3.6)	19.2 (3.1)	0.073	-0.20
BMI-for-age z-score	317	-1.1 (0.9)	-1.1 (0.9)	-1.2 (0.9)	0.252	-0.10
Height-for-age z-score	317	-0.8 (1.1)	-0.7 (1.1)	-0.9 (1.1)	0.059	-0.23
Weight-for-age z-score	317	-1.2 (0.9)	-1.2 (0.9)	-1.4 (0.9)	0.024	-0.27
Haemoglobin (g/dL)	317	11.0 (2.1)	11.1 (2.1)	10.9 (2.1)	0.480	-0.08
White blood cell count (×10^9/L)	317	7.1 (1.9)	7.1 (2.0)	7.0 (1.7)	0.483	-0.08
Haematocrit (%)	317	33.8 (5.4)	33.9 (5.3)	33.6 (5.8)	0.624	-0.06
Platelets (×10^9/L)	317	254.9 (100.8)	260.3 (106.0)	244.1 (88.9)	0.151	-0.16
Adiponectin (µg/mL)	317	67.3 (65.3, 69.4)	67.8 (65.7, 69.9)	66.5 (62.2, 71.0)	0.890	-0.07
Leptin (ng/mL)	317	3.0 (2.9, 3.1)	3.0 (2.9, 3.2)	2.9 (2.8, 3.1)	0.509	-0.08
Resistin (ng/mL)	317	3.9 (3.6, 4.2)	3.8 (3.5, 4.2)	4.0 (3.5, 4.5)	0.410	0.07
Leptin-to-adiponectin ratio	317	0.04 (0.04, 0.05)	0.04 (0.04, 0.05)	0.04 (0.04, 0.05)	0.366	-0.03

Continuous variables are mean (SD), except adipocytokines shown as geometric mean (95% CI). Effect size is the standardised mean difference for continuous variables and Cramer's V for categorical variables. Socioeconomic status N = 302 because of incomplete parental questionnaires.

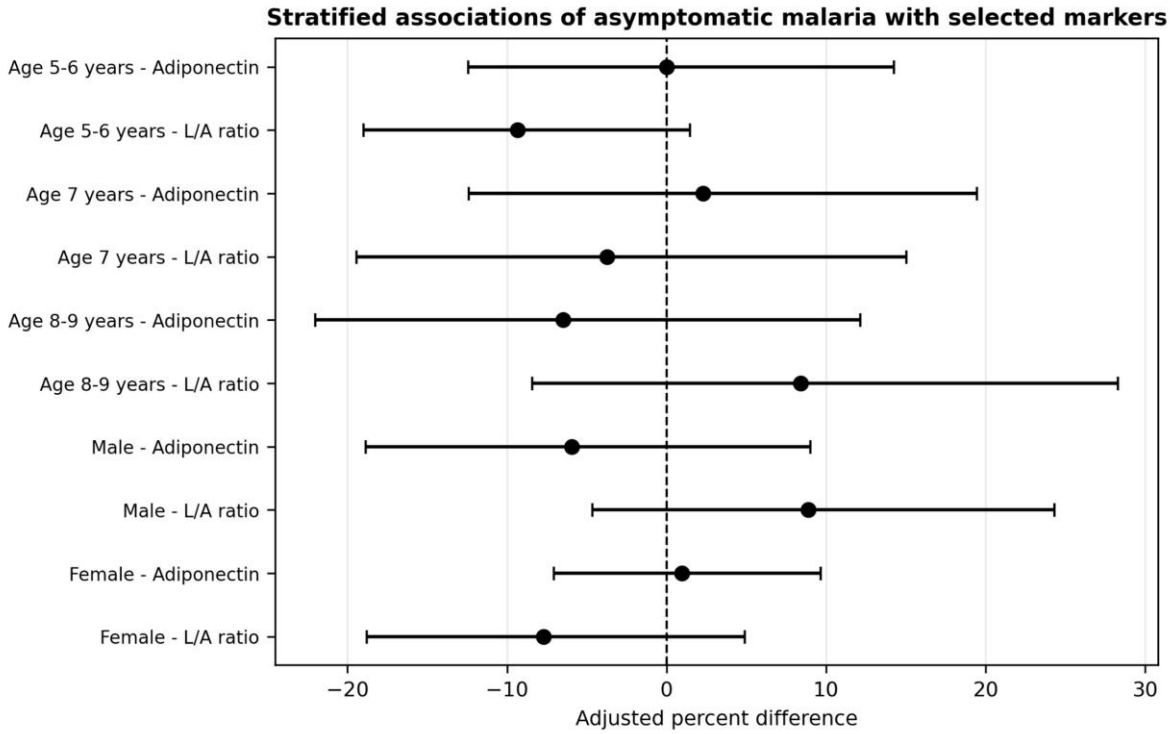
Supplementary Table II. Associations between parasite density and adipocytokines among malaria-positive children.

Marker	Spearman rho (95% CI)	N	Raw P value	FDR-adjusted P value
Adiponectin	0.31 (0.13, 0.48)	101	0.002	0.007
Leptin	0.12 (-0.07, 0.29)	101	0.251	0.334
Resistin	-0.06 (-0.24, 0.12)	101	0.532	0.532
Leptin-to-adiponectin ratio	-0.13 (-0.31, 0.06)	101	0.194	0.334

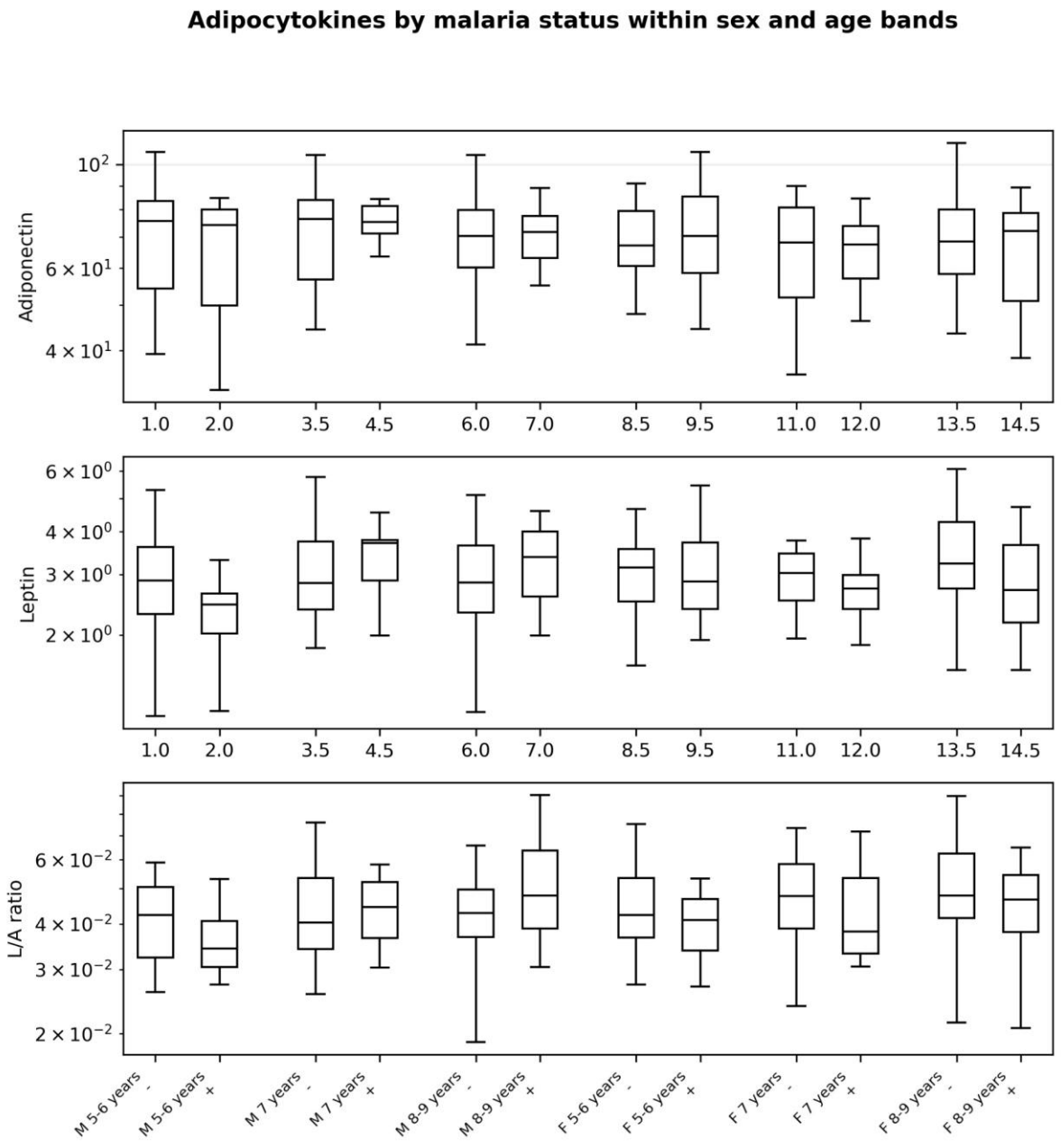
FDR = false discovery rate; CI = Confidence Interval



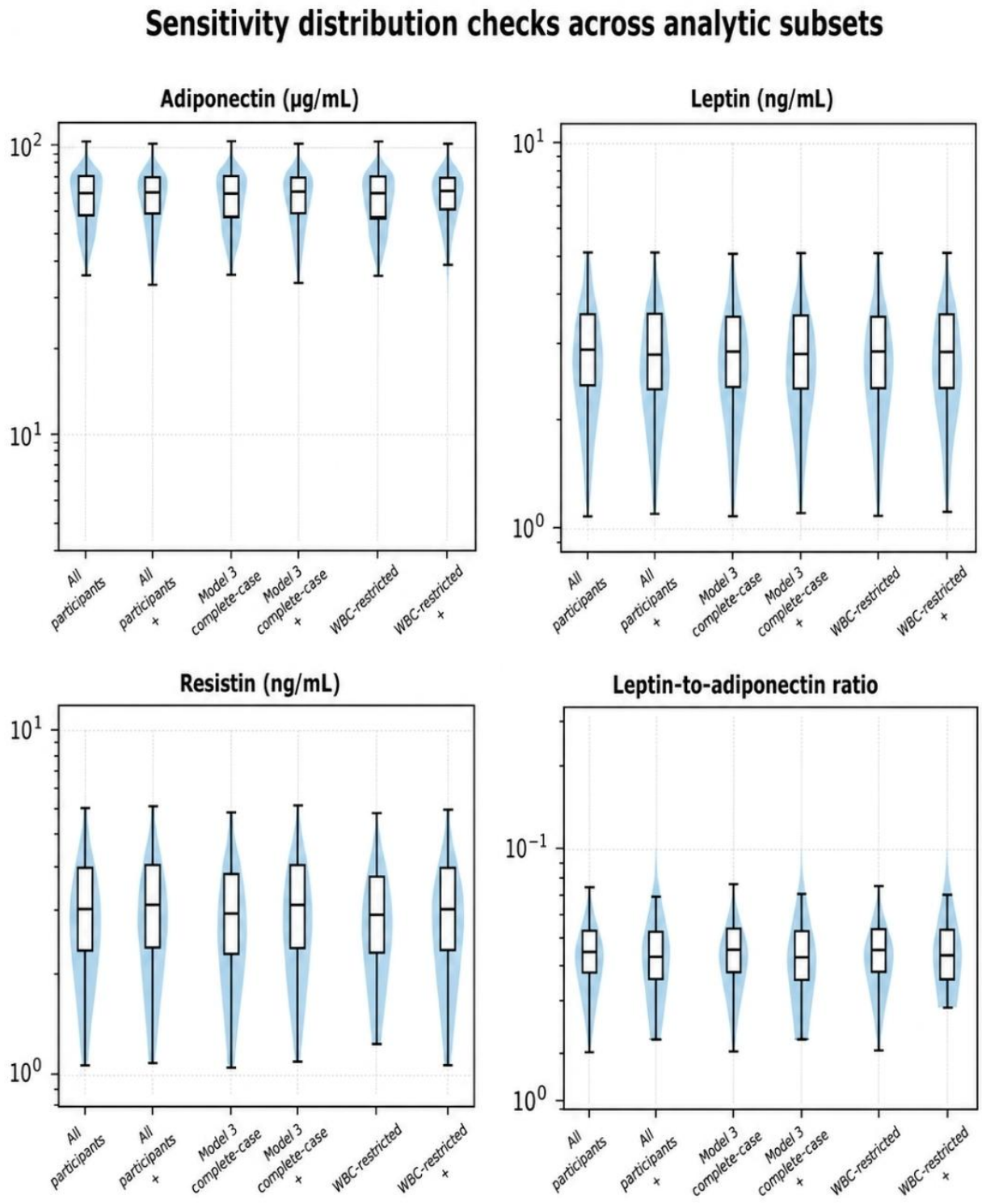
Supplementary Figure 1. Adipocytokine distributions by microscopy malaria status. Violins show distributional density; boxes show median and interquartile range; points show individual observations.



Supplementary Figure 2. Stratified adjusted associations of asymptomatic malaria with selected markers across age and sex subgroups.



Supplementary Figure 3. Adiponectin, leptin and leptin-to-adiponectin ratio by malaria status within sex and age bands.



Supplementary Figure 4. Sensitivity distribution checks for adipocytokines across analytic subsets.