The Association between Recent Infections and Anemia in Children: A Secondary Analysis of the Nepal Demographic and Health Survey

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Abstract

Background: Studies have reported transient decreases in hemoglobin levels during febrile illnesses, such as pneumonia. Nevertheless, the duration of the impact of common childhood infections on anemia assessment has not been fully elucidated. This study investigates the potential associations between recent episodes of fever, diarrhea, or acute respiratory infection (ARI) and anemia in children.

Materials and Methods: A secondary analysis of the Nepal Demographic and Health Survey datasets was conducted. Parental reports of fever, diarrhea, or ARI within the 2 weeks preceding the survey were analyzed for children aged 6–59 months. Anemia was defined as a hemoglobin level of <11.0 g/dL. The prevalence of anemia and mean hemoglobin levels were compared among children with and without recent infections, stratified by age. The association between recent infections and anemia was assessed by multiple logistic regression.

Results: Among the 6,483 children, the prevalence of anemia was 47%. Fever, diarrhea, and ARI occurred in 22%, 11%, and 11% of them, respectively. Children aged 6–11 months with recent fever had a higher prevalence of anemia. However, regarding anemia prevalence or mean hemoglobin levels, this trend was not observed in the other age groups. Multiple logistic regression analyses showed no significant associations between fever (odds ratio [OR], 1.10; 95% confidence interval [CI], 0.97–1.26, *P*-value = 0.13), diarrhea (OR, 0.94; 95% CI, 0.79–1.12, *P*-value = 0.50), or ARI (OR, 1.06; 95% CI, 0.86–1.30, *P*-value = 0.59) and anemia. **Conclusion:** Based on the findings of this study, fever, diarrhea, or ARI were not significantly associated with anemia during the two weeks prior to the survey, with the exception of fever in infants aged 6–11 months. These findings imply that the hemoglobin levels measured two weeks post-infection likely reflect the underlying anemia status rather than the transient infection-related effects.

Keywords: Diarrhea, Fever, Hemoglobin, Infant, Respiratory Tract Infections

Introduction

Anemia, a deficiency in red blood cells or hemoglobin, is a major global health concern, particularly affecting pregnant women and young children (1). Although iron deficiency is the primary cause of childhood anemia (2), inflammation and infection can also contribute to it (3). Fever, which is commonly caused by infectious diseases in children (4), has been associated with decreased hemoglobin levels (5, 6). Evidence suggests correlations between the severity of inflammation or duration of infection and anemia development. However, the mechanisms underlying anemia in acute

infectious diseases have not been fully understood. Most studies have focused on the acute infection phase in small clinical settings (5, 6), leaving a knowledge gap regarding its prolonged effects on hemoglobin levels. This study aimed to investigate the associations between recent episodes of fever, diarrhea, or acute respiratory infection (ARI) and anemia in children within the two weeks proceeding to the study and by using a nationally representative survey Nepal. in Understanding this relationship may improve the interpretation of hemoglobin measurement and inform public health strategies.

Materials and Methods Data Source and Participants

This secondary data analysis used the Nepal Demographic and Health Survey (DHS) datasets in 2011, 2016, and 2022 (7–9). The Nepal DHS is a nationally representative cross-sectional survey. This study was conducted by the Ministry of Health and Population/Nepal, New ERA/Nepal, and ICF International. The survey aims to provide comprehensive information on the health and population status of Nepal. It monitors the health and population and supports the improvement and planning of health services. The study included children aged 6-59 months from households eligible for blood testing, and excluded those with missing information on hemoglobin levels. The Ethics Committee of the Nepal Health Research approved the Nepal Council DHS program. Written informed consent was obtained from each participant's parents/guardians before data collection. The DHS dataset was publicly available on the website of ICF's DHS program. This study was conducted based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (10).

Anemia

Anemia was assessed by measuring hemoglobin levels and by using a portable battery-operated device (HemoCue® system) on site. Anemia was defined as a hemoglobin level of <11.0 g/dL, and classified into three types, namely mild (10.0–10.9 g/dL), moderate (7.0–9.9 g/dL), and severe (<7.0 g/dL).

Fever, Diarrhea, and ARI

Data on whether children had experienced fever, diarrhea, or ARI within the preceding 2 weeks was collected from their parents/guardians and their responses classified as "Yes," "No," or "Unknown/Missing." ARI was defined as chest-related short, rapid breathing and/or difficult breathing. Fever cases were further categorized based on their antibiotic use.

Covariates

Based on the previous studies, the following variables were selected as covariates: child age, child gender, child body mass index (BMI), birth order, number of household members, maternal age, maternal education level, wealth index, and place of residence.

Statistical Analysis

Children with and without fever, diarrhea, or ARI were compared based on their anthropometric and socio-demographic characteristics. The prevalence of anemia and mean hemoglobin levels were compared between children with and without fever, diarrhea, or ARI within the preceding 2 weeks. Subgroup analyses were conducted by considering age and antibiotic use. Independent-samples t tests were run to compare continuous variables between groups, and chi-square tests were used to compare the proportions of categorical variables. To investigate if there were any associations between fever, diarrhea, or ARI and anemia, multiple logistic regression analyses were performed using complete cases without missing values. The following variables were included as adjustment factors: child age (categorized as 6-11, 12-23, 24-35, 36-47, or 48-59 months of age), child gender (boy or girl), child BMI (categorized as underweight, normal, or obese). birth order (categorized as firstborn, secondborn, or thirdborn and beyond), number of household members (categorized as 2-4, 5-7, or 8 and more), maternal age (categorized as 15-24, 25-34, 35–44, or \geq 45 years), maternal (categorized education level as no education, basic, secondary, or higher), wealth index (categorized as very poor, poor, middle-class, rich, or very rich), and place of residence (rural areas or urban areas).

All statistical analyses were performed using the R software (version 4.3.2; R Core Team, 2023). A two-tailed significance level of 5% (P < 0.05) was used for all statistical tests.

Results

Of the 6,723 initially enrolled children, aged 6–59 months, 6,483 underwent blood testing, and were included in the analysis. The overall prevalence of anemia (a hemoglobin level of <11.0 g/dL) was 47% (3,037/6,483). A decreasing trend in anemia prevalence was observed with an increase in age: 72% (6–11 months), 66% (12–23 months), 45% (24–35 months), 37% (36–47 months), and 28% (48–59 months) (Table I). The prevalence of fever, diarrhea, and ARI at any time during the 2 weeks preceding the interview was 22%, 11%, and 11%, respectively.

Table II shows anemia prevalence and mean hemoglobin levels in children with and without fever in different age groups. In children aged 6-11 months, a recent fever was significantly associated with a higher prevalence of anemia (P = 0.012). Although there was a trend toward lower mean hemoglobin levels in children with recent fever, this difference was not statistically significant (P = 0.2). The trends in anemia prevalence and mean hemoglobin levels were not observed in the other age groups (anemia prevalence: *P*-value range from 0.3 to >0.9; mean hemoglobin levels: P-value range from 0.4 to 0.5), Regarding diarrhea and ARI, Similar trends were not observed in anemia prevalence (diarrhea: P-value range from 0.4 to >0.9; ARI: P-value range from 0.075 to 0.9) and mean hemoglobin levels (diarrhea: P-value range from 0.3 to 0.8; ARI: P-value range from 0.094 to >0.9). No significant differences were found in anemia prevalence (P = 0.6) or mean hemoglobin levels (P > 0.9)between the groups with and without antibiotic use (Table III).

Multiple logistic regression analysis results, adjusted for socio-demographic and anthropometric factors, revealed no significant associations between fever (odds ratio [OR], 1.10; 95% confidence interval [CI], 0.97–1.26, P = 0.13), diarrhea (OR, 0.94; 95% CI, 0.79–1.12, P = 0.50), or ARI (OR, 1.06; 95% CI, 0.86–1.30, P = 0.59) within the 2 weeks following the interview and anemia (Figure 1).

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Kuniyoshi et al.

| | Fever | | | Diarrhea | , | | ARI | | |
|------------------------|-------------------------|------------------------|-----------------|-----------------------|----------------------|-----------------|-----------------------|----------------------|-----------------|
| | Absence, N = $5,044$ | Presence, N = 1,437 | <i>P</i> -value | Absence, N = 5,782 | Presence, N = 695 | <i>P</i> -value | Absence, N = 4,335 | Presence, N = 514 | <i>P</i> -value |
| Survey year, n (%) | | | < 0.001 | | | < 0.001 | | | < 0.001 |
| 2011 | 1,670 (33) | 413 (29) | | 1,786 (31) | 297 (43) | | 241 (5.6) | 217 (42) | |
| 2016 | 1,643 (33) | 452 (31) | | 1,943 (34) | 147 (21) | | 1,971 (45) | 123 (24) | |
| 2022 | 1,731 (34) | 572 (40) | | 2,053 (36) | 251 (36) | | 2,123 (49) | 174 (34) | |
| Missing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Sex, n (%) | | | 0.029 | | | 0.061 | | | 0.034 |
| Boy | 2,591 (51) | 785 (55) | | 2,986 (52) | 385 (55) | | 2,249 (52) | 292 (57) | |
| Girl | 2,453 (49) | 652 (45) | | 2,796 (48) | 310 (45) | | 2,086 (48) | 222 (43) | |
| Missing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Age, n (%) | | | < 0.001 | | | < 0.001 | | | < 0.001 |
| 6-11 months | 469 (9.3) | 201 (14) | | 537 (9.3) | 131 (19) | | 427 (9.9) | 100 (19) | |
| 12-23 months | 1,080 (21) | 367 (26) | | 1,224 (21) | 224 (32) | | 997 (23) | 135 (26) | |
| 24-35 months | 1,175 (23) | 321 (22) | | 1,342 (23) | 153 (22) | | 1,006 (23) | 116 (23) | |
| 36-47 months | 1,186 (24) | 296 (21) | | 1,375 (24) | 107 (15) | | 975 (22) | 86 (17) | |
| 48-59 months | 1,134 (22) | 252 (18) | | 1,304 (23) | 80 (12) | | 930 (21) | 77 (15) | |
| Missing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Body mass index, n (%) | | | 0.006 | | | < 0.001 | | | < 0.001 |
| Obese | 53 (1.1) | 8 (0.6) | | 56 (1.0) | 5 (0.7) | | 33 (0.8) | 6 (1.2) | |
| Normal | 4,649 (93) | 1,300 (91) | | 5,338 (93) | 608 (88) | | 4,021 (93) | 449 (88) | |
| Underweight | 318 (6.3) | 120 (8.4) | | 360 (6.3) | 76 (11) | | 267 (6.2) | 55 (11) | |
| Missing | 24 | 9 | | 28 | 6 | | 14 | 4 | |
| Birth order, n (%) | | | < 0.001 | | | 0.8 | | | 0.8 |
| First | 1,619 (33) | 495 (36) | | 1,879 (33) | 232 (34) | | 1,474 (35) | 172 (35) | |
| Second | 1,316 (27) | 408 (30) | | 1,537 (27) | 186 (28) | | 1,166 (28) | 145 (29) | |

Table I: Characteristics of study participants based on fever, diarrhea or acute respiratory infection

Iran J Ped Hematol Oncol. 2025, Vol 15, No 3, 530-542

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533

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| Third a | above | 1,981 (40) | 472 (34) | | 2,198 (39) | 255 (38) | | 1,524 (37) | 179 (36) | |
|---------------------------------------|--------|------------|-----------|---------|------------|----------|---------|------------|----------|---------|
| Mi | issing | 128 | 62 | | 168 | 22 | | 171 | 18 | |
| Number of household members, n (%) | | | 0.002 | | | 0.6 | | | 0.4 | |
| | 2-4 | 1,626 (32) | 533 (37) | | 1,913 (33) | 243 (35) | | 1,472 (34) | 184 (36) | |
| | 5-7 | 2,413 (48) | 626 (44) | | 2,718 (47) | 321 (46) | | 2,011 (46) | 223 (43) | |
| 8 a | above | 1,005 (20) | 278 (19) | | 1,151 (20) | 131 (19) | | 852 (20) | 107 (21) | |
| Mi | issing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Maternal age, n (%) | | | | 0.014 | | | < 0.001 | | | 0.4 |
| 15-24 | years | 1,959 (39) | 607 (42) | | 2,234 (39) | 331 (48) | | 1,740 (40) | 220 (43) | |
| 25-34 | years | 2,549 (51) | 704 (49) | | 2,948 (51) | 303 (44) | | 2,206 (51) | 244 (47) | |
| 35-44 | years | 494 (10) | 122 (8.5) | | 554 (10) | 61 (8.8) | | 369 (8.5) | 49 (9.5) | |
| 45 years | over | 42 (0.8) | 4 (0.3) | | 46 (0.8) | 0 (0.0) | | 20 (0.5) | 1 (0.2) | |
| Mi | issing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Maternal education level | , n | | | < 0.001 | | | 0.6 | | | 0.080 |
| No educ | ation | 1,820 (36) | 410 (29) | | 1,976 (34) | 253 (36) | | 1,247 (29) | 171 (33) | |
| 1 | Basic | 1,258 (25) | 372 (26) | | 1,452 (25) | 178 (26) | | 1,190 (27) | 125 (24) | |
| Secon | ndary | 1,597 (32) | 540 (38) | | 1,920 (33) | 216 (31) | | 1,522 (35) | 183 (36) | |
| Hi | igher | 369 (7.3) | 115 (8.0) | | 434 (7.5) | 48 (6.9) | | 376 (8.7) | 35 (6.8) | |
| Mi | issing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Wealth index, n (%) | | | | < 0.001 | | | 0.6 | | | >0.9 |
| Ро | orest | 1,595 (32) | 379 (26) | | 1,767 (31) | 207 (30) | | 1,260 (29) | 147 (29) | |
| Po | oorer | 1,076 (21) | 302 (21) | | 1,242 (21) | 136 (20) | | 921 (21) | 110 (21) | |
| М | liddle | 977 (19) | 315 (22) | | 1,144 (20) | 147 (21) | | 889 (21) | 103 (20) | |
| r | icher | 798 (16) | 269 (19) | | 940 (16) | 124 (18) | | 763 (18) | 96 (19) | |
| Ri | ichest | 598 (12) | 172 (12) | | 689 (12) | 81 (12) | | 502 (12) | 58 (11) | |
| Mi | issing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Place of residence, n (%) | | | | 0.002 | | | 0.040 | | | < 0.001 |

534

Iran J Ped Hematol Oncol. 2025, Vol 15, No 3, 530-542

Kuniyoshi et al.

| | Urban | 2,077 (41) | 659 (46) | | 2,465 (43) | 268 (39) | | 2,237 (52) | 206 (40) | |
|--------------------------------|------------|--------------|--------------|---------|--------------|--------------|---------|--------------|--------------|-------|
| | Rural | 2,967 (59) | 778 (54) | | 3,317 (57) | 427 (61) | | 2,098 (48) | 308 (60) | |
| | Missing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Anemia, n (%) | | | | 0.002 | | | 0.004 | | | 0.013 |
| | Severe | 21 (0.4) | 8 (0.6) | | 25 (0.4) | 4 (0.6) | | 19 (0.4) | 4 (0.8) | |
| | Moderate | 1,037 (21) | 310 (22) | | 1,173 (20) | 172 (25) | | 921 (21) | 122 (24) | |
| | Mild | 1,245 (25) | 414 (29) | | 1,467 (25) | 192 (28) | | 1,098 (25) | 152 (30) | |
| | Not anemia | 2,741 (54) | 705 (49) | | 3,117 (54) | 327 (47) | | 2,297 (53) | 236 (46) | |
| | Missing | 0 | 0 | | 0 | 0 | | 0 | 0 | |
| Hemoglobin levels mean (SD) | (g/dL), | 11.01 (1.36) | 10.86 (1.30) | < 0.001 | 11.00 (1.34) | 10.77 (1.38) | < 0.001 | 10.96 (1.33) | 10.82 (1.36) | 0.014 |

Continuous variables between groups were compared using independent samples t-tests, and proportions of categorical variables were compared using chi-square tests. A two-tailed significance level of 5% (P < 0.05) was used for all statistical tests.

ARI, acute respiratory infection

Iran J Ped Hematol Oncol. 2025, Vol 15, No 3, 530-542

| (A) Fever | | 14 | | | | | | | | noui jever i | | | | | |
|---|-----------------------------|-----------------------------|-----------------|-----------------------------|-------------------------------|-----------------|-----------------------------|-------------------------------|-----------------|-----------------------------|-------------------------------|-----------------|----------------------------|-------------------------------|-----------------|
| | 6–11 mo | onths of age | | 12–23 mc | onths of age | | 24–35 mc | onths of age | | 36–47 ma | onths of age | | 48–59 mo | onths of age | |
| | Fever (+), N = 201 | Fever (–), N = 469 | P-value | Fever (+), N = 367 | Fever (–), N = 1,080 | <i>P</i> -value | Fever (+), N = 321 | Fever (–), N = 1,175 | <i>P</i> -value | Fever (+), N = 296 | Fever (–), N = 1,186 | <i>P</i> -value | Fever (+), N = 252 | Fever (–), N = 1,134 | <i>P</i> -value |
| Anemia, n (%) | | | 0.012 | | | 0.3 | | | >0.9 | | | 0.9 | | | 0.8 |
| Severe | 3 (1.5) | 1 (0.2) | | 4 (1.1) | 12 (1.1) | | 1 (0.3) | 4 (0.3) | | 0 (0.0) | 3 (0.3) | | 0 (0.0) | 1 (0.1) | |
| Moderate | 77 (38) | 187 (40) | | 108 (29) | 367 (34) | | 62 (19) | 226 (19) | | 39 (13) | 158 (13) | | 24 (10) | 99 (8.7) | |
| Mild | 77 (38) | 139 (30) | | 130 (35) | 330 (31) | | 84 (26) | 296 (25) | | 73 (25) | 270 (23) | | 50 (20) | 210 (19) | |
| Not anemia | 44 (22) | 142 (30) | | 125 (34) | 371 (34) | | 174 (54) | 649 (55) | | 184 (62) | 755 (64) | | 178 (71) | 824 (73) | |
| Hemoglobin levels (g/dl), mean (SD) | 10.11 (1.14) | 10.27 (1.29) | 0.2 | 10.43 (1.22) | 10.37 (1.31) | 0.4 | 10.92 (1.24) | 10.99 (1.25) | 0.4 | 11.23 (1.22) | 11.29 (1.24) | 0.4 | 11.58 (1.16) | 11.63 (1.24) | 0.5 |
| (B) Diarrhea | | | | | | | | | | | | | | | |
| _ | 6–11 mo | onths of age | | 12–23 mc | onths of age | | 24–35 mc | onths of age | | 36–47 mc | onths of age | | 48–59 mo | onths of age | |
| 25-07-02 | Diarrhea (+), N = 131 | Diarrhea (-), N = 537 | <i>P</i> -value | Diarrhea (+), N = 224 | Diarrhea (−), N = 1,224 | <i>P</i> -value | Diarrhea (+), N = 153 | Diarrhea (−), N = 1,342 | <i>P</i> -value | Diarrhea (+), N = 107 | Diarrhea (−), N = 1,375 | <i>P</i> -value | Diarrhea (+), N = 80 | Diarrhea (-), N = 1,304 | <i>P</i> -value |
| anemia, n (%) | | | 0.4 | | | 0.5 | | | 0.4 | | | 0.9 | | | >0.9 |
| Severe | 2 (1.5) | 2 (0.4) | | 2 (0.9) | 14 (1.1) | | 0 (0.0) | 5 (0.4) | | 0 (0.0) | 3 (0.2) | | 0 (0.0) | 1 (0.1) | |
| Moderate | 54 (41) | 208 (39) | | 65 (29) | 410 (33) | | 31 (20) | 257 (19) | | 16 (15) | 181 (13) | | 6 (7.5) | 117 (9.0) | |
| Mild | 42 (32) | 174 (32) | | 80 (36) | 381 (31) | | 31 (20) | 349 (26) | | 23 (21) | 320 (23) | | 16 (20) | 243 (19) | |
| Not anemia | 33 (25) | 153 (28) | | 77 (34) | 419 (34) | | 91 (59) | 731 (54) | | 68 (64) | 871 (63) | | 58 (73) | 943 (72) | |
| Hemoglobin Elevels (g/dl), mean (SD) | 10.13 (1.28) | 10.25 (1.24) | 0.3 | 10.43 (1.29) | 10.38 (1.29) | 0.5 | 11.05 (1.31) | 10.97 (1.24) | 0.5 | 11.25 (1.31) | 11.28 (1.23) | 0.8 | 11.64 (1.23) | 11.62 (1.23) | 0.7 |
| C) ARI | | | | | | | | | | | | | | | |
| | 6–11 mo | onths of age | | 12–23 mc | onths of age | | 24–35 mc | onths of age | | 36–47 mc | onths of age | | 48–59 mo | onths of age | |
| [6] | ARI (+), N = 100 | ARI (-), N = 427 | <i>P</i> -value | ARI (+), N = 135 | ARI (-), N = 997 | <i>P</i> -value | ARI (+), N = 116 | ARI (-), N = 1.006 | <i>P</i> -value | ARI (+), N = 86 | ARI (-), N = 975 | <i>P</i> -value | ARI (+), N = 77 | ARI (-), N = 930 | <i>P</i> -value |
| ⁸ . Anemia, n (%) | | | 0.075 | | | 0.3 | | | 0.088 | | | 0.9 | | | 0.5 |
| Severe | 2 (2.0) | 2 (0.5) | | 2 (1.5) | 11 (1.1) | | 0 (0.0) | 3 (0.3) | | 0 (0.0) | 3 (0.3) | | 0 (0.0) | 0 (0.0) | |
| 536 Iran J Ped Hematol Oncol. 2025, Vol 15, No 3, 530-542 This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 Unported License. | | | | | | | | | | | | | | | |

Table Π : Anomia provalence and mean hemoglobin levels in children with and without fever in different are around

Kuniyoshi et al.

| Moderate | 38 (38) | 164 (38) | | 41 (30) | 346 (35) | | 25 (22) | 198 (20) | | 13 (15) | 127 (13) | | 5 (6.5) | 86 (9.2) | |
|---|-----------------|-----------------|-----|-----------------|-----------------|-------|-----------------|-----------------|-----|-----------------|-----------------|-----|-----------------|-----------------|------|
| Mild | 39 (39) | 132 (31) | | 36 (27) | 305 (31) | | 39 (34) | 241 (24) | | 19 (22) | 230 (24) | | 19 (25) | 190 (20) | |
| Not anemia | 21 (21) | 129 (30) | | 56 (41) | 335 (34) | | 52 (45) | 564 (56) | | 54 (63) | 615 (63) | | 53 (69) | 654 (70) | |
| Hemoglobin levels (g/dl), mean (SD) | 10.10 (1.25) | 10.29 (1.28) | 0.2 | 10.53 (1.35) | 10.34 (1.29) | 0.094 | 10.88 (1.27) | 10.98 (1.24) | 0.2 | 11.35 (1.28) | 11.26 (1.22) | 0.6 | 11.60 (1.12) | 11.57 (1.20) | >0.9 |

mean (SD)

Continuous variables between groups were compared using independent samples t-tests, and proportions of categorical variables were compared using chi-square tests. A two-tailed significance level of 5% (P < 0.05) was used for all statistical tests.

ARI, acute respiratory infection; SD, standard deviation

Iran J Ped Hematol Oncol. 2025, Vol 15, No 3, 530-542

537

| | | use | | |
|-------------------------------------|-----------------------------|--------------------------------|-----------------|-------------------|
| | | Fever (+), | | Fever (–), |
| | | N = 698 | | N = 5,044 |
| | Antibiotics (+), N = 395 | Antibiotics $(-)$, N = 303 | <i>P</i> -value | |
| Anemia, n (%) | | | 0.6 | |
| Severe | 1 (0.3) | 3 (1.0) | | 21 (0.4) |
| Moderate | 101 (26) | 76 (25) | | 1,037 (21) |
| Mild | 109 (28) | 77 (25) | | 1,245 (25) |
| Not anemia | 184 (47) | 147 (49) | | 2,741 (54) |
| Hemoglobin levels (g/dl), mean (SD) | 10.79 (1.29) | 10.76 (1.32) | >0.9 | 11.01 (1.36) |

Table III: Anemia prevalence and mean hemoglobin levels in children with and without antimicrobial

Continuous variables between groups were compared using independent samples t-tests, and proportions of categorical variables were compared using chi-square tests. A two-tailed significance level of 5% (P < 0.05) was used for all statistical tests.

SD, standard deviation



Figure 1. Association between fever, diarrhea, or acute respiratory infection and anemia

Multiple logistic regression was used to assess the association between recent infections and anemia, adjusted for child age (categorized as 6–11, 12–23, 24–35, 36–47, or 48–59 months of age), child sex (boy or girl), child body mass index (categorized as underweight, normal, or obese), birth order (categorized as first, second, or third and above), number of household members (categorized as 2–4, 5–7, 8 and above), maternal age (categorized as 15–24, 25–34, 35–44, or \geq 45 years), maternal education level (categorized as no education, basic, secondary, or higher), wealth index (categorized as poorest, poorer, middle, richer, or richest), and place of residence (rural or urban). ARI, acute respiratory infection; CI, confidence interval

538

Discussion

This study investigated the potential associations between recent fever. diarrhea, or ARI and anemia in children aged 6-59 months. The findings of this study can suggest that from least two weeks after the onset of infection, the presence of these symptoms is unlikely to significantly influence the interpretation of hemoglobin levels, except for infants aged 6-11 months with fever. Further research is warranted to investigate the potential role of infection in anemia development, particularly in the vulnerable 6-11-month age group. The observed association between recent fever and anemia in this age group warrants careful consideration and further discussion because this age range represents a critical window of development characterized by heightened susceptibility to both infectious diseases nutritional deficiencies. and Indeed, infants in this age group experience a decline in passively acquired maternal antibodies, coinciding with a period of rapid growth that elevates iron demand and increased iron requirements (11, 12). This combination of factors suggests that the synergistic interplay between infection and nutritional status may be particularly pronounced in this period, potentially exacerbating anemia. Fever, as a marker of infection. could contribute to the development of anemia through multiple mechanisms, including decreased iron absorption, increased iron utilization for immune response, inflammatory and cytokine-mediated suppression of erythropoiesis, potentially exacerbating the impact of fever on hemoglobin levels (3). Therefore, to elucidate the precise role of infection in the etiology of anemia within this specific infant population, further research, including longitudinal studies and mechanistic investigations, is crucial. The results of this study are aligned with a small clinical study reporting increased

hemoglobin levels 7-10 days after the acute phase in children (13). This consistency supports the study findings of no significant difference in anemia risk or mean hemoglobin levels measured approximately 2 weeks post-infection between groups with or without acute infection symptoms. However, it is worth mentioning that the precise timing and magnitude of hemoglobin recovery postinfection may vary depending on such factors as type and severity of infection as well as individual's nutritional status and immune response. Further research is needed to fully characterize the temporal dynamics of infection-related hemoglobin fluctuations across different age groups and infection etiologies. The link between acute inflammation and anemia is welldocumented in the literature (5,6) with several studies reporting a positive correlation between acute phase reactants, such as C-reactive protein, and the development of anemia of inflammation (also known as anemia of chronic disease) (14-16). Several mechanisms have been proposed to explain the infection-related hemoglobin reduction, including hemophagocytosis, hemolysis, erythrocyte pooling, hemodilution, and, importantly, impaired erythropoiesis due to cytokinemediated suppression of iron utilization and erythropoietin production (3, 17, 18). In the context of acute infection, iron deficiency is unlikely to be the primary driver of anemia. This is supported by the hemoglobin observation that levels frequently exhibit spontaneous improvement as the infection resolves, often without the need for iron supplementation. This transient nature of infection-associated anemia is distinguished from chronic iron deficiency which requires anemia. longer-term interventions. This study has several limitations. First, reliance on retrospective self-reported information about recent

illnesses introduces potential recall bias. Future research should collect more detailed information on the characteristics of infection, including microbiological confirmation when possible. Second, hemoglobin measurement via capillary puncture may introduce errors when compared with venous blood sampling. Ideally, future research should use venous blood samples for hemoglobin analysis to enhance accuracy of their findings. Third, a cross-sectional study design prevents identification of pre-infection hemoglobin levels, thereby, limiting the ability to assess the individual effect of infection on hemoglobin levels. A longitudinal study design would provide more robust evidence of the impact of infection on hemoglobin levels, allowing for a clearer understanding of individual changes and the recovery process. Fourth, this study is unavailability limited by the of comprehensive data on several potentially covariates. These include detailed nutritional factors (such as dietary iron intake, supplementation, and breastfeeding history), pre-existing chronic conditions known to affect hematopoiesis (e.g., thalassemia), and direct biochemical markers of inflammatory status (e.g., Creactive protein or ferritin). The exclusion of these variables may temper the complete interpretation of factors influencing post-infection hemoglobin levels, and their systematic inclusion is recommended for future research to provide a more nuanced understanding. Despite these limitations, the present findings have several important implications for both public health and clinical practice. The findings of this study suggest that, beyond the immediate acute phase of infection, hemoglobin levels measured approximately 2 weeks after the onset of infection are likely to provide a reliable picture of a child's more underlying hematologic status, and are not significantly confounded by transient infection-related effects. This information

can guide clinicians in assessing and managing anemia in children, particularly in resource-limited settings. However, it is crucial to emphasize that caution must be exercised when generalizing these findings to diverse populations and settings. Factors such as background nutritional status, the local prevalence of specific infectious diseases (e.g., malaria, and helminth infections), variations in healthcare access and infrastructure, and distinct age-specific vulnerabilities may significantly modify the observed relationships and necessitate context-specific adaptations of anemia management strategies.

Conclusion

This study provides evidence that episodes common childhood infection. of specifically fever, diarrhea, and ARI, are unlikely to substantially confound the interpretation of hemoglobin levels when measured at least approximately 2 weeks after symptom onset, except in case of fever in infants aged 6-11 months. To ensure appropriate diagnosis and targeted management, clinicians should consider and investigate other potential and more persistent underlying etiologies of anemia, including nutritional deficiencies, chronic infections, hemoglobinopathies, and other underlying medical conditions.

Data Availability Statement

Data are available through the DHS Program. Access and use require application and approval.

Ethical Considerations

The Nepal DHS program was approved by the Ethics Committee of the Nepal Health Research Council. Written informed consent was obtained from each participant prior to data collection.

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Authors' Contributions

YK conceptualized and designed the study, collected the data, and drafted the manuscript. YK reviewed and edited the final version of the manuscript.

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Conflict of Interest

The authors declare no conflict of interest for this article.

References

1. Stevens GA, Paciorek CJ, Flores-Urrutia MC. National, regional, and global estimates of anemia by severity in women and children for 2000–19: a pooled analysis of population-representative data. Lancet Glob Health 2022; 10(5): e627e639.

2. Wang M. Iron deficiency and other types of anemia in infants and children. Am Fam Physician 2016; 93(4): 270-278.

3. Weiss G, Ganz T, Goodnough LT. Anemia of inflammation. Blood 2019; 133(1): 40-50.

4. Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kuppermann N, O'Leary ST, et al. Clinical practice guideline: evaluation and management of well-appearing febrile infants 8 to 60 days old. Pediatrics 2021; 148(2): e2021052228-e2021052232.

5. Ballin A, Lotan A, Serour F, Ovental A, Boaz M, Senecky Y, et al. Anemia of acute infection in hospitalized children—No evidence of hemolysis. J Pediatr Hematol Oncol 2009; 31(10): 750-752.

6. Ballin A, Senecky Y, Rubinstein U, Schaefer E, Peri R, Amsel S, et al. Anemia associated with acute infection in children. Isr Med Assoc J IMAJ 2012; 14(8): 484-487.

7. Ministry of Health and Population [Nepal], New ERA, and ICF. Nepal Demographic and Health Survey 2022. Kathmandu: Ministry of Health and Population [Nepal]; 2023.

8. Ministry of Health and Population -MOHP/Nepal, New ERA/Nepal, and ICF International. Nepal Demographic and Health Survey 2011. Kathmandu: MOHP/Nepal, New ERA/Nepal, and ICF International; 2012.

9. Ministry of Health - MOH/Nepal, New ERA/Nepal, and ICF. Nepal Demographic and Health Survey 2016. Kathmandu: MOH/Nepal, New ERA/Nepal, and ICF; 2017.

10. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008; 61(4): 344-349.

11. Engle-Stone R, Aaron GJ, Huang J, Wirth JP, Namaste SM, Williams AM, et al. Predictors of anemia in preschool children: biomarkers reflecting inflammation and nutritional determinants of anemia (BRINDA) project. Am J Clin Nutr 2017; 106: 402S-415S.

12. Armitage AE, Agbla SC, Betts M, Sise EA, Jallow MW, Sambou E, et al. Rapid growth is a dominant predictor of hepcidin suppression and declining ferritin in Gambian infants. Haematologica 2019; 104(8): 1542-1553.

13. Fekri K, Kianpour F, Kheiri S, Khoshdel N, Khoshdel A. Changes in hemoglobin level and mean corpuscular volume during the convalescent phase of acute febrile illness in children: a study of

the possible role of hemolysis. Acta Med Iran 2020; 9-14.

14. Moran-Lev H, Weisman Y, Cohen S, Deutsch V, Cipok M, Bondar E, et al. Interrelationship between hepcidin, vitamin D, and anemia in children with acute infectious disease. Pediatr Res 2018; 84(1): 62-65.

15. Sales MC, Queiroz EOD, Paiva ADA. Association between anemia and subclinical infection in children in Paraíba State, Brazil. Rev Bras Hematol E Hemoter 2011; 33(2): 96-99.

16. Shinoda N, Sullivan KM, Tripp K, Erhardt JG, Haynes BM, Temple VJ, et al. Relationship between markers of inflammation and anemia in children of Papua New Guinea. Public Health Nutr 2013; 16(2): 289-295.

17. Roy CN. Anemia of inflammation. Hematology Am Soc Hematol Educ Program 2010; 2010: 276-280.

18. Ganz T. Anemia of Inflammation. N Engl J Med 2019; 381(12):1148-1157.