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Associations Between Inflammation Biomarkers and Serum Ferritin and Zinc Concentrations in Preschool Children in Nepal

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Abstract: Concentration of trace nutrients is affected by inflammation; however, there has been limited research on iron and zinc, particularly in children. The objective of the current was to assess associations between inflammation biomarkers and serum ferritin and zinc concentrations., The study used α-1 glycoprotein (AGP) as a second biomarker because C-reactive protein (CRP) detection as a biomarker for inflammation is less sensitive in chronic infections The study utilized cross-sectional data of 1649 preschool Nepalese children from Nepal National Micronutrient Status Survey 2016. A standardized, highly sensitive technique was used to measure CRP and AGP. To obtain associations between CRP and AGP, nutrient concentrations were stratified across classifications of CRP and AGP. Concentrations level greater and smaller than several CRP and AGP cut-off points, namely, 0.5 mg/L, 1.0 mg/L, 3.0 mg/L and 5.0 mg/L (CRP) and 0.5 mg/L, 1.0 mg/L, 1.5 mg/L and 2.0 mg/L (AGP). With CRP biomarker at interval of > 0.5-1 mg/L, the median (25th and 75th percentiles) was 21.6 (11.5, 37.8) mg/L for ferritin; and 83.9 (63.8, 108.8) mg/L for zinc. Corresponding values for ferritin and zinc with AGP biomarker were 22.2 (10.9, 35.9) mg/L and 83.9 (65.6, 106.9) mg/L respectively. CRP concentration at interval of ≥ 5 mg/L was negatively associated with ferritin concentration [adjusted odds ratio (aOR)= 0.44, 95% confidence interval (CI): (0.24, 0.82)]. AGP concentration at interval of ≥ 1.0 mg/L was negatively associated with zinc concentration [aOR: 0.71; 95% CI: (0.50, 1.00)]. High CRP and AGP levels as defined by their low cut-off points (below0.5 mg/L) had no influence on zinc and ferritin concentrations. Using both CRP and AGP as biomarkers for inflammation provides higher precision in the detection of inflammation. This combination of biomarkers is therefore recommended in future research for assessing zinc and iron deficiencies. The negative association of CRP and AGP with serum ferritin and zinc concentrations highlight the need to pay special attention to non-biological factors with elevated levels of the two inflammation biomarkers.

Keywords: α-1 Acid Glycoprotein, C-reactive Protein, Ferritin, Zinc, Children, Inflammation, Nepal

1. Introduction

Inflammation is a body's immune system's response against infection and injuries that involves different types of immune cells, clotting proteins and signaling molecules. The cells of immune system move to the injury or infection sites and causes the inflammation [1]. The four key cardinal signs of inflammation are redness, heat, swelling, pain, and loss of function [1]. The NNMSS assessed inflammation considering its possible association with nutritional status of children.

This in turn could influence the interpretation of biomarkers. Two key blood test markers for inflammation are C-reactive protein (CRP) and α-1 acid glycoprotein (AGP). CRP is produced in the liver that is classified as an acute phase reactant and is measured through blood test. Typically, CRP is not detected in the blood unless a certain level of inflammation is present in the body. AGP is defined as an acute phase protein in all mammals. During an acute phase response, serum concentration of AGP rises by many folds which is the systemic response to a local inflammatory stimulus [2]. An acute inflammation is indicated by a CRP ≥ 5.0 mg/L, whilst chronic inflammation is indicated by a AGP > 1.0 g/L [3].

There has not been any previous country level data related to inflammation in Nepal. However, NNMSS 2016 revealed that, prevalence of inflammation is likely high [4].

Inflammation can profoundly affect serum ferritin. Inflammation has different effects on iron status' conditional distribution. A study conducted among Cuban children under 5 years of age showed that inflammation exerted less influence on serum ferritin concentrations among children who had the highest iron reserves [29]. Whilst little effect was found on low ferritin prevalence with adjustment of inflammation. Serum Zinc concentration is supposed to be affected by inflammation [31]. Serum zinc concentration gets reduced with inflammation [30] suggesting a possibly less strong impact of inflammation on zinc concentrations than previously thought [32] and appears to produce high prevalence estimates of nutritional zinc deficiency.

The relations between inflammatory markers and serum ferritin and zinc concentration are inconsistent which signifies the need to further investigate the association between inflammatory biomarkers and serum ferritin and zinc concentration.

The inflammatory process influences many indicators of micronutrient statuses. Generally, in the presence of inflammation, there is a decline in levels of retinol and RBP, which consequently overestimates the prevalence of Vitamin A deficiency [3]. The 1998 NNMSS did not assess and account for any indicators of inflammation in describing the prevalence of vitamin A deficiency. The concentration of serum zinc gets decreased with inflammation. [4]. Iron status indicators, including ferritin, gets affected by the inflammatory process and more often increases the values of ferritin which in turn underestimate the prevalence of iron deficiency [3]. Therefore, it is crucial to collect information on inflammatory markers to adjust the influence of inflammation on certain biomarkers to correctly interpret indicators of micronutrient status.

According to the NNMSS, the prevalence of elevated AGP (only) and elevated CRP (only) among children was 18% and 2% respectively. While percentage of children with both (elevated CRP and AGP) was 9%. There was variation in Elevated AGP (only) by wealth quintile, ethnicity and ecological zone. Nearly twenty percent (20%) of children from the Mountain and Terai and 15 % of children from Hill had elevated AGP (only). Variation in elevated CRP (only) was reported by age of child wealth. The prevalence of elevated CRP ranged from 8% among children with 6-8 months of age to 0.3% among children with 48-59 months of age [4]. By wealth, elevated CRP (only) ranged from 4% among children from the second wealth quintile to below1% (0.5%-0.6%) among children with household belonging to fourth and fifth quintiles. There was variation in the prevalence of having both elevated CRP and AGP based on the age and sex of the children. Its prevalence was 17% among children aged 9-11 months while 5% among children 48-59 months. Male child has higher (10%) elevated CRP and AGP (both) compared to females (7%).

The objective of the current paper was to examine the effects of inflammation on nutrient concentrations by investigating the associations between inflammation biomarkers and zinc concentrations serum ferritin. The study used α-1 glycoprotein (AGP) as a second biomarker because C-reactive protein (CRP) detection as a single biomarker for inflammation is less sensitive in chronic infections [5].

Findings of this study could provide evidence to public health professionals in Nepal to adjust for inflammation in apparently healthy child, particularly when AGP and CRP are used as biomarkers for inflammation.

1.1. Ethical Consideration

The Ministry of Health and Population (MoHP), Government of Nepal (GoN), approved the NNMSS. The consent was taken from mothers for the child participating in the study. The permission to use secondary dataset was taken from MoHP to use.

1.2. Key Messages

a) The median values for Serum ferritin were 21.4 µg/L and zinc concentrations was 84.7 µg/L for acute inflammation.
b) CRP concentration at interval of ≥ 5 mg/L was negatively associated with serum ferritin concentration.
c) AGP concentration at interval of ≥ 1.0 mg/L but not CRP concentration at interval of ≥ 5 mg/L is negatively associated with serum zinc concentrations.
d) AGP concentration at interval of ≥ 1.0-1.5 mg/L was negatively associated with serum zinc.
e) AGP concentration at interval of ≥ 1.0 mg/L was significantly lower serum zinc concentrations and ferritin concentrations.

2. Methodology

2.1. Study Design and Study Participants

The current study covered 1649 Nepalese pre-school children aged 6-59 months. The 2016 Nepal National Micronutrient Status Survey (NNMSS) dataset was used as source of data for the study. Details of sampling design, data collection, specimen collection and processing are described in the NNMSS final report [4].

2.2. Outcome Variable of the Study

The outcome variables for this study were iron deficiency (BRINDA adjusted ferritin levels (ferritin)) and zinc deficiency (BRINDA adjusted zinc deficiency). BRINDA adjusted serum ferritin level cut-off points were 0 µg/L and 15 µg/L and BRINDA adjusted serum zinc deficiency level cut-off points were 10 µg/L and 57 µg/L. Zinc deficiency was categorised as 1; otherwise, 0, whilst ferritin iron deficiency was coded as 1, and non-occurrence of ferritin iron deficiency was coded as 0.

2.3. Exposure Variables

We categorized continuous variables by using cut-offs which were study-specific of conventional definitions. Serum CRP concentrations were classified into 6 intervals, namely 0.0-0.5 mg/L, > 0.5-1.0 mg/L, > 1-3 mg/L, ≥ 5 mg/L, and < 5 mg/L. Serum AGP concentrations were categorized into 0.0-0.5 mg/L, 0.5-1.0 mg/L, 1.0-1.5 mg/L, 1.5-2.0 mg/L, > 2 mg/L and < 1.0 mg/L. The choice of these values was based on CRP and AGP cut-offs, and the range of CRP and AGP values in normal and healthy children in the United States of America [6-10]. The low serum zinc level was defined as serum zinc concentration less than 65 µg/dL [11-13] and low serum ferritin level was defined as serum ferritin concentration less than 15 µg/L, as recommended by the World Health Organization (WHO) for assessing iron deficiency in children above 5 years of age [14].

2.4. Potential Confounding Variables

Our choice of possible confounding variables was based on recent existing literature on factors related to micronutrient deficiencies [15-18] and their accessibility in the NNMSS dataset. The potential confounding variables were classified into individual level, household level and community-level factors, health status factors (a day prior to the survey) anthropometric and nutrition factors as well as water and sanitation factors.

In this study, geographical region, province, type of residence (urban/rural), and ecological zone and ethnicity (caste) constituted the community-level factors. The household-level factors were household wealth index and ethnicity. A principal components analysis (PCA) [19] was used to construct the wealth index. Scores were assigned to the household facilities and assets of respondents after computation of the index, ranking each member of the sample by their score. In this study, wealth index was divided into five classes, namely, lowest, second, middle, fourth and highest. Lowest quintile represented the bottom 20% of the households; The next bottom 20% represented the second, the next 20% the middle, the next 20% the fourth and the top 20% represented the highest wealth quintile. Factors which constituted individual level were child's age, gender and relationship to the career. Contraction of fever, cough and diarrhoea constituted the health status factors.

Anthropometric and nutrition factors were made up of the stunting, wasting and underweight status of children as well as their dietary diversity. Water and sanitation factors comprised drinking water quality, type of sanitation facilities used at participants' households and their water treatment practices.

2.5. Statistical Analyses

In the current study, all statistical analysis was carried out by using STATA/MP version 14 (Stata Corp, College Station, TX, USA). 'Svy' commands was employed in this study to allow adjustments for cluster-sampling design and weight. Firstly, we carried out frequency tabulations for exposure and all confounding factors and for CRP and AGP levels by serum ferritin and zinc concentrations, we reported the weighted continuous variables as medians with interquartile ranges. Following this univariate and multivariate analyses was carried out. We employed a staged modelling technique, as part of the multivariate analyses. The multivariate analyses were used to assess the association between both inflammation biomarkers (CRP and AGP) and serum ferritin and zinc concentrations.

As a technique in multivariate modelling, first all household and community level factors were entered into the baseline multivariable model. This was followed by an elimination process to get rid of statistically insignificant factors (Model 1). Thereafter, we examined individual level factors with model 1 (Model 2). In the subsequent stage, we assessed health-related factors with model 2 (Model 3) and anthropometric and nutrition factors with model 3 (Model 4). This was followed by the fifth modelling stage, in which we examined water and sanitation factors with model 4 (Model 5). In the last stage (model 6), we assessed the exposure variables (CRP and AGP) with those variables which were significant in models 1-5.

Any co-linearity was tested and reported. Odds ratios with 95% confidence intervals (CIs) was calculated for assessing the adjusted odds ratio (AOR) of independent variables.

3. Results

3.1. Characteristics of Sample

The demographic and nutritional characteristics of the 1649 children with complete data on serum CRP, AGP, ferritin and zinc required for this analysis are summarised in Table 1. Over fifty percent of the children (54%) were male, and more than two-thirds of them (70%) were aged 24-59 months. The proportion of children who had fever, cough and diarrhoea was 36%, 38% and 20% respectively. Of the total children, 35% were stunted, 12% were wasted and 29% were overweight. The majority of children were from rural areas (87%), Province 2 (23%), Terai ecological zone (50%) and came from households with the lowest wealth index 21%). More than three-quarters of the children (77%) consumed food from less than four food groups, and only 8% of them came from households with severe food security. The majority of the children were from households with improved sources of drinking water (92%), with flush or pour flush

toilet facility (71%) and no water treatment habit (83%).

3.2. Concentration of Serum Ferritin and Zinc Within Ithin CRP and AGP Intervals

With CRP biomarker at interval of > 0.5-1 mg/L, the median (25^{th} and 75^{th} percentiles) was 21.6 (11.5, 37.8) mg/L for ferritin; and 83.9 (63.8, 108.8) mg/L for zinc. Corresponding values for ferritin and zinc with AGP biomarker were 22.2 (10.9, 35.9) mg/L and 83.9 (65.6, 106.9) mg/L respectively (Table 2).

3.3. Association of CRP and AGP with Serum Ferritin and Zinc Concentrations

CRP concentration at interval of ≥ 5 mg/L was negatively associated with serum ferritin [adjusted odds ratio (AOR): 0.44 (0.24, 0.82; 95% CI)). AGP concentration at interval of ≥ 1.0 mg/L was negatively associated with ferritin concentration [AOR: 0.64; 95% CI: (0.44, 0.93)] (Figure 1). AGP concentration at interval of ≥ 1.0-1.5 mg/L was negatively associated with serum zinc [AOR: 0.64; 95% CI: (0.44, 0.93)] (Figure 2). AGP concentration at interval of ≥ 1.0 mg/L was negatively associated serum ferritin [AOR: 0.64; 95% CI: (0.44, 0.93)] (Figure 1). Additionally, no significant association between low intervals of both CRP and AGP concentrations and concentration of serum ferritin and zinc. was found.

Our study revealed other factors associated with serum ferritin and serum zinc (with both CRP and AGP levels as biomarkers) among the preschool children. Other factors that were associated positively with serum zinc concentrations were: children residing in rural areas, in the Far-western region and those from middle-level households (Table 3). Other factors positively associated with serum ferritin concentrations included: children resident in Province 5, children from ethnicities other than the Janajati and Dalit and Brahmin/Chettri, stunted children and children consuming food from more than four food groups.

Table 1. *Demographic and nutritional characteristics of children aged 6-59 months.*

Characteristic	**N (%)**
Community level factors	
Residence	
Urban	208 (12.6)
Rural	1440 (87.4)
State	
Province 1	270 (16.4)
Province 2	379 (23.0)
Province 3	315 (19.1)
Province 4	144 (8.7)
Province 5	270 (16.4)
Province 6	104 (6.3)
Province 7	167 (10.1)
Geographical region	
Eastern	354 (21.5)
Central	611 (37.1)
Western	283 (17.2)
Mid-western	234 (14.2)
Far-western	167 (10.0)
Ecological zone	
Mountain	127 (7.7)
Hill	686 (41.6)
Terai	835 (50.7)
Ethnicity (Caste)	
Brahmin/Chettri	498 (30.2)
Dalit	299 (18.1)
Janajati	486 (29.5)
Others*	365 (22.2)
Household level factors	
Household wealth index	
Lowest	359 (21.8)
Second	319 (19.4)
Middle	318 (19.3)
Fourth	335 (20.3)
Highest	317 (19.3)
Individual level factors	
Child's age (months)	
6-23	490 (29.7)
24-59	1159 (70.3)
Child's gender	
Male	891 (54.1)
Female	757 (45.9)

Characteristic	N (%)
Relation to child	
Biological parents	1594 (96.7)
Others	55 (3.3)
Health status	
Child had fever	
Yes	598 (36.3)
No	1051 (63.7)
Child had cough	
Yes	626 (38.0)
No	1023 (62.0)
Child had diarrhoea	
Yes	326 (19.7)
No	1323 (80.3)
Anthropometry and nutrition	
Child was stunted (< - 2 SD)	
No	1062 (64.6)
Yes	583 (35.4)
Child was wasted (< - 2 SD)	
No	1445 (88.2)
Yes	193 (11.8)
Child was underweight (< - 2 SD)	
No	1164 (70.8)
Yes	480 (29.2)
Child had BMIz (< - 2 SD)	
No	1493 (90.8)
Yes	152 (9.2)
Dietary diversity	
< 4 foods	1268 (76.9)
4 or more foods	381 (23.1)
Water and sanitation	
Sources of drinking water	
Improved	1515 (91.9)
Unimproved	134 (8.1)
Type of toilet facility	
Flush or pour flush toilet	1176 (71.4)
Pit latrine	472 (28.6)
Water treatment habit	
Yes	274 (16.6)
No	1375 (83.4)
* Newar, Other Terai Caste and Muslims	

Table 2. *Serum ferritin and zinc concentrations within C-reactive Protein (CRP) and α-1 acid glycoprotein (AGP) intervals.*

Intervals	N*	BRINDA Adjusted Ferritin (µg/L)	BRINDA Adjusted zinc (µg/L)
C-reactive Protein (mg/L)		median (25th, 75th percentiles)	median (25th, 75th percentiles)
0.0–0.5	835	21.7 (11.4, 35.4)	84.0 (64.9, 105.2)
> 0.5–1	257	21.6 (11.5, 37.8)	83.9 (63.8, 108.8)
> 1–3	307	21.2 (9.5, 37.5)	83.9 (69.3, 109.7)
> 3–5	83	24.1 (11.3, 31.5)	79.8 (63.9, 109.5)
≥ 5	165	21.4 (13.6, 39.3)	84.7 (64.1, 107.5)
C-reactive Protein (mg/L)			
< 5	1482	21.7 (11.2, 35.7)	83.9 (65.3, 107.4)
≥ 5	165	21.4 (13.6, 39.3)	84.7 (64.1, 107.5)
α-1 acid glycoprotein (mg/L)			
0.0–0.5	317	19.6 (11.2, 33.1)	82.5 (63.8, 106.1)
> 0.5–1	894	22.2 (10.9, 35.9)	83.9 (65.6, 106.9)
≥ 1-1.5	252	21.6 (11.9, 39.3)	90.7 (66.9, 117.0)
> 1.5–2	116	21.7 (11.6, 33.8)	79.7 (65.5, 98.6)
> 2	68	21.8 (14.9, 46.6)	84.7 (67.7, 102.9)
α-1 acid glycoprotein (mg/L)			
< 1	1211	21.6 (10.9, 35.5)	83.8 (64.9, 106.7)
≥ 1	436	21.7 (11.9, 37.5)	84.7 (66.4, 109.3)
N* = weighted number			

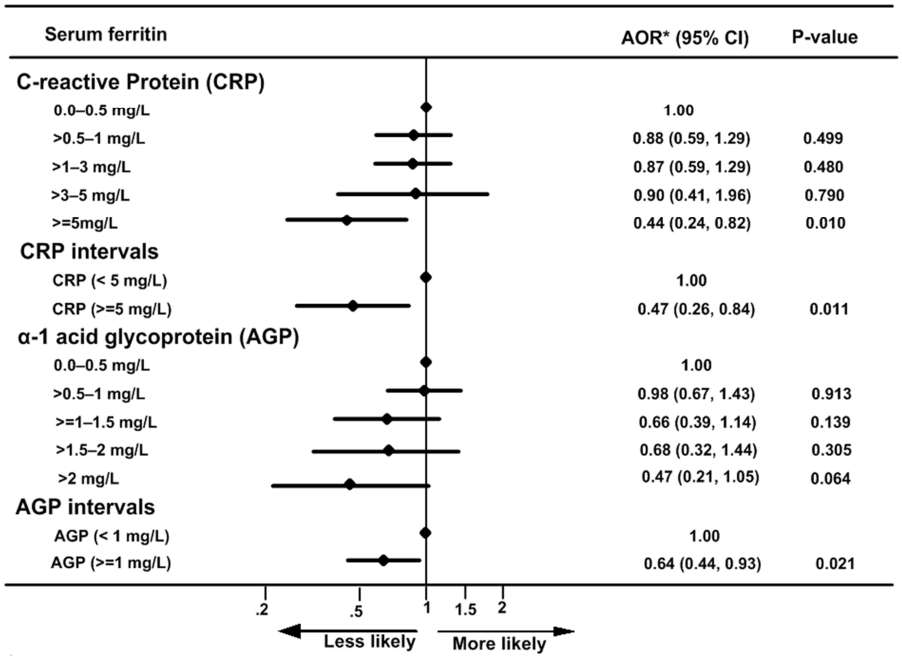

Figure 1. *Association of CRP and AGP with serum ferritin concentration.*

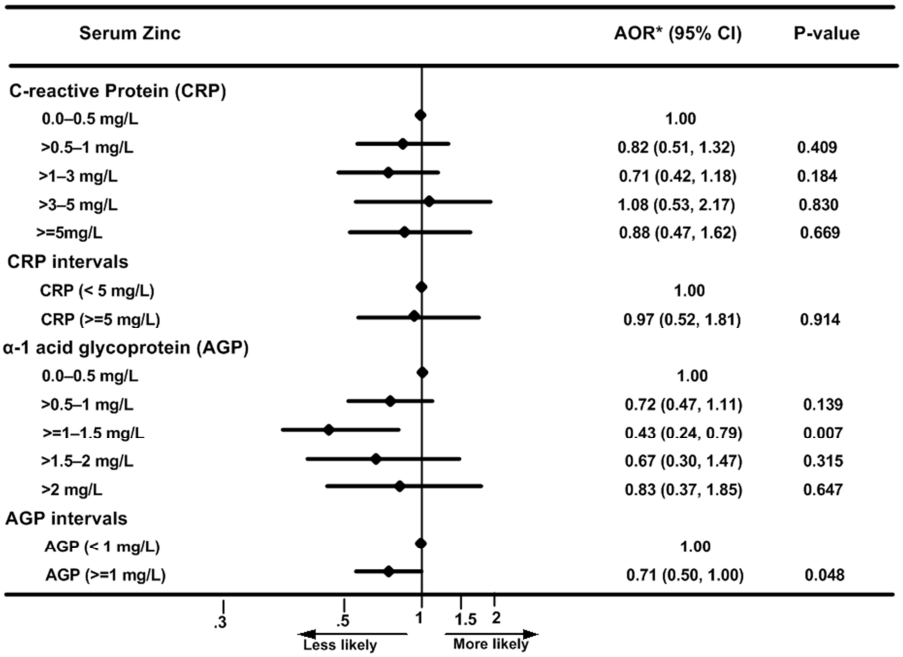

Figure 2. *Association of CRP and AGP with serum zinc concentration.*

Table 3. *Association between CRP and AGP on Ferritin and Serum Zinc in preschool children in Nepal: Unadjusted and adjusted odd ratios.*

Characteristic	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
	BRINDA adjusted ferritin (µg/L)				BRINDA adjusted zinc (µg/L)			
Residence								
Urban	-	-	-	-	1.00		1.00	
Rural	-	-	-	-	2.79 (1.32, 5.88)	0.008	2.79 (1.32, 5.88)	0.026
Geographical region								
Eastern	-	-	-	-	1.00		1.00	
Central	-	-	-	-	1.02 (0.56, 1.86)	0.946	1.08 (0.66, 1.92)	0.792
Western	-	-	-	-	0.81 (0.46, 1.43)	0.461	0.79 (0.44, 1.42)	0.429
Mid-western	-	-	-	-	1.47 (0.81, 2.65)	0.192	1.29 (0.73, 2.28)	0.374
Far-western					2.09 (1.16, 3.79)	0.016	1.81 (1.03, 0.88)	0.040

Characteristic	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
	BRINDA adjusted ferritin (µg/L)				BRINDA adjusted zinc (µg/L)			
Household Wealth Index								
Lowest	-	-	-	-	1.00		1.00	
Second	-	-	-	-	0.51 (0.34, 0.77)	0.001	0.57 (0.38, 0.87)	0.010
Middle	-	-	-	-	0.50 (0.33, 0.75)	0.001	0.60 (0.41, 0.90)	0.014
Fourth	-	-	-	-	0.54 (0.34, 0.86)	0.009	0.69 (0.44, 1.08)	0.102
Highest	-	-	-	-	0.43 (0.23, 0.79)	0.008	0.64 (0.34, 1.24)	0.187
State								
Province 1	1.00		1.00		-	-	-	-
Province 2	2.46 (1.57, 3.87)	<0.001	2.06 (1.20, 3.55)	0.010	-	-	-	-
Province 3	1.00 (0.66, 1.53)	0.996	1.13 (0.65, 1.96)	0.652	-	-	-	-
Province 4	1.27 (0.75, 2.15)	0.365	1.48 (0.75, 2.93)	0.259	-	-	-	-
Province 5	1.83 (1.29, 2.60)	0.001	1.71 (1.10, 2.65)	0.018	-	-	-	-
Province 6	1.35 (0.63, 2.87)	0.433	1.15 (0.47, 2.82)	0.756	-	-	-	-
Province 7	1.38 (0.99, 1.93)	0.061	1.36 (0.86, 2.16)	0.188	-	-	-	-
Ethnicity (Caste)								
Brahmin/Chettri	1.00		1.00		-	-	-	-
Dalit	1.99 (1.36, 2.93)	0.001	1.72 (1.10, 2.70)	0.019	-	-	-	-
Janajati	1.98 (1.34, 2.95)	0.001	1.80 (1.14, 2.82)	0.012	-	-	-	-
Others	2.99 (1.98, 4.53)	<0.001	2.26 (1.50, 3.40)	<0.001	-	-	-	-
Child's age (months)								
6-23	1.00		1.00		-	-	-	-
24-59	3.59 (2.71, 4.77)	<0.001	4.37 (3.12, 6.11)	<0.001	-	-	-	-
Child Stunted (< -2 SD)								
No	1.00		1.00		-	-	-	-
Yes	1.34 (1.02, 1.75)	0.037	1.61 (1.18, 2.19)	0.003	-	-	-	-
Dietary Diversity								
< 4 foods	1.00		1.00		-	-	-	-
4 or more foods	1.23 (0.91, 1.67)	0.183	1.39 (1.01, 1.94)	0.046	-	-	-	-

4. Discussions

Prior studies related to iron status conducted in developing nations have used inflammation biomarkers to assess its influence on the distribution of iron status biomarkers [6, 7, 20, 21].

In this current study, we examined the association of inflammation biomarkers (CRP and AGP) and serum ferritin and zinc concentrations by analyzing data for 1649 Nepalese preschool children. The analysis of the association between biomarkers of iron and zinc and inflammation biomarkers revealed number of findings. The current study found negative association between the inflammation biomarkers and serum ferritin and zinc concentrations. Other factors associated with serum zinc concentrations included rural residence, residence in the Far-western region; those associated with serum ferritin concentrations included other ethnicities other than the Janajati, Dalit and Brahmin/Chettri, older children aged 24-59 months and stunted children.

In this current study, we found that serum ferritin concentration was the only biomarker of iron status which was in consistent relation to either CRP or AGP, consistent with results of a previous study [22]. We also found that the preschool children with evidence of infection had decreased median serum zinc concentration, which is in consonance with results of past studies [23-25]. Stronger association was found between serum ferritin and AGP compared to the association between serum ferritin and CRP. This finding was consistent with a past study [22].

The current study found low influence of inflammation biomarkers on the distribution of iron status (ferritin) and is in consonance with a past study [22]. This finding suggests that in the case of a low prevalence of clinical signs of inflammation, there is only a small influence on prevalence estimates of iron deficiency.

Furthermore, the study found negative association between acute inflammation (CRP $\geq$ 5 mg/L) and serum ferritin concentration. This was consistent with results from past studies which indicated that some vitamins and iron were negatively associated with CRP [26, 27].

The current study found no significant association between CRP concentrations and serum zinc concentrations, in consonance with a previous other study in Peruvian children [23].

In addition, the study also found that there were decreased odds of serum zinc for AGP $\geq$ 1 mg/L. This finding was consistent with results from previous research conducted in Congo among children aged 6-59 months [28].

Findings of this current study may have significant implications for assessing iron and zinc status among children. Using low cut-offs for CRP and AGP may increase the ability to adjust for inflammation children who are apparently healthy when both are used as biomarkers from inflammation.

This study had several strengths. Firstly, it utilized dataset from a nationally representative and population-based survey, results of which may be generalized for the entire country of Nepal. Secondly, it used both CPR and AGP as inflammation markers, which increased the sensitivity in determining inflammation in chronic infections [8]. However, one

important limitation was that causality could not be established as the dataset used was cross-sectional in design.

5. Conclusions

In conclusion, this study found negative association between CRP ≥ 5mg/L and serum ferritin concentration and AGP ≥ 1.0 Mg/L serum ferritin. Whilst no significant association was found between CRP and serum zinc, whereas and was negatively association was found between AGP ≥ 1.0 mg/L and serum zinc concentration. These findings highlight the importance of inflammation in determining if a healthy-looking child may have iron and/or zinc deficiency. The Nepal Ministry of Health and Population should pay particular attention to non-biological factors associated with elevated levels of the two inflammation biomarkers.

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