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Factors Associated with Inflammation in Preschool Children and Women of Reproductive Age in Nepal

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Abstract: Not much is known about the correlates of inflammation among pre-school children and women of reproductive age in Nepal. This study assessed the socio-demographic factors associated with increased levels of inflammation in Nepalese children and women of reproductive age. We analysed data from 3159 participants (1709 children aged 6-59 months, 1243 non-pregnant women aged 15-49 years and 207 pregnant women aged 15-49 years) from the 2016 Nepal National Micronutrient Status Survey (NNMSS), a population-based and nationally representative sample conducted by the Nepal Ministry of Health and Population, with support from UNICEF. Multivariate regression models were used to evaluate associations between predictors and continuous high-sensitivity inflammation among the various participants. Increased inflammation levels were significantly associated with children from the Province 7, children who contracted fever and cough, and children from households with no water treatment habit. Increased levels of inflammation were significantly associated with non-pregnant women from the Dalit caste, pregnant women who had a cough, and non-pregnant women who had high dietary diversity. Increased levels of inflammation were significantly associated with pregnant women from rich households, pregnant women who had a cough and pregnant women from severely food insecure households. Interventions to address the burden of inflammation in Nepal should target individuals who contracted illnesses such as fever and cough and pregnant women from severely food insecure households.

Keywords: Inflammation, Children, Pregnant, Women, Nepal

1. Introduction

Inflammation is a complex process that involves various types of immune cells, clotting proteins and signalling molecules, all of which may undergo change over time. Inflammation is used to describe the body's protective response against infection. Cells of the immune often travel to the sites of an injury or infection to cause the inflammation [1]. There are four common signs of inflammation; these are warmth, redness, swelling and pain [1]. C-reactive protein (CRP) and α-1 acid glycoprotein (AGP) constitute the two key blood test biomarkers for inflammation. CRP is classified as an acute phase reactant, is produced in the liver, and its level is measured by testing the blood. AGP is defined as an acute phase protein in all mammals. During an acute phase response, concentration of its serum rises several fold, which is the systemic answer to a local inflammatory stimulus [2]. A CRP $\geq$ 5.0 mg/L indicates an acute inflammation, whilst a AGP > 1.0 g/L [3] indicates chronic inflammation.

A previous study has established that inflammation might play a central role in the pathogenesis of atherosclerosis, and consequently coronary heart diseases (CHD) [4]. Although markers of inflammation, such as CRP, have been known to be associated with an increased risk of incident coronary heart diseases (CHD), the causes of increased CRP are not completely understood [5].

The NNMSS assessed inflammation among participants of the survey, as it anticipated an association between inflammation and nutritional status. According to the NNMSS final report, prevalence of elevated AGP (only) and CRP (only) among the children aged 6-59 months, was 18%

and 2% respectively, and that 9% of the children had both elevated AGP and CRP [6]. Elevated levels of AGP (only) were found to vary with ecological zone, household wealth and ethnicity (caste). Further, elevated levels of CRP (only) varied with age of the child as well as the household wealth. In addition, elevated levels of a combination of AGP and CRP were found to vary with age and sex of the child.

Prevalence of elevated AGP (only) and CRP (only) among the non-pregnant women aged 15-49 years, was 4% each, and that 2% of the non-pregnant women had both elevated AGP and CRP [6]. Elevated levels of AGP (only) were found to vary with age; and elevated levels of CRP (only) varied with developmental region and age. In addition, elevated levels of a combination of AGP and CRP were found to vary with lactation status of the woman.

Prevalence of elevated AGP (only) and CRP (only) among the pregnant women aged 15-49 years, was < 4% and 13% respectively, and 2% of the children had both elevated AGP and CRP [6]. Eighty five of the pregnant women were found to have no inflammation [6]. Elevated levels of CRP (only) varied with trimester of the pregnancy. In addition, elevated levels of a combination of AGP and CRP were found to vary with age and sex of the child.

Despite the significance of inflammation, there has not been any study in Nepal that assessed the socio-demographic factors associated with it. Our current study aimed to utilise data from the 2016 NNMSS to examine the significant factors associated with inflammation among pre-school children, non-pregnant women as well as pregnant women. Findings of our study might have significant implications for primary prevention and/or amelioration of many inflammation-related diseases in Nepal.

Key Messages:

i. Children who contracted fever and/or a cough were significantly more likely to suffer from inflammation than those who did not.
ii. The likelihood of inflammation was significantly higher among children from households with no water treatment habit.
iii. Non-pregnant women from the Dalit caste were significantly more predisposed to inflammation than those from the Brahmin/Chettri caste.
iv. The likelihood of inflammation was significantly higher among non-pregnant women with high dietary diversity.
v. Pregnant women from severely food insecure households were significantly more prone to inflammation compared with their counterparts from food secure households.

2. Methods

2.1. Study Design and Participants

The cross-sectional and nationally representative 2016 Nepal National Micronutrient Status Survey (NNMSS) was used as the source of data for this current study. The NNMSS involved a stratification process to provide representative estimates for the five development regions of Nepal, namely, Eastern, Central, West, Midwest and Far West regions. It also involved a similar stratification across the three ecological zones of the entire the country, namely, Terai (plains), Hills, and Mountains, to obtain representative estimates. Details of the study design may be obtained from the NNMSS final report [6]. Participants of this study were pre-school children aged 6-59 months, and women aged between 15 and 49 years.

Data collection and specimen analysis: Specialised questionnaires for the participants were used to collect information on socio-demographic characteristics, dietary diversity scale, two week recall of contraction of fever, cough and diarrhoea and documenting the collection of biological data. The survey also collected the two key indicators of inflammation, namely, AGP and CRP. Sample sizes were increased to account for an assumed prevalence of inflammation of 40%. Details of collection of inflammation indicators may be obtained from the final report of the NNMSS [6].

2.2. Study Outcomes

The outcome variable for this current study was inflammation. The cut-off points for acute inflammation level were set at CRP≥12.0, and AGP<1.0. The cut-off points for chronic inflammation level were set at CRP<5.0, and AGP≥1.0. To determine inflammation, acute inflammation and chronic inflammation were combined. Inflammation was categorised as 1; otherwise 0.

2.2.1. Descriptive Study Variables

For this current study, the outcome variable was inflammation. Potential covariates, choice of which was informed by the extant literature on factors associated with micronutrient deficiencies [7-10], included individual-, household- and community-level factors. Other potential covariates included environmental factors (type of toilet facility used in households, quality of drinking water, health status), household security status of households, as well as the diet habits of the participants.

Type of residence (urban/rural), state, geographical region, and ecological zone constituted the community-level factors. Household level factors were household wealth index and ethnicity (caste). The household wealth index (an indicator of wealth) was represented as a score of household assets through the principal components analysis method (PCA) [11]. Scores were assigned to each de jure household member after the index was calculated, ranking each member of the sample by their score. In our study, the wealth index was categorized into five quintiles, namely, poor, middle, rich and rich. The bottom 40% of the households was referred to as poor, the next 40% as the middle-class, and the top 20% as rich. The individual-level factors included participants' age and gender (children). Our analysis included all socio-demographic variables contained in the dataset of the NNMSS.

2.2.2. Statistical Analysis

STATA/MP version 14 (Stata Corp, College Station, TX, USA) was used to conduct all statistical analyses in this current study. The 'Svy' commands were used to allow for adjustments for the cluster-sampling design and weight. Firstly, frequency tabulations to describe the data used in the study were carried out. We then created contingency tables to examine the impact of all potential covariates of inflammation. We utilised the Taylor series linearization method during the estimation of confidence intervals (CIs) around prevalence estimates. In addition, we calculated the multivariable logistic regression that adjusted for clustering and sampling weights to determine the unadjusted odds ratios of inflammation. As part of the multivariable logistic regression analysis, a six-stage model to determine the adjusted odds ratios of inflammation was performed.

In the stage model, we entered the community-level factors into the first model, and conducted a manually executed elimination procedure to assess factors associated with inflammation at a 0.05 significance level. In the second model, we added the significant factors in the first stage to the household-level factors. This was then followed by the elimination procedure. We used a similar approach for the individual-level, health status and diet habits factors in the third, fourth, fifth and sixth stages, respectively.

Any co-linearity in the final model was tested and reported, and the odds ratios with 95% confidence intervals to determine the adjusted odds ratios (possible confounding) variables were calculated.

2.3. Ethical Consideration

Due to concerns about creating fear and high refusal rates among illiterate participants, oral informed consent procedures were carried out with participants. The interviewers or supervisors read the informed consent to each participant (or carer in the case of the children). Parents/carers of children were asked to provide permission and consent for their children's participation, and each woman or parent/carer of a child was asked to provide assent before interviewing or biological data collection. Permission was sought from the Nepal Ministry of Health and Population (which approved the NNMSS) for use of available dataset.

3. Results

3.1. Characteristics of the Sample

Of the 1709 children sampled, approximately 87% of them came from rural settings, and the majority of them were from the Province 2 (~23%) and the Terai ecological zone (~51%) (Table 1). Less than 20% of the children were from rich households, and the majority of them were from the Brahmin/Chettri caste. Male children outnumbered their female counterparts (54% versus 46% respectively), while the majority of them (~70%) were aged 24-59 months. A large majority of the children were cared by their biological parents. Less than one-half of the children did have fever, cough and diarrhoea in the last two weeks preceding the survey. Similarly, less than one-half of them were stunted, wasted or overweight. More than 50% of the children came from food secured households, but the majority of them had low dietary diversity (52%). A large majority of the participants (92%) came from households with improved drinking water sources; more than 7 out of every 10 of them came from households which had flush or pour flush toilet facilities, and the majority of them (83%) came from households which did not have any culture of water treatment.

Table 1. *Characteristics of the study samples.*

Characteristic	Children aged 6-59 months		Non-pregnant women aged 15-49 years		Pregnant women aged 15-49 years	
Community level factors	**N = 1709**	**%**	**N = 1243**	**%**	**N = 207**	**%**
Residence						
Urban	223	13.1	295	13.7	21	10.0
Rural	1486	86.9	1849	86.3	186	90.0
State						
Province 1	280	16.4	373	17.4	36	17.2
Province 2	391	22.9	435	20.3	64	31.0
Province 3	323	18.9	433	20.2	32	15.5
Province 4	152	8.9	217	10.1	16	7.6
Province 5	284	16.6	378	17.6	33	15.8
Province 6	107	6.2	106	5.0	13	6.2
Province 7	172	10.1	201	9.4	14	6.8
Geographical region						
Eastern	369	21.6	484	22.6	53	25.7
Central	625	36.6	756	35.3	79	38.0
Western	300	17.5	418	19.5	34	16.3
Mid-western	243	14.2	283	13.2	28	13.3
Far-western	172	10.1	201	9.4	14	6.8
Ecological zone						
Mountain	131	7.7	134	6.3	9	4.5
Hill	708	41.4	925	43.2	82	39.7
Terai	870	50.9	1083	50.6	116	55.8
Household level factors						

Characteristic	Children aged 6-59 months		Non-pregnant women aged 15-49 years		Pregnant women aged 15-49 years	
Community level factors	**N = 1709**	**%**	**N = 1243**	**%**	**N = 207**	**%**
Household wealth index						
Poor	699	40.9	729	34.0	77	37.3
Middle	673	39.8	874	40.8	102	49.2
Rich	330	19.3	540	25.2	28	13.5
Ethnicity (Caste)						
Brahmin/Chettri	518	30.3	788	36.8	60	29.1
Dalit	314	18.4	330	15.4	38	18.3
Janajati	499	29.2	667	31.1	55	26.5
Others*	377	22.1	358	16.7	54	26.1
Individual level factors						
Age (years)						
15-24			669	31.2	93	44.8
25-34			769	35.9	30	14.5
35-49			706	32.9	84	40.7
Body mass index (kg/m^2)						
≤18.5			211	9.9		
19-25			1433	67.0		
25+			494	23.1		
Child's age (months)						
6-23	521	30.5				
24-59	1188	69.5				
Child's gender						
Male	917	53.7				
Female	792	46.3				
Relation to child						
Biological parents	1594	96.5				
Others	55	3.5				
Health status						
Had fever						
Yes	624	36.6	296	13.8	32	15.7
No	1085	63.4	1848	86.2	175	84.4
Had cough						
Yes	655	38.3	314	14.7	44	21.1
No	1054	61.7	1829	85.4	163	78.9
Had diarrhoea						
Yes	335	19.6	196	9.2	12	5.8
No	1374	80.4	1945	90.8	195	94.2
Anthropometric and Nutrition						
Stunting (< - 2 SD)						
No	1095	64.4				
Yes	605	35.6				
Wasting (< - 2 SD)						
No	1495	88.3				
Yes	199	11.7				
Underweight (< - 2 SD)						
No	1206	71.0				
Yes	494	29.0				
Dietary diversity						
Low	890	52.1	1098	51.2	68	32.6
Moderate	424	24.8	469	21.9	83	40.2
High	395	23.1	577	26.9	56	27.2
Household food insecurity status						
Food secure	912	53.4	1207	56.3	119	57.5
Mild insecurity	184	10.8	222	10.4	22	10.5
Moderate insecurity	469	27.4	587	27.4	51	24.4
Severe insecurity	144	8.4	127	5.9	16	7.6
Water and sanitation						
Source of drinking water						
Improved	1573	92.0	1951	91.0	195	94.3
Unimproved	136	8.0	192	9.0	12	5.7
Type of toilet facility						
Flush or pour flush toilet	1218	71.3	1648	76.9	143	68.9
Pit latrine	491	28.7	496	23.1	64	31.2
Water treatment habit						
Yes	286	16.7	1650	77.0	175	84.6
No	1423	83.3	494	23.0	32	15.4

Of the 1243 non-pregnant women sampled, approximately 86% of them came from rural settings, and the majority of them were also from the Province 2 (20.3%) and the Terai ecological zone (~51%). Slightly more than 25% of the women were from rich households, and the majority of them were from the Brahmin/Chettri caste. While 36% of the women were aged 25-34 years, less than one-half of them did contract fever, cough or diarrhoea in the last two weeks preceding the survey; and less than 10% of them had a body mass index (BMI) of less than 18.5 kg/m^2. More than one-half of the women came from food secured households, but the majority of them had low dietary diversity (51%). A large majority of the participants (91%) came from households with improved drinking water sources; approximately 77% of them came from households which had flush or pour flush toilet facilities, and more than three-quarters came from households which had a culture of water treatment.

Of the 207 pregnant women sampled, 9 out of every 10 of them came from rural settings, and the majority of them were also from the Province 2 (31%) and the Terai ecological zone (~56%). Only 14% of the women were from rich households, and the majority of them were from the Brahmin/Chettri caste. The majority of the women (45%) were aged 15-24 years, the large majority of them did not contract fever, cough or diarrhoea in the last two weeks preceding the survey. More than one-half of the women came from food secured households, and the minority of them had high dietary diversity (27%). A large majority of the participants (94%) came from households with improved drinking water sources; approximately 69% of them came from households which had flush or pour flush toilet facilities, and more than three-quarters came from households which had a culture of water treatment.

3.2. Prevalence of Inflammation Status

The inflammation statuses among the participants are presented in figures 1 and 2. The highest proportion of the children (19%) had inflammation (combination of chronic and acute inflammation), whilst the lowest proportion (2%) had acute inflammation only, with the proportion of those with chronic inflammation lying in between (18%) (Figure 1). The highest proportion of the non-pregnant (7.3%) had inflammation (combination of chronic and acute inflammation), whilst the lowest proportion (3.6%) had acute inflammation only, with the proportion of those with chronic inflammation lying in between (3.7%) (Figure 2) The highest proportion of the pregnant (13%) had inflammation (combination of chronic and acute inflammation), whilst the lowest proportion (0.4%) had acute inflammation only, with the proportion of those with chronic inflammation lying in between (12.4%) (Figure 3).

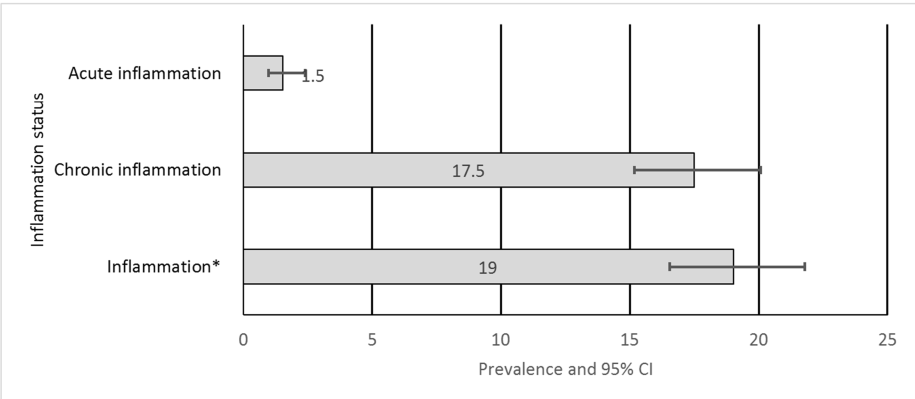

*Figure 1. Prevalence and 95% confidence Intervals of inflammation status among children aged 6-59 months. *Combined chronic and acute.*

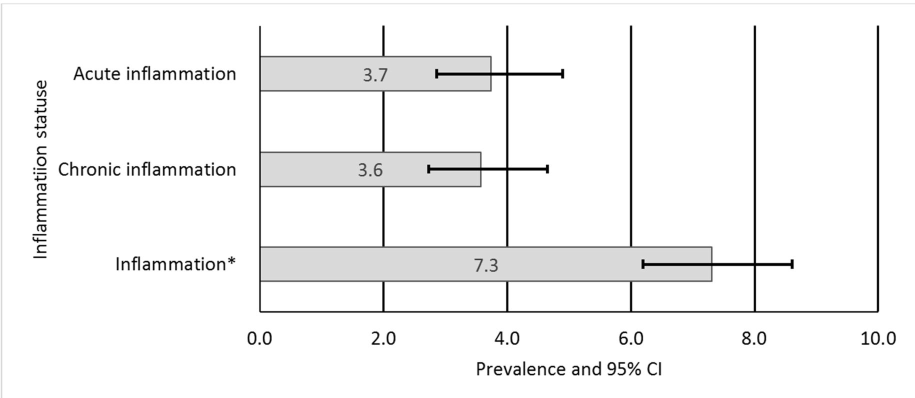

*Figure 2. Prevalence and 95% confidence Intervals of acute, chronic and combined acute and chronic inflammation among non-pregnant women aged 15-49 years. *Combined chronic and acute.*

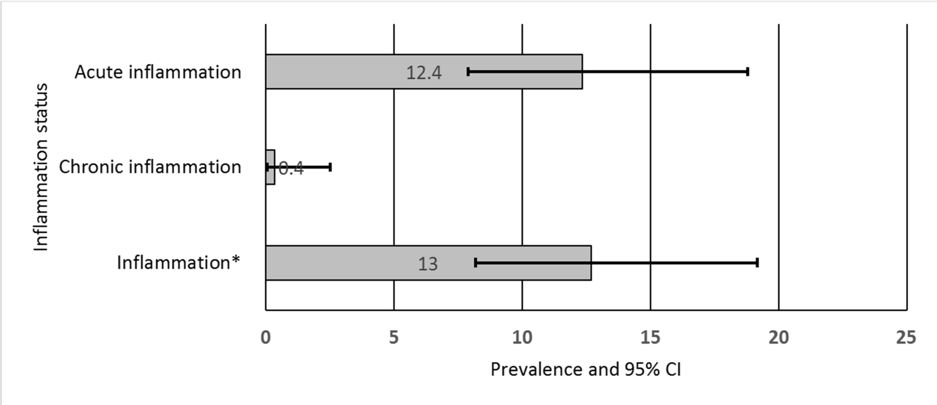

Figure 3. *Prevalence and 95% confidence Intervals of inflammation status among pregnant women aged 15-49 years. *Combined chronic and acute.*

3.3. Prevalence and Factors Associated with Inflammation Among Children Aged 6-59 Months

Of the children who had inflammation, rural and urban children were almost equally represented (19.1% and 18.4% respectively) (Table 2). The majority of the children who had inflammation came from the Province 7 (24.2%) and the Mountain ecological zone [Prevalence (P): 21.5, 95% confidence interval (CI): (17.0, 26.9)]. The majority of the children who had inflammation were from poor households [P: 20.8%, 95% CI: (17.4, 24.8)]. Inflammation was higher among the older-age children (25-59 months) [P: 15.8%; 95% CI: (8.2, 28.1)]; and females who had the disease outnumbered their male counterparts [P: 19.1%, 95% CI: (15.7, 23.0)]. Most of the children who had inflammation came from households with severe food insecurity [P: 28.8%, 95% CI: (17.9, 37.9)], with pit latrine facility [P: 23.8%, 95% CI: (19.5, 28.7)], and no habit of water treatment [P: 20.5%, 95% CI: (17.8, 23.4)].

After adjusting for potential covariates, our analyses revealed that children from the Province 7 were significantly more predisposed to inflammation compared with their counterparts from Province 1 [adjusted odds ratio (AOR): 1.57; 95% CI: (1.03, 2.39)] (Table 2). Further, children who contracted fever in the two weeks preceding the survey were significantly more likely to suffer from inflammation than those who did not [AOR: 1.61; 95% CI: (1.20, 2.17)]. In addition, the likelihood of inflammation was significantly higher among children who had cough in the two weeks preceding the survey compared with those who had not [AOR: 1.54; 95% CI: (1.17, 2.02)].

Table 2. *Prevalence and factors associated with inflammation among children aged 6-59 months: unadjusted and adjusted odd ratios.*

Characteristic	Prevalence 95% CI	Unadjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Community level factors					
Residence					
Urban	18.7 (14.2, 24.4)	1.00			
Rural	19.1 (16.3, 22.2)	1.02 (0.69, 1.52)	0.909		
State					
Province 1	16.9 (13.3, 21.4)	1.00		1.00	
Province 2	21.6 (18.1, 25.6)	1.35 (0.94, 1.95)	0.102	1.22 (0.91, 1.65)	0.186
Province 3	15.1 (9.7, 22.9)	0.88 (0.49, 1.58)	0.655	1.00 (0.56, 1.79)	0.988
Province 4	9.6 (4.1, 20.6)	0.52 (0.20, 1.33)	0.169	0.58 (0.22, 1.50)	0.257
Province 5	21.8 (14.4, 31.7)	1.37 (0.76, 2.45)	0.286	1.43 (0.82, 2.48)	0.200
Province 6	24.1 (19.2, 29.9)	1.56 (1.03, 2.35)	0.035	1.48 (0.99, 2.20)	0.055
Province 7	24.2 (18.9, 30.4)	1.56 (1.02, 3.40)	0.040	1.57 (1.03, 2.39)	0.037
Geographical region					
Eastern	16.7 (13.7, 20.3)	1.00			
Central	19.1 (22.2, 54.1)	1.17 (0.81, 1.69)	0.385		
Western	15.5 (8.7, 26.1)	0.91 (0.45, 1.83)	0.792		
Mid-western	23.0 (17.4, 29.9)	1.49 (0.97, 2.27)	0.065		
Far-western	24.2 (18.9, 30.4)	1.59 (1.07, 2.35)	0.021		
Ecological zone					
Mountain	21.5 (17.0, 26.9)	1.00			
Hill	16.6 (12.9, 21.1)	0.73 (0.48, 1.10)	0.128		
Terai	20.8 (17.1, 24.6)	0.95 (0.65, 1.37)	0.769		
Household level factors					
Household wealth index					
Poor	20.8 (17.4, 24.8)	1.00			
Middle	17.6 (13.3, 22.8)	0.81 (0.54, 1.21)	0.293		
Rich	18.2 (13.6, 24.1]	0.85 (0.56, 1.28)	0.422		
Ethnicity (Caste)					

Characteristic	Prevalence 95% CI	Unadjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Brahmin/Chettri	19.6 (16.3, 23.4)	1.00			
Dalit	22.5 (17.9, 27.8)	1.19 (0.87, 1.63)	0.273		
Janajati	11.4 (7.9, 15.9)	0.53 (0.35, 0.80)	0.003		
Others*	25.3 (19.4, 32.3)	1.39 (0.91, 2.11)	0.121		
Individual level factors					
Child's age (months)					
6-23	11.7 (6.4, 20.3)	1.00			
24-59	15.8 (8.2, 28.1]	1.41 (0.53, 1.79)	0.491		
Child's gender					
Male	18.9 (15.9, 22.4)	1.00			
Female	19.1 (15.7, 23.0)	1.01 (0.76, 1.34)	0.953		
Relation to child					
Biological parents	19.0 (16.6, 21.8)	1.00			
Others	18.5 (9.0, 34.3)	0.97 (0.43, 2.19)	0.935		
Health status					
Had fever					
No	14.9 (12.2, 18.2)	1.00		1.00	
Yes	26.0 (22.2, 30.4)	2.00 (1.48, 2.69)	<0.001	1.61 (1.20, 2.17)	0.002
Had cough					
No	15.2 (12.3, 18.5)	1.00		1.00	
Yes	25.2 (21.8, 29.1)	1.89 (1.43, 2.50)	<0.001	1.54 (1.17, 2.02)	0.003
Had diarrhoea					
No	17.6 (14.9, 20.6)	1.00			
Yes	25.0 (19.7, 31.3)	1.57 (1.09, 2.25)	0.016		
Anthropometric and Nutrition					
Stunting (< - 2 SD)					
No	17.9 (15.0, 21.2)	1.00			
Yes	21.1 (16.9, 25.9)	1.23 (0.88, 1.71)	0.227		
Wasting (< - 2 SD)					
No	18.3 (15.8, 21.0)	1.00			
Yes	24.7 (17.9, 32.9)	1.46 (0.98, 2.19)	0.063		
Underweight (< - 2 SD)					
No	17.2 (14.7, 20.1)	1.00			
Yes	23.4 (18.7, 28.9)	1.47 (1.06, 2.04)	0.023		
Dietary diversity					
Low	20.3 (16.7, 24.4)	1.00			
Moderate	16.2 (12.4, 20.8)	0.76 (0.51, 1.13)	0.170		
High	19.3 (15.1, 24.3)	0.94 (0.67, 1.32)	0.710		
Household food insecurity status					
Food secure	18.5 (15.3, 22.1)	1.00			
Mild food insecurity	20.3 (14.0, 28.4)	1.13 (0.69, 1.84)	0.632		
Moderate food insecurity	17.3 (12.9, 22.6)	0.92 (0.62, 1.37)	0.682		
Severe food insecurity	28.8 (17.9, 37.9)	1.61 (0.94, 2.79)	0.085		
Water and sanitation					
Source of drinking water					
Improved	19.0 (16.4, 21.9)	1.00			
Unimproved	19.1 (13.4, 25.9)	1.01 (0.67, 1.51)	0.969		
Type of toilet facility					
Flush or pour flush toilet	17.1 (14.6, 19.9)	1.00			
Pit latrine	23.8 (19.5, 28.7)	1.51 (1.12, 2.04)	0.008		
Water treatment habit					
Yes	11.3 (8.7, 15.6)	1.00		1.00	
No	20.5 (17.8, 23.4)	1.94 (1.37, 2.75)	<0.001	1.74 (1.18, 2.57)	0.005

3.4. Prevalence and Factors Associated with Inflammation Among Non-pregnant Women Aged 15-49 Months

Of the women who had inflammation, those who lived rural settings outnumbered their urban counterparts (7.4% and 6.8% respectively) (Table 3). The minority of the women who had inflammation came from the Province 4 (4.6%) and the Hill ecological zone [Prevalence (P): 5.6, 95% CI: (5.1, 8.2)]. The majority of the women who had inflammation were from rich households [P: 8.5%, 95% CI: (6.9, 10.5)]. Inflammation was higher among the women in the oldest age bracket (35-49 years) [P: 8.8%; 95% CI: (6.5, 11.9)]. Most of the women who had inflammation had a BMI of 25+ [P: 14.2%, 95% CI: (11.4, 17.6)], came from households with severe food insecurity [P: 7.5%, 95% CI: (3.5, 15.3)], with high dietary diversity [P: 10.7%, 95% CI: (7.9, 14.1)], with improved drinking water source [P: 7.6%, 95% CI: (6.1, 8.9)], with pit latrine facility [P: 23.8%, 95% CI: (19.5, 28.7)], and no habit of water treatment [P: 8.2%, 95% CI: (5.6, 11.6)].

After adjusting for potential covariates, we found that non-pregnant women from the Dalit caste were significantly more predisposed to inflammation compared with their counterparts from the Brahmin/Chettri caste [adjusted odds ratio (AOR): 1.76; 95% CI: (1.06, 2.91)] (Table 3). Further, women who had a cough in the two weeks preceding the survey were significantly more likely to suffer from inflammation than those who did not [AOR: 3.13; 95% CI: (1.04, 9.20)]. Finally, the likelihood of inflammation was significantly higher among non-pregnant women who had high dietary diversity, compared with those who had not [AOR: 1.76; 95% CI: (1.08, 2.86)].

Table 3. *Prevalence and factors associated with inflammation among non-pregnant women aged 15-49 years: unadjusted and adjusted odd ratios.*

Characteristic	Prevalence 95% CI	Unadjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Community level factors					
Residence					
Urban	6.8 (4.9, 9.5)	1.00			
Rural	7.4 (6.1, 8.9)	1.09 (0.71, 1.66)	0.690		
State					
Province 1	7.8 (5.5, 11.1)	1.00			
Province 2	7.8 (4.9, 12.4)	0.99 (0.53, 1.88)	0.999		
Province 3	7.8 (6.1, 9.9)	1.00 (0.63, 1.59)	0.986		
Province 4	4.6 (1.7, 11.1)	0.56 (0.19, 1.65)	0.291		
Province 5	7.8 (5.4, 11.2)	0.99 (0.58, 1.73)	0.997		
Province 6	7.1 (4.0, 12.3)	0.90 (0.44, 1.84)	0.773		
Province 7	6.0 (4.9, 7.4)	0.75 (0.49, 1.67)	0.202		
Geographical region					
Eastern	8.6 (5.9, 12.4)	1.00			
Central	7.4 (5.8, 9.3)	0.84 (0.52, 1.35)	0.468		
Western	7.6 (4.9, 11.5)	0.87 (0.48, 1.59)	0.654		
Mid-western	5.4 (3.7, 7.7)	0.60 (0.35, 1.05)	0.071		
Far-western	6.0 (4.9, 7.4)	0.68 (0.43, 1.07)	0.095		
Ecological zone					
Mountain	7.4 (4.9, 10.9)	1.00			
Hill	6.5 (5.1, 8.2)	0.87 (0.53, 1.44)	0.586		
Terai	7.9 (6.2, 10.2)	1.09 (0.65, 1.81)	0.740		
Household level factors					
Household wealth index					
Poor	7.3 (5.5, 9.5)	1.00			
Middle	6.6 (4.8, 8.9)	0.90 (0.59, 1.37)	0.619		
Rich	8.5 (6.9, 10.5)	1.19 (0.83, 1.72)	0.330		
Ethnicity (Caste)					
Brahmin/Chettri	7.6 (5.9, 9.8)	1.00		1.00	
Dalit	11.9 (8.5, 16.4)	1.64 (0.99, 2.70)	0.054	1.76 (1.06, 2.91)	0.028
Janajati	5.7 (3.9, 8.5)	0.74 (0.44, 1.25)	0.253	0.79 (0.46, 1.34)	0.370
Others*	5.3 (3.4, 8.1)	0.68 (0.38, 1.21)	0.188	0.69 (0.38, 1.23)	0.208
Individual level factors					
Age (years)					
15-24	6.4 (4.3, 9.5)	1.00			
25-34	6.7 (5.1, 8.6]	1.04 (0.60, 1.82)	0.881		
35-49	8.8 (6.5, 11.9)	1.40 (0.79, 2.47)	0.234		
Body mass index (kg/m^2)					
≤18.5	9.9 (4.8, 19.2)	1.00			
19-25	4.6 (3.6, 5.8)	0.44 (0.19, 1.00)	0.051		
25+	14.2 (11.4, 17.6)	1.51 (0.63, 3.61)	0.348		
Health status					
Had fever					
No	7.6 (5.0, 11.3)	1.00			
Yes	7.3 (5.9, 8.8)	0.95 (0.57, 1.59)	0.847		
Had diarrhoea					
No	9.8 (5.8, 16.0)	1.00			
Yes	7.1 (5.9, 8.4))	0.70 (0.38, 1.28)	0.245		
Nutrition					
Dietary diversity					
Low	6.6 (5.0, 8.5)	1.00		1.00	
Moderate	4.9 (3.0, 7.9)	0.74 (0.42, 1.31)	0.294	0.75 (0.43, 1.32)	0.313
High	10.7 (7.9, 14.1)	1.69 (1.04, 2.76)	0.033	1.76 (1.08, 2.86)	0.024
Household food insecurity status					
Food secure	6.8 (5.3, 8.8)	1.00			
Mild insecurity	6.9 (4.0, 11.5)	1.00 (0.50, 2.01)	0.999		
Moderate insecurity	8.4 (5.8, 12.1)	1.25 (0.74, 2.09)	0.398		

Characteristic	Prevalence 95% CI	Unadjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Severe insecurity	7.5 (3.5, 15.3)	1.09 (0.47, 2.52)	0.829		
Water and sanitation					
Source of drinking water					
Improved	7.6 (6.4, 8.9)	1.00			
Unimproved	4.0 (1.8, 8.9)	0.51 (0.21, 1.21)	0.123		
Type of toilet facility					
Flush or pour flush toilet	7.4 (6.1, 8.9)	1.00			
Pit latrine	6.9 (5.3, 9.2)	0.94 (0.66, 1.33)	0.716		
Water treatment habit					
Yes	7.1 (5.7, 8.7)	1.00			
No	8.2 (5.6, 11.6)	1.17 (0.72, 1.91)	0.526		

3.5. Prevalence and Factors Associated with Inflammation Among Pregnant Women Aged 15-49 Months

Of the pregnant women who had inflammation, those who lived urban settings outnumbered their rural counterparts (20.4% and 11.8% respectively) (Table 4). The majority of the pregnant women who had inflammation came from the Province 6 (26.2%) and the Mountain ecological zone [P: 20.2, 95% CI: (4.4, 58.0)]. In addition, the majority of the pregnant women who had inflammation were from rich households [P: 23.7%, 95% CI: (9.8, 47.2)]. Inflammation was higher among the middle-age pregnant women (aged 25-34 years) [P: 15.8%; 95% CI: (8.2, 28.1)]. Most of the pregnant women who had inflammation did have fever, cough or diarrhoea in the two weeks preceding the survey, came from households with severe food insecurity [P: 37.9%, 95% CI: (15.1, 67.7)], with high dietary diversity [P: 15.5%, 95% CI: (7.1, 30.7)], with improved drinking water source [P: 13.1%, 95% CI: (8.3, 19.9)], with flush or pour flush toilet facility [P: 12.9%, 95% CI: (7.8, 20.8)], and with habit of water treatment [P: 13.2%, 95% CI: (8.2, 20.5)].

After adjusting for potential covariates, we found that pregnant women from rich households were significantly more prone to inflammation compared with their counterparts from the poor households [adjusted odds ratio (AOR): 4.99; 95% CI: (1.11, 22.40)] (Table 4). Further, pregnant women who had a cough in the two weeks preceding the survey were significantly more likely to suffer from inflammation than those who did not [AOR: 3.13; 95% CI: (1.04, 9.20)]. Finally, the likelihood of inflammation was significantly higher among pregnant women from severely food insecure households, compared with those from food secure households [AOR: 5.93; 95% CI: (1.07, 12.89)].

Table 4. *Prevalence and factors associated with inflammation among pregnant women aged 15-49 years: unadjusted and adjusted odd ratios.*

Characteristic	Prevalence 95% CI	Unadjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Community level factors					
Residence					
Urban	20.4 (7.5, 44.7)	1.00			
Rural	11.8 (7.3, 18.7)	0.52 (0.15, 1.86)	0.316		
State					
Province 1	11.7 (3.6, 31.9)	1.00			
Province 2	13.8 (5.8, 29.4)	1.21 (0.25, 5.87)	0.813		
Province 3	8.2 (1.5, 34.5)	0.68 (0.08, 5.93)	0.723		
Province 4	16.1 (3.8, 47.9)	1.44 (0.19, 10.82)	0.719		
Province 5	6.9 (2.2, 19.8)	0.57 (0.10, 3.20)	0.518		
Province 6	26.2 (9.6, 54.2)	2.67 (0.47, 15.27)	0.269		
Province 7	17.3 (7.9, 33.9)	1.58 (0.34, 7.39)	0.562		
Geographical region					
Eastern	17.8 (8.1, 34.6)	1.00			
Central	7.9 (2.733, 21.02)	0.40 (0.10, 1.67)	0.211		
Western	10.0 (3.1, 28.0)	0.52 (0.11, 2.41)	0.398		
Mid-western	17.4 (7.6, 34.9)	0.98 (0.27, 3.45)	0.969		
Far-western	17.3 (7.9, 33.9)	0.97 (0.27, 3.45)	0.963		
Ecological zone					
Mountain	20.2 (4.4, 58.0)	1.00			
Hill	11.7 (5.9, 21.7)	0.52 (0.08, 3.34)	0.491		
Terai	12.8 (6.9, 22.6)	0.58 (0.09, 3.65)	0.563		
Household level factors					
Ethnicity (Caste)					
Brahmin/Chettri	16.4 (8.3, 29.6)	1.00			
Dalit	16.6 (6.9, 34.6)	1.02 (0.29, 3.53)	0.980		
Janajati	7.4 (2.1, 22.6)	0.41 (0.09, 1.84)	0.241		
Others*	11.2 (4.1, 27.1)	0.64 (0.17, 2.41)	0.512		
Individual level factors					

Characteristic	Prevalence 95% CI	Unadjusted OR 95% CI	p-value	Adjusted OR 95% CI	p-value
Age (years)					
15-24	11.7 (6.4, 20.3)	1.00			
25-34	15.8 (8.2, 28.1]	1.41 (0.53, 1.79)	0.491		
35-49	0	0.00			
Health status					
Had fever					
No	11.4 (6.7, 18.7)	1.00			
Yes	19.7 (9.0, 37.5)	1.90 (0.65, 5.53)	0.237		
Had cough					
No	9.1 (5.1, 15.9)	1.00		1.00	
Yes	26.1 (13.6, 44.4)	3.53 (1.26, 9.89)	0.017	3.13 (1.04, 9.2)	0.042
Had diarrhoea					
No	12.6 (8.0, 19.2))	1.00			
Yes	15.1 (2.2, 58.9)	1.24 (0.14, 10.62)	0.843		
Nutrition					
Dietary diversity					
Low	7.5 (2.6, 19.6)	1.00			
Moderate	14.9 (7.9, 26.3)	2.17 (0.59, 7.98)	0.243		
High	15.5 (7.1, 30.7)	2.26 (0.56, 9.20)	0.252		
Household food insecurity status					
Food secure	11.7 (6.6, 20.1)	1.00		1.00	
Mild insecurity	8.4 (1.2, 41.4)	0.69 (0.08, 5.86)	0.729	0.66 (0.08, 5.28)	0.686
Moderate insecurity	9.1 (3.1, 23.8)	0.75 (0.20, 2.78)	0.664	0.68 (0.17, 2.67)	0.583
Severe insecurity	37.9 (15.1, 67.7)	4.58 (1.14, 18.40)	0.032	5.93 (1.07, 12.89)	0.042
Water and sanitation					
Source of drinking water					
Improved	13.1 (8.3, 19.9)	1.00			
Unimproved	6.5 (1.4, 25.3)	0.47 (0.09, 2.44)	0.364		
Type of toilet facility					
Flush or pour flush toilet	12.9 (7.8, 20.8)	1.00			
Pit latrine	12.1 (4.9, 26.4)	0.92 (0.30, 2.80)	0.879		
Water treatment habit					
Yes	13.2 (8.2, 20.5)	1.00			
No	9.9 (2.9, 28.2)	0.72 (0.18, 2.87)	0.644		

4. Discussion

In this cross-sectional study among pre-school children and women of reproductive age, contraction of fever, and living in households with no water treatment habits (pre-school children); living in the Dalit ecological zone, having a cough and having a high dietary diversity (non-pregnant women) and living in rich households, having a cough and living in severely food insecure households (pregnant women) was associated with higher inflammation levels, after adjusting for other potential covariates.

In our current study, we found that inflammation was significantly higher among pre-school children who had a fever, compared with those who did not have the disease. Our finding was consistent with a study in Japan that examined the relationship between causes of fever and inflammatory biomarkers [12] and another study that utilised cross-sectional data from the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anaemia (BRINDA) project that involved 29765 pre-school children in 16 surveys and 25731 women of reproductive age in 10 surveys [13]. This finding should not be surprising because there is evidence that fever in itself is (one of 5 signs of inflammation) an inflammatory response which extends beyond the site of infection and may affect the entire body, leading to an overall rise in body temperature [14].

Univariate analysis of the NNMSS data revealed that for the pre-school children increased predisposition to inflammation was positively associated with those who had diarrhoea two weeks prior to the survey, consistent with a result from a past study in Brazil which analysed stool samples collected for a diarrhoeal study among children [15]. The finding may be due to high rates of faecal lactoferrin, reminiscent of cryptosporidium in developing countries, which has been shown to stimulate an inflammatory response in children who are malnourished [16, 17]. In addition, increased likelihood of inflammation in the pre-school children was found to be associated with those who were underweight. This finding is in contradiction with past studies which revealed that obese children had significantly higher odds of inflammation compared with their non-obese counterparts [18, 19]. Epidemiological studies among adults and children [20] have revealed that elevated BMI is associated with elevated systemic markers of inflammation such as CRP [19]. There have been few clinical studies that have investigated paediatric obesity and inflammation using CRP and other inflammatory cytokines [21]. However, those studies were either limited in scope, with a relatively small sample size [22-24] or had used BMI as a surrogate marker of obesity status [19]. Although BMI correlates fairly well with body fat in adult populations, it is an imperfect measure of adiposity, particularly in paediatric populations [25, 26].

Furthermore, we found that the pre-school children from households with pit latrines were significantly more prone to inflammation compared with their counterparts from households with flush or pour flush toilets. Children from households with pit latrines rather than flush or pour flush toilets are more prone to unhygienic practices; and poor hygienic practices as well as low socio-economic status have been shown to be the commonest risk factors for the presence of inflammatory trachoma [27-29].

The likelihood of inflammation was found to be significantly higher among pre-school children and non-pregnant women who had a cough in the two weeks preceding the survey. This finding was consistent with a previous study on airway inflammation in non-asthmatic subjects with chronic cough, in which subjects with chronic cough had an increased number of inflammatory cells in broncho-alveolar lavage fluid [30].

We found that there was an increased likelihood of inflammation among pregnant women from severely food insecure households. This finding was consistent with a finding from a study in the US which conducted a cross-sectional analysis of the US National Health and Nutrition Examination Survey (1999–2006) involving 12 191 adults, and which revealed that food insecurity was associated with CRP [31]. This finding may suggest that inflammation could be a mechanism through which food insecurity has been proven to predispose people to chronic diseases including cardio-vascular disease [32-36].

The main strength of this current study was that the NNMSS is population-based and nationally-representative, and therefore findings could be generalised to other parts of Nepal where data were not collected.

The study, however, had a number of limitations. Firstly, causality could not be inferred, because of the cross-sectional nature of survey. Secondly, the presumptions on the recall bias for the process of recalling and recording the dietary and physical activity habits, required attention and involved perception. Thirdly, as dietary assessment involved perception, underreporting was likely, because of participant's awareness of the importance of diet and their ability to readily identify healthful and not so healthful foods. Consequently, there was the probability that some databases were unable to reflect the precise food intake. Finally, general environmental data to represent participants' exposures rather than personal monitoring data were used.

5. Conclusions

This current study revealed the factors associated with inflammation among pre-school children and women of reproductive age. Having fever and cough was one of the prominent factors associated with inflammation in the participants, especially among the pre-school children and non-pregnant women. Other factors associated with inflammation, particularly among pregnant women were living in rich households and living in severely food insecure households. Further longitudinal investigations are required to ascertain these associations. Additionally, further investigations are required to identify the temporal and biosocial mechanisms that mediate the association between food insecurity and specific chronic diseases, such as diabetes and cardiovascular disease, toward the ultimate aim to develop cost-effective, sustainable, and effective public health programmes.

References

[1] SickKids Staff. *Inflammation and the immune system*. [cited 2018 Sep 26]; Available from: https://www.aboutkidshealth.ca/Article?contentid=926&language=English.

[2] Hochepied, T., et al., *α1-Acid glycoprotein: an acute phase protein with inflammatory and immunomodulating properties.* Cytokine & growth factor reviews, 2003. 14 (1): p. 25-34.

[3] Suchdev, P. S., et al., *Overview of the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) Project–*. Advances in Nutrition, 2016. 7 (2): p. 349-356.

[4] Libby, P., P. M. Ridker, and A. Maseri, *Inflammation and atherosclerosis.* Circulation, 2002. 105 (9): p. 1135-1143.

[5] Kelishadi, R., et al., *Lifestyle and environmental factors associated with inflammation, oxidative stress and insulin resistance in children.* Atherosclerosis, 2009. 203 (1): p. 311-319.

[6] Ministry of Health Nepal, et al., *Nepal National Micronutrient Status Survey – 2016*. 2017, Minisry of Health, Nepal: Kathmandu, Nepal.

[7] Balcı, Y. I., et al., *Prevalence and risk factors of anemia among adolescents in Denizli, Turkey.* Iranian journal of pediatrics, 2012. 22 (1): p. 77.

[8] Alzaheb, R. A. and O. Al-Amer, *The Prevalence of Iron Deficiency Anemia and its Associated Risk Factors Among a Sample of Female University Students in Tabuk, Saudi Arabia.* Clinical Medicine Insights: Women's Health, 2017. 10: p.1179562X17745088.

[9] Alaofè, H., et al., *Prevalence of anaemia, deficiencies of iron and vitamin A and their determinants in rural women and young children: a cross-sectional study in Kalalé district of northern Benin.* Public health nutrition, 2017. 20 (7): p. 1203-1213.

[10] Harding, K. L., et al., *Determinants of anemia among women and children in Nepal and Pakistan: An analysis of recent national survey data.* Maternal & child nutrition, 2017.

[11] Filmer, D. and L. H. Pritchett, *Estimating Wealth Effects Without Expenditure Data—Or Tears: An Application To Educational Enrollments In States Of India**. Demography, 2001. 38 (1): p. 115-132.

[12] Naito, T., et al., *Relationships between causes of fever of unknown origin and inflammatory markers: a multicenter collaborative retrospective study.* Internal Medicine, 2015. 54 (16): p. 1989-1994.

[13] Merrill, R. D., et al., *Factors associated with inflammation in preschool children and women of reproductive age: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project.* The American journal of clinical nutrition, 2017. 106 (suppl_1): p. 348S-358S.

[14] *Inflammation and fever*. Available from: https://courses.lumenlearning.com/microbiology/chapter/inflammation-and-fever/.

[15] Kohli, A., et al., *Giardia duodenalis assemblage, clinical presentation and markers of intestinal inflammation in Brazilian children.* Transactions of the Royal Society of Tropical Medicine and Hygiene, 2008. 102 (7): p. 718-725.

[16] Alcantara, C. S., et al., *Interleukin-8, tumor necrosis factor-α, and lactoferrin in immunocompetent hosts with experimental and Brazilian children with acquired cryptosporidiosis.* The American journal of tropical medicine and hygiene, 2003. 68 (3): p. 325-328.

[17] Kirkpatrick, B. D., et al., *Cryptosporidiosis stimulates an inflammatory intestinal response in malnourished Haitian children.* The Journal of infectious diseases, 2002. 186 (1): p. 94-101.

[18] Singer, K., et al., *The relationship between body fat mass percentiles and inflammation in children.* Obesity, 2014. 22 (5): p. 1332-1336.

[19] Skinner, A. C., et al., *Multiple markers of inflammation and weight status: cross-sectional analyses throughout childhood.* Pediatrics, 2010: p. peds. 2009-2182.

[20] Visser, M., et al., *Elevated C-reactive protein levels in overweight and obese adults.* Jama, 1999. 282 (22): p. 2131-2135.

[21] Tam, C., et al., *Obesity and low-grade inflammation: a paediatric perspective.* Obesity Reviews, 2010. 11 (2): p. 118-126.

[22] Wang, G., et al., *C-reactive protein in adolescent twins: patterns and relationship to adiposity.* The Journal of Clinical Endocrinology & Metabolism, 2011. 96 (10): p. 3226-3233.

[23] Parrett, A. L., et al., *Adiposity, activity, fitness, and C-reactive protein in children.* Medicine and science in sports and exercise, 2010. 42 (11): p. 1981-1986.

[24] Barbeau, P., et al., *Hemostatic and inflammatory markers in obese youths: effects of exercise and adiposity.* The Journal of pediatrics, 2002. 141 (3): p. 415-420.

[25] Freedman, D. S., et al., *Classification of body fatness by body mass index–for-age categories among children.* Archives of pediatrics & adolescent medicine, 2009. 163 (9): p. 805-811.

[26] Dugas, L. R., et al., *Adiposity Is Not Equal in a Multi-Race/Ethnic Adolescent Population: NHANES 1999–2004.* Obesity, 2011. 19 (10): p. 2099-2101.

[27] Taylor, H. R., et al., *Hygiene factors and increased risk of trachoma in central Tanzania.* Archives of ophthalmology, 1989. 107 (12): p. 1821-1825.

[28] Tielsch, J. M., et al., *The epidemiology of trachoma in southern Malawi.* The American journal of tropical medicine and hygiene, 1988. 38 (2): p. 393-399.

[29] Cumberland, P., G. Hailu, and J. Todd, *Active trachoma in children aged three to nine years in rural communities in Ethiopia: prevalence, indicators and risk factors.* Transactions of the Royal society of Tropical Medicine and Hygiene, 2005. 99 (2): p. 120-127.

[30] Boulet, L.-P., et al., *Airway inflammation in nonasthmatic subjects with chronic cough.* American journal of respiratory and critical care medicine, 1994. 149 (2): p. 482-489.

[31] Gowda, C., C. Hadley, and A. E. Aiello, *The association between food insecurity and inflammation in the US adult population.* American journal of public health, 2012. 102 (8): p. 1579-1586.

[32] Vozoris, N. T. and V. S. Tarasuk, *Household food insufficiency is associated with poorer health.* The Journal of nutrition, 2003. 133 (1): p. 120-126.

[33] Seligman, H. K., et al., *Food insecurity is associated with diabetes mellitus: results from the National Health Examination and Nutrition Examination Survey (NHANES) 1999–2002.* Journal of general internal medicine, 2007. 22 (7): p. 1018-1023.

[34] Seligman, H. K., B. A. Laraia, and M. B. Kushel, *Food insecurity is associated with chronic disease among low-income NHANES participants.* The Journal of nutrition, 2009. 140 (2): p. 304-310.

[35] Stuff, J. E., et al., *Household food insecurity is associated with adult health status.* The Journal of nutrition, 2004. 134 (9): p. 2330-2335.

[36] Olson, C. M., *Nutrition and health outcomes associated with food insecurity and hunger.* The Journal of nutrition, 1999. 129 (2): p. 521S-524S.