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Assessment of Iron Deficiency Anemia as a Risk Factor for Acute Lower Respiratory Tract Infections in Nepalese Children- A Cross-Sectional Study.

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ABSTRACT

Background: Anemia and acute lower respiratory tract infections are persistent and pervasive public health problems. Objective-To determine the relation of iron deficiency anemia with lower respiratory tract infection. **Methods:** The study included 82 diagnosed cases of acute lower respiratory tract infection in infants and children of age 6 months to 5 years. Detailed history and physical examination was done according to predesigned proforma. Laboratory investigations like complete blood count, red blood cell morphology and serum ferritin was carried out. Data was statistically analyzed. **Results:** Out of 82 cases, 34 cases were iron deficiency positive. Among 82 cases, majority of them were below 24 months. Gender wise, male population was higher compared to female. Sixty one percent of the cases belonged to middle class and 39% belonged to lower class. Cough was present in all acute lower respiratory tract infection patients followed by fast breathing, fever, chest in drawing, noisy breathing, poor feeding and the least of all was bluish discoloration of face/lips. The overall mean temperature, pulse rate and respiratory rate were 100.36^{0}F, 113.41 per minute and 58.49 per minute respectively. Among signs, tachypnea for age was present in all cases. Auscultatory chest findings revealed normal auscultatory findings in 12.2% patients, only crepitation in 42.7%, only rhonchi in 17.1% and both crepitation and rhonchi in 28%. Pneumonia was predominant with 79.3% among 82 cases. Except eosinophil and monocyte counts, mean of other counts significantly differ among the bronchiolitis patients and pneumonia patients. Out of 82 cases, 22% had Hb≥11gm/dl and remaining had Hb<11gm/dl. Out of 18 cases with Hb≥11gm/dl, 14 were pneumonia and 4 cases were bronchiolitis. **Conclusion:** Simple intervention with cheap, dependable and cost effective prevention of lower respiratory tract infection with iron supplementation in children under 5 years of age might the reduce incidence of morbidity and mortality.

Keywords: Anemia, Acutelower respiratory tract infections, Iron deficiency.

INTRODUCTION

Anemia is a major nutritional global problem of immense public health significance, affecting persons of all ages, sex and economic group.[1]Most recently, the prevalence of anemia was estimated 38% in pregnant women, 29% in non-pregnant women and 43% in children, with reductions since 1995 in each group.[2]

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Iron deficiency is the most widespread and common nutritional disorder in the world with estimated 30% of the global population suffering from iron deficiency anemia (IDA) and most of them living in developing countries.[3] Acute lower respiratory tract infection (ALRTI) is the leading cause of mortality and one of the common causes of morbidity in children under 5 years of age in most of the developing countries like Nepal.[4,5] Balanced and adequate nutritional supplementation to the growing children is of immense importance for development and maturity of immunity, consequently development of resistance against the infections. So nutritional inadequacy including the iron deficiency forms an indirect risk factor for the contracting ALRTI.[6]

Hence, this study was aimed to determine the relationship between IDA as a risk factor for ALRTI among children of age 6 months to 5 years.

MATERIALS AND METHODS

Study Design and Setting

This study employed a hospital-based cross-sectional study and was conducted in the Department of Pediatrics, Nepalgunj Medical College and Teaching Hospital (NGMCTH), Nepalgunj, Nepal for the period of one year from January 2015 to February

2016. The study was approved by the institutional review board. Eighty two diagnosed cases of ALRTI in infants and children of age 6 months to 5 years admitted in NGMCTH, Nepal were taken as study population.

The inclusion criteria included children of age 6 months to 5 years with ALRTI as per WHO criteria.[7]The exclusion criteria considered was: a. children suffering from other systemic illness like congenital heart disease, tuberculosis and protein energy malnutrition (PEM ≥ Grade 3 as per Indian Academy of Paediatrics (IAP) classification)[8] b. children who already received antibiotics from outside c. congenital malformation of the chest wall d. those taking iron supplements and e. those patients whose guardians do not give consent for study.

Socio-demographic variables, clinical signs and symptoms, general appearance, vital signs, respiratory examination and hematological investigations were carried out in all the participants.

The following criteria was used to define IDA in the participants-[9-14]

1. Hemoglobin (Hb) <11 gm/dl,
2. MCV <76 femto litres and MCH <24 picograms,
3. RDW >14.5%,
4. Serum ferritin <30 ng/ml in the presence of infection, and
5. PBS showing microcytic, hypochromic red blood cells with or without significant anisocytosis.

The norms considered for ALRTI was defined as per WHO criteria ie, presence of fever, cough with fast breathing of >60 per minute in <2 month of age, >50 per minute in 2 to 12 month of age and>40 per minute in 12 month to 5 years of age, the duration of illness being <30 days.[7]

Within Child Health Epidemiology Reference Group (CHERG) of WHO among ALRTI cases, a decision was made to concentrate on pneumonia and bronchiolitis because they were considered as major components of ALRTI that accounted for global burden of disease from acute respiratory infection among young children.[15] So, cases with pneumonia or bronchiolitis were taken in this study.

Pneumonia was further classified into pneumonia, severe pneumonia and very severe pneumonia as per WHO criteria for assessing severity of pneumonia.[7]

Data collection procedure

Before starting interview, brief introduction was given to parents or who brought the child and informed consent of their willingness was taken from them. They were also informed about the aims of the study. Detailed history and physical examination was done according top redesigned proforma. History of relevant symptoms like fever, cough, rapid breathing, nasal flaring, chest retraction, refusal of feeds, lethargy, wheeze etcwas taken. Socioeconomic status was graded according to modified Kuppus wamy's scale for use in Nepal.[16]

The CBC count was quantified using fully automatic complete analyser, Nihon Kohdencelltac E with five differential parts, 22 parameters. Serum ferritin level was assessed through a machine – Lumace CB 962, Centro LIA/pc using chemiluminance immunoassay.

Data processing and analysis

Data was analyzed using SPSS 17.0 version. Descriptive analysis was done for demographic and clinical variables and presented by tabulation, pie chart and bar charts. Bivariate analysis using '*t*' independent test and chi square test was done between demographic, laboratory variable and ALRTI (with or without IDA) presented with mean difference and p-value. Bivariate analysis using chi square test was done between demographic, laboratory variables and ALRTI (with or without IDA) presented with odds ratio (OR) and p-value. Variables in bivariate analysis with p-value up to 0.2 are used for multivariate analysis. Linear regression was done for multivariate analysis and presented with beta coefficient or OR with 95 % CI.

RESULTS

In the present study, a total of 82 cases with ALRTI were enrolled and IDA was labelled as those fulfilling the all six criteria as mentioned on operational definition. Out of 82 cases, 34 cases were IDA positive fulfilling all six criteria, remaining was labelled as IDA negative.

Among 82 cases, majority of them 87.8% (72) were below 24 months and minority 12.2% (10) were above 24 months of age. In both age groups, IDA negative outnumber IDA positive cases (51.2% vs 36.6%) and (7.3% vs 4.9%) respectively. However, there was no significant association observed between two age groups (p=0.92).Gender wise, male population were higher compared to female [49(59.8%) vs 33(40.2%)] with approximately 1.5:1 male to female ratio. It was not statistically significant (p=0.75).Sixty one percent (50) of the cases belonged to middle class including upper middle and lower middle and 39% (32) belonged to lower class including upper lower and lower class. In both classes, IDA negative cases exceeded IDA positive cases and with no significant difference between two groups(p=0.73).Fifty three(64.6%) out of 82 patients were from mid western development region and remaining 29 (35.4%) were from far western development region. Sixteen cases from far western development region were IDP compared to 13 cases who were negative for iron deficiency. However, there was no statistical significance between cases from these two developmental region (p=0.06)**[Table 1].**

Table 1: Relationship of iron deficiency with socio-demographic variables.

Demographic variables	All n(%)	Iron deficiency Positive n(%)	Iron deficiency negative n(%)	OR(95% CI)	p-value
Age (months)					
≥24 months	10(12.2%)	4(4.9%)	6(7.3%)	1	0.92
<24 months	72(87.8%)	30(36.6%)	42(51.2%)	1.07(0.27-4.12)	
Gender					
Male	49(59.8%)	21(25.6%)	28(34.1%)	1	0.75
Female	33(40.2%)	13(15.9%)	20(24.4%)	1.15(0.47-2.83)	
Socioeconomic status					
Upper and lower middle	50(61%)	20(24.4%)	30(36.6%)	1	0.73
Upper lower and lower	32(39%)	14(17%)	18(22%)	1.16(0.47-2.86)	
Residence					
Mid western development region	53(64.6%)	18(22%)	35(42.7%)	1	0.06
Far western development region	29(35.4%)	16(19.5%)	13(15.9%)	2.39(0.94-6.04)	

According to modified Kuppuswamy's scale[16], socioeconomic status had been classified into five classes. None of the family was there from upper socioeconomic status. In upper middle socioeconomic status, 13 cases were IDA negative whereas none of the cases were IDA positive. Maximum number of cases belonged to lower middle socioeconomic status with IDA positive cases exceeding IDA negative cases (20 vs17). Similarly, 23 patients belonged to upper lower economic status with 15 cases having IDA. Least number of cases (total 9 cases)belonged to family with lower socioeconomic status with ratio 2:1 for IDA positive to IDA negative [Figure 1].

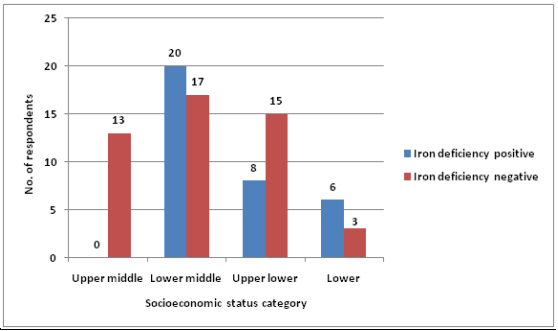

Figure 1: Association of socioeconomic status with and without iron deficiency in ALRTI.

As per chief complaints given by the informant, cough was present in all patients with ALRTI followed by fast breathing 79 (96.3%) out 82, fever 86.8%, chest indrawing (difficulty in breathing) 62.2%, noisy breathing 19.5%, poor feeding 14.6% and the least of all was bluish discoloration of face/lips 6.1%. As patients without iron deficiency exceeded iron deficiency anemia, symptoms like fever, cough, fast breathing and chest in drawing appeared to be higher in patient without iron deficiency whereas noisy breathing and poor feeding were present equally in both category and out of 5 cases with bluish discoloration of face/lips, 4 belonged to having IDA positive [Table 2].

Cough had the maximum duration with the mean of 5.07 days and SD 1.83, followed by noisy breathing, fever, fast breathing, difficulty in breathing, poor feeding and finally bluish discoloration of face. Mean duration of fever, fast breathing, difficulty in breathing were higher in IDA positive cases while mean duration of cough and noisy breathing were higher in IDA negative cases. There was no difference in mean duration of poor feeding and bluish discoloration among two groups [Table 3].

Out of 82 cases, 42 were alert while 40 had sick look on general appearance. Among sick looking patient, 15 (18.3%) were irritable and 6 (7.3%) were restless. Equal numbers of cases (20 in each) were sick look in both IDA positive and negative category. Out of 6, 4 cases were restless in IDA positive category[Table 4].

The overall mean temperature, pulse rate and respiratory rate were 100.36^0F,113.41 per minute and 58.49 per minute respectively. Mean of these variables were higher in IDA cases as compared to those without iron deficiency [Table 5].

Among signs, tachypnea for age was present in all cases. Subcostal/intercostals retraction was present in 51 cases (62.2%), pallor was seen in 52 cases (63.4%),nasal flaring and cyanosis in 6 (7.3%) and 5 (6.1%) cases respectively. Iron deficiency negative cases were higher for chest retraction (28 vs 23 cases)and tachypnea (48 vs 34 cases) as compared to IDA positive cases while pallor, cyanosis and nasal flaring were higher in IDA positive cases. Auscultatory chest findings reveals only crepitation in 35 (42.7%), only rhonchi in 14 (17.1%), both crepitation and rhonchi in 23 (28%) and normal auscultatory findings in 10 (12.2%) patients [Table 6].

Table 2: Symptoms of ALRTI as briefed by informants.

Symptoms as per informants	All n(%)	Iron deficiency positive n(%)	Iron deficiency negative n(%)
Fever			
Present	71(86.6%)	30(36.6%)	41(50%)
Absent	11(13.4%)	4(4.9%)	7(8.5%)
Cough			
Present	82(100%)	34(41.5%)	48(58.5%)
Absent	0(0%)	0(0%)	0(0%)
Fast breathing			
Present	79(96.3%)	31(37.8%)	48(58.5%)
Absent	3(3.7%)	3(3.7%)	0(0%)
Chest indrawing (Difficulty inbreathing)			
Present	51(62.2%)	23(28.1%)	28(34.1%)
Absent	31(37.8%)	11(13.4%)	20(24.4%)
Noisy breathing			
Present	16(19.5%)	8(9.8%)	8(9.8%)
Absent	66(80.5%)	26(31.7%)	40(48.8%)
Bluish discoloration of face/ lips			
Present	5(6.1%)	4(4.9%)	1(1.2%)
Absent	77(93.9%)	30(36.6%)	47(57.3%)
Poor feeding			
Present	12(14.6%)	6(7.3%)	6(7.3%)
Absent	70(85.4%)	28(34.2%)	42(51.2%)

Table 3: Duration of clinical symptoms of ALRTI prior to admission.

Duration of clinical symptoms of ALRTI (days)	All		Iron deficiency Positive		Iron deficiency negative	
	Mean	S.D	Mean	S.D	Mean	S.D
Duration of cough	5.07	1.83	5	1.93	5.13	1.77
Duration of fever	4.44	1.82	4.63	1.86	4.29	1.8
Duration of fast breathing	3.44	1.43	3.52	1.31	3.4	1.52
Duration of difficulty in breathing/chest indrawing	3.38	1.9	3.65	2.03	3.19	1.81
Duration of noisy breathing	4.75	1.48	4.63	1.4	4.88	1.64
Duration of poor feeding/refusal toeat	1.67	0.49	1.67	0.51	1.67	0.51
Duration of bluish discoloration of face	1	0	1	0	1	0

Table 4: General appearance of cases at the time of admission.

General Appearance	All n(%)	Iron deficiency positive n(%)	Iron deficiency negative n(%)
Alertness			
Alert	42(51.2%)	14(17.1%)	28(34.1%)
Not alert	40(48.8%)	20(24.4%)	20(24.4%)
Restless			
Yes	6(7.3%)	4(4.9%)	2(2.4%)
No	76(92.7%)	30(36.6%)	46(56.1%)
Irritable			
Yes	15(18.3%)	7(8.5%)	8(9.8%)
No	67(81.7%)	27(32.9%)	40(48.8%)
Sick looking			
Yes	40(48.78%)	20(24.4%)	20(24.4%)
No	42(51.21%)	14(17.1%)	28(34.1%)

Pneumonia was predominant with 65 (79.3%) among 82 cases. Remaining cases were bronchiolitis (20.7%). Iron deficiency negative had higher number of cases as compared to IDA positive **[Table 7].**

Table 5: Vital signs of cases.

Vitals	All		Iron deficiency Positive		Iron deficiency negative	
	Mean	S.D	Mean	S.D	Mean	S.D

Temperature(ºF)	100.36	1.64	100.88	1.84	99.98	1.39
Pulse rate(per minute)	113.41	13.4	117.35	8.23	110.63	10
Respiratory rate(per minute)	58.49	8.68	59.06	8.23	58.08	9.05

Table 6: Signs present during clinical examination at the time of admission.

Signs at presentation	All n(%)	Iron deficiency Positive n(%)	Iron deficiency Negative n(%)
Subcostal/intercostal retraction			
Present	51(62.2%)	23(28.1%)	28(34.1%)
Absent	31(37.8%)	11(13.4%)	20(24.4%)
Tachypnea for age			
Present	82(100%)	34(41.5%)	48(58.5%)
Absent	0(0%)	0(0%)	0(0%)
Pallor			
Present	52(63.4%)	33(40.2%)	19(23.2%)
Absent	30(36.6%)	1(1.2%)	29(35.4%)
Cyanosis			
Present	5(6.1%)	4(4.9%)	1(1.2%)
Absent	77(93.9%)	30(36.6%)	47(57.3%)
Nasal flaring			
Present	6(7.3%)	4(4.9%)	2(2.4%)
Absent	76(92.7%)	30(36.6%)	46(56.1%)
Auscultatory chest findings			
Normal	10(12.2%)	4(4.9%)	6(7.31%)
Crepitation	35(42.7%)	13(15.9%)	22(26.8%)
Rhonchi	14(17.1%)	6(7.3%)	8(9.8%)
Rhonchi andCrepitation	23(28%)	11(13.4%)	12(14.6%)

Table 7: Types of ALRTI on basis of clinical features, clinical examination and radiological findings.

Types of ALRTI	All n(%)	Iron deficiency positive n(%)	Iron deficiency negative n(%)
Bronchiolitis	17(20.7%)	7(8.5%)	10(12.2%)
Pneumonia	65(79.3%)	27(33%)	38(46.3%)

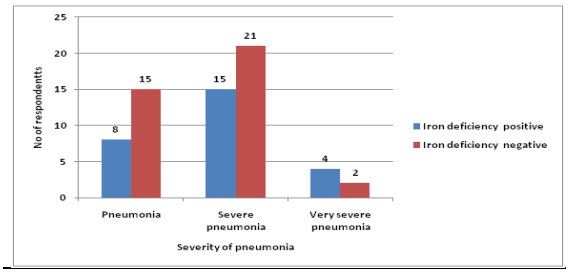

Figure 2: Comparison of severity of pneumonia with respect to iron deficiency.

As per WHO criteria for assessing severity of pneumonia, 23 out of 65 (35.4%) were diagnosed as a cases of pneumonia, 36 (55.4%) as severe pneumonia and 6 (9.2%) as very severe pneumonia. Very severe pneumonia cases were higher in IDA positive group whereas pneumonia and severe pneumonia cases were higher in other group [Figure 2].

Radiological evidence of pneumonia was present in 48 (58.5%) patients, hyperinflated lungs suggestive of bronchiolitis in 12 (14.6%) patients and normal in 22 (26.8%) patients [Table 8].

Table 8: Radiological findings on chest X-ray.

Chest X-ray report	All n(%)	Iron deficiency Positive n(%)	Iron deficiency negative n(%)
Normal	22(26.8%)	9(11%)	13(15.8%)
Suggestive of Bronchiolitis	12(14.6%)	5(6.1%)	7(8.5%)
Suggestive of Pneumonia	48(58.5%)	20(24.4%)	28(34.1%)

Maximum number of ALRTI cases belonged to age group 6-12 months, followed by age 13-24 months and the least number of age 25-60 months [Figure 3].

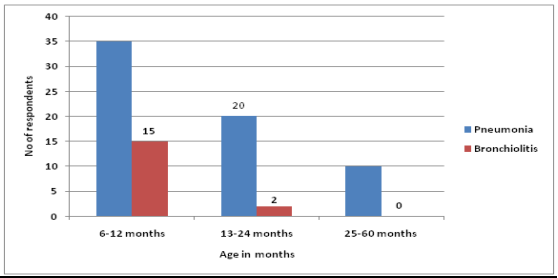

Figure 3: Prevalence of ALRTI according to different age groups.

Except eosinophil and monocyte counts, mean of other counts significantly differ among the bronchiolitis patients and pneumonia patients. Among TLC and neutrophil count, mean counts were higher in pneumonia patients whereas mean lymphocyte count was higher in bronchiolitis patients. Among the above parameter, TLC,

neutrophil and lymphocyte count between bronchiolitis and pneumonia were statistically significant [Table 9].

Table 9: Association of total leucocyte count (TLC) and differential count with ALRTI.

Variables	Bronchiolitis		Pneumonia		Mean difference	P value
	Mean	S.D	Mean	S.D		
TLC	10529.41	3041.33	14766.15	5768.72	-4236.74[(-7129.45-(-1344.02)]	0.005*
Neutrophil	49.65	7.5	61.48	16.45	-11.83(-17.3-(-6.35)	0.00*
Lymphocyte	48.41	8.03	37.03	16.26	11.38(2.8-5.75)	0.00*
Eosinophils	1.24	1.25	1.11	1.32	0.12(-0.58-0.83)	0.72
Monocytes	0.53	0.8	0.42	0.72	0.11(0.2-(-0.28)	0.57

Out of 82 cases, 18 (22%) had haemoglobin level ≥11gm/dl and 64 (88%) had haemoglobin level <11gm/dl. Out of 18 cases with Hb≥11 gm/dl, 14 were pneumonia and 4 cases were bronchiolitis. Fifty one cases out of 64 with Hb<11 gm/dl had pneumonia and remaining 13 had bronchiolitis [Table 10].

Table 10: ALRTI with respect to hemoglobin level.

Hemoglobin level(gm/dl)	Pneumonia n(%)	Bronchiolitis n(%)
Hb≥11	14(17.1%)	4(4.9%)
Hb<11	51(62.2%)	13(15.8%)

Maximum number [50 (60.9%)] of IDA cases belonged to age group 6-12 months. Out of 50 cases, 46% had IDA. Seven out of 22 (31.8%) in age group 13-24 months had IDA and 4 out of 10 (40%) in age group 25-60 months had IDA [Figure 4].

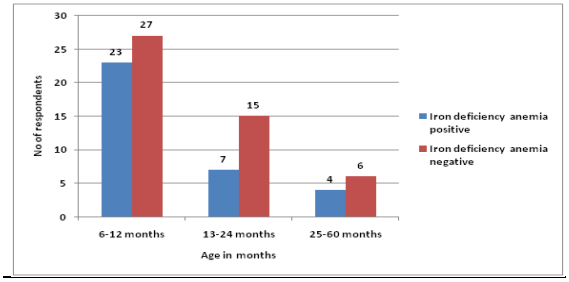

Figure 4: Distribution of iron deficiency anemia according to age group.

Independent "*t*" test result shows, mean of the laboratory parameters Hb, total RBC count, hematocrit, MCV, MCH, MCHC, RDW, serum ferritin were significantly different among the IDA positive and negative group with highly significant p-value<0.01. Whereas TLC, differential counts and platelets were statistically insignificant between IDA positive and negative group with p-value>0.05 [Table 11].

Table 11: Mean difference of laboratory parameters in relation with IDA among ALRTI.

Laboratory parameters of anemia	All		Iron deficiency Positive		Iron deficiency negative		Mean difference	P value
	Mean	S.D	Mean	S.D	Mean	S.D		
Hemoglobin (gm/dl)	9.46	1.85	7.99	0.96	10.5	1.61	2.51 (1.89-3.12)	0.00*
TotalRBC (million/mm^3)	4.02	0.62	3.81	0.5	4.17	0.65	0.35 (0.09-0.62	0.00*
Hematocrit (%)	29.41	5.45	25.34	2.94	32.29	4.96	6.94 (5.2-8.69)	0.00*
MCV (femtolitre)	72.61	9.05	64.49	6.05	78.36	5.84	13.87 (111.22-16.51)	0.00*
MCH (picogram)	23.46	3.8	19.92	2.2	25.97	2.46	6.04 (4.99-7.09)	0.00*
MCHC (gm/dl)	31.95	1.61	31.13	1.57	32.52	1.38	1.39 (0.73-2.04)	0.00*
RDW (%)	17.15	2.93	19.24	1.73	15.67	2.71	-3.56[-4.54-(-2.58)]	0.00*
TLC (cells/mm^3)	13887.8	5577.38	14126.47	6290.7	13718.75	5074.91	-407.72 (-2909.54-2094.1)	0.74
Neutrophil (%)	59.02	15.76	57.88	16.51	59.83	15.32	1.95 (-5.11-9.01)	0.58
Lymphocytes (%)	39.39	15.6	40.47	16.77	38.62	14.85	-1.84 (-8.83-5.14)	0.6
Eosinophils (%)	1.14	1.3	1.12	1.57	1.15	1.09	0.02 (-0.61-0.65)	0.93
Monocytes (%)	0.44	0.73	0.47	0.82	0.42	0.67	-0.05 (-0.38-0.27)	0.74
Platelets (lakhs/mm^3)	3.37	1.08	3.49	1.15	3.28	1.03	-0.21 (-0.69-0.27)	0.38

Serum ferritin (ng/ml)	66.52	47.65	40.21	41.46	85.15	43.02	44.94 (26.03-63.84)	0.00*

Among 82 cases, 27.33% had normocytic normochromic RBC in peripheral blood smear. Remaining cases had microcytic hypochromic RBC. Anisocytosis was present in 46.56% of microcytic hypochromic cases [Figure 5].

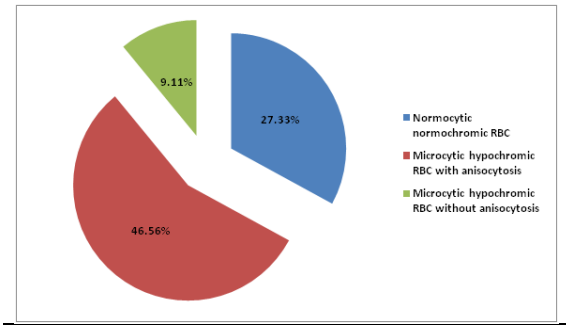

Figure 5: RBC morphology in peripheral blood smear.

Mean value of MCV, MCH and serum ferritin were markedly lower in macrocytic hypochromic as compared to normocytic normochromic RBCs. However there was minimal difference in mean value of MCHC between two groups [Figure 12].

Chi square test of association showed strong association between Hb level and IDA with odds ratio of 3(2.03-4.42), p value<0.01 among the patients with Hb level <11 gm/dl as compared to those with Hb ≥11 gm/dl. Similarly, there was strong association between MCV <76fl with IDA with odds ratio of 3.42(2.2-5.32) and p<0.01 as compared to MCV>76fl. Similar association was seen with other parameter like MCH, MCHC, RDW, serum ferritin and microcytic hypochromic RBC in PBS with IDA having p-value<0.01 [Figure 13].

Table 12: Mean value of MCV, MCH, MCHC and serum ferritin with respect RBC morphology in PBS.

Parameters	Microcytic hypochromic		Normocytic normochromic	
	Mean	S.D	Mean	S.D
MCV(fl)	67.73	6.87	82.54	2.15
MCH(pg)	21.36	2.74	27.75	0.98
MCHC(gm/dl)	31.58	1.69	32.7	1.12
Serum ferritin(ng/ml)	50.19	45.66	99.79	32.07

In multivariate analysis, total eight independent variables were entered, multiple regression analysis was done using enter method to predict dependent variable IDA. In multiple linear regressions, coefficient of determination (R2) showed 64% variability in dependent variable IDA was explained by this regression model. Regression model is statistically significant through F statistics with p-value of 0.00. Among the laboratory parameters MCV, MCH were statistically significant predictors of IDA with OR [-0.01(-0.03-0.01)], pvalue of 0.02 and OR [-0.07(-0.13—0.003)], p value of 0.04 respectively. If there is one unit change in MCV, the iron level in blood will decrease by 0.01 unit which is statistically significant. One unit change in MCH will decrease the iron level in blood by 0.07 unit which is statistically significant [Figure 14].

Table 13: Relationship between laboratory parameters and IDA among ALRTI.

Laboratory parameters category	All n(%)	Irondeficiency Anemia positive n(%)	Irondeficiency Anemia negative n(%)	OR(95%CI)	P value
Hemoglobin(mg/dl)					
≥11	18(22%)	0(0%)	18(22%)	1	0.00*
<11	64(78%)	34(41.4%)	30(36.6%)	3(2.03-4.42)	
MCV(fl)					
≥76	34(41.5%)	0(0%)	34(41.5%)	1	0.00*
<76	48(58.5%)	34(41.5%)	14(17.07%)	3.42(2.2-5.32)	
MCH(picogram)					
≥24	33(40.2%)	0(0%)	33(40.2%)	1	0.00*
<24	49(59.8%)	34(41.5%)	15(18.3%)	12.33(4.16-36.49)	
RDW (%)					
≤14.5	28(34.1%)	0(0%)	28(34.1%)	1	0.00*
>14.5	54(65.9%)	34(41.5%)	20(24.4%)	2.7(1.9-3.82)	
MCHC(gm/dl)					
≥30	73(89%)	26(31.7%)	47(54.9%)	1	0.002*
<30	9(11%)	8(9.8%)	1(1.2%)	14.46(1.71-122.09)	
Serum ferritin(ng/ml)					
≥30	48(58.5%)	0(0%)	48(58.5%)	1	0.002*
<30	9(11%)	8(9.8%)	1(1.2%)	14.46(1.71-122.09)	
Peripheral blood smear for RBC					
Normocytic normochromic RBC	27(32.9%)	0(0%)	27(32.9%)	1	0.00*

Microcytic hypochromic RBC	55(67.1%)	34(41.5%)	21(25.6%)	2.61(1.87-3.66)	

Table 14: Multivariate linear regression analysis.

Variables	Unstandarized Beta coefficient OR (95%CI)	P value
Hemoglobin(gm/dl)	-0.55(-0.33-0.22)	0.69
Total RBC count(million/mm^3)	0.06(-0.16-0.28)	0.58
Hematocrit (%)	-0.003(-0.09-0.08)	0.95
MCV(femolitre)	-0.01(-0.03-0.01)	0.02*
MCH(70ictogram)	-0.07(-0.13—0.003)	0.04*
MCHC(gm/dl)	-0.01(-0.1-0.06)	0.66
RDW (%)	0.006(-0.04-0.05)	0.79
Serum ferritin(ng/ml)	2.21(-0.002-0.002)	0.98

DISCUSSION

A total number of 82 cases of age 6 months to 5 years with ALRTI were enrolled in this study among which maximum children i.e. 72 out of 82 (87.8%) were between 6-24 months. Fifty cases (60.9%) were infants from 6 months to 1 year of age and 22 children (26.8%) belonged to age group 13-24 months, which is quite comparable to studies conducted by Malla T et al[1], Hussain SQ et al[17] and Rijal P et al[18]. This signifies that ALRTI is most common in age group of <1 year. Higher frequency of ALRTI in infancy can be explained by the fact that various anatomical and physiological risk factors in infants such as they are obligate nose breathers, tongue relatively large, airway narrow, increase metabolic demand and less elasticity of alveoli; associated with incomplete establishment of immunity.[19] This is the time when a child starts having low hb levels secondary to inadequate and inappropriate supplementary and complementary feeding practices. However, there was no significant difference between the two age groups (≥24 months and <24 months).

Male preponderance was found (59.8%) with male to female ratio 1.5:1. Similar results were found in different studies, 70.7% in Malla T et al[1], 57.3% in Hussain SQ et al[17], 63% in Ramakrishnan K et al[20] and 64.42% in Savitha MR et al[21]. The gender wise discrimination of the children continues even before birth and continues throughout the life, and utilization of health care services is another example of this continued discrimination as evident by less number of female in the above studies. However, no significant difference (p=0.75) occurred between two sex in the study.

According to modified Kuppuswamy's scale[16] for use in Nepal, 50(61%) patients belonged to middle class family, among them 13 patients was from upper middle class and 37 patients from lower middle class. Remaining 32(39%) belonged to lower socioeconomic status with 23 patients from upper lower class and 6 from lower class. No patients belonged to upper socioeconomic status. A study conducted in Nepal by Yadav S et al[22] had similar proportion of patient in terms of socioeconomic status i.e. 61.5% belongs to mid-upper class and 38.5% to lower class. In contrast, a study conducted by Savitha MR et al[21] to identify modifiable risk factors for ALRTI showed that majority of patients (>90%) belonged to lower and upper lower socioeconomic class. No statistical significance observed between patients with middle and lower socioeconomic status (p=0.73).

As Nepalgunj is situated in mid-western development region, approximately two-third patients belong to the districts of this region and the remaining from districts located in far western development region. Patients fulfilling all the six criteria for IDA as mentioned in operational definition was less (34 vs 48), in most demographic variables IDA negative cases outnumbered IDA positive cases. However, IDA positive cases exceeded IDA negative cases in patients with lower middle and lower socioeconomic status and patients from far western development region.

Symptoms and signs of patient had usual presentation of ALRTI with cough as the common symptoms present in all patients followed by fast breathing (96.3%), fever 86.8%, chest indrawing 62.2%, noisy breathing 19.5%, poor feeding 14.6% and the least of all was bluish discoloration of face/lips 6.1%. Also, mean duration of cough was highest followed by noisy breathing, fever, fast breathing, difficulty in breathing, poor feeding and least of all was bluish discoloration of face. Mean duration of fever, fast breathing, difficulty in breathing were higher in iron deficiency anemia positive cases while mean duration of cough and noisy breathing were higher in iron deficiency negative cases. There was no difference in mean duration of poor feeding and bluish discoloration among two groups. In study done by Malla T et al[1], cough was present in all cases with ALRTI followed by fever (96.42%), chest indrawing (85.71%), fast breathing (71.42%), shortness of breath (57.85%), poor feeding (57.14%) and noisy breathing (35.71%). In study done by Hussian SQ et al[17], all cases presented with cough followed by fever (94.5%), chest indrawing (83.6%) and fast breathing (67.3%).

Among vital signs, mean of temperature, pulse rate and respiratory rate were higher in IDA cases as compared to those without iron deficiency. This type of findings was not reflected in previous studies.

Among signs, tachypnea for age was present in all cases. Subcostal/intercostals retraction in 62.2%, nasal flaring in 7.3% and cyanosis was present in 6.1% of total cases. Pallor was noted in 63.4% of cases. Iron deficiency negative cases were higher for chest retraction and tachypnea as compared to IDA positive cases while pallor, cyanosis and nasal

flaring were higher in IDA positive cases. Auscultatory chest findings reveal only crepitation in 42.7%, only rhonchi in 17.1%, both crepitation and rhonchi in 28% and normal auscultatory findings in 12.2% of total patients.

Among 82 cases with ALRTI, 65 (79.3%) patients were diagnosed as pneumonia and remaining 17 (20.7%) cases as bronchiolitis on the basis of clinical features, clinical examination, laboratory findings such as TLC/DLC and radiological findings on chest X-ray. Out of 17 bronchiolitis cases, maximum number of case i.e. 15 (88.2%) belonged to 6-12 months age group. Similarly maximum number of pneumonia (53.5%) belonged to <1 year of age. Patients with pneumonia were further classified as pneumonia (35.4%), severe pneumonia (55.4%) and very severe pneumonia (9.2%), as per WHO criteria of assessing severity of pneumonia. Very severe pneumonia cases were higher in IDA positive group whereas pneumonia and severe pneumonia cases were higher in other group. Radiological evidence of pneumonia in chest X-ray was present in 58.5% of patients, hyper inflated lungs suggestive of bronchiolitis in 14.6% and normal chest X-ray in 26.8% of patients. A study done by Rijal P et al[18] showed similar results with pneumonia in 83.6% and bronchiolitis in 16.4%. In contrast, study done by Malla T et al[1] showed approximately equal number of bronchopneumonia and bronchiolitis (51.4 vs 48.6%) and radiological findings of pneumonia and hyperinflation was 50% and 29% respectively. The reason for increase number of bronchiolitis in study done by Malla T et al[1] may be due to inclusion of patients below 6 months of age as bronchiolitis has a peak incidence between 2-6 months of age.[23,24]

Among the TLC and neutrophil count, mean counts were higher in pneumonia patients whereas for lymphocyte, mean count was higher in bronchiolitis patients. Among the above parameter, TLC, neutrophil count and lymphocyte count between bronchiolitis and pneumonia were statistically significant with p-value<0.05. Bacterial pneumonia is often associated with an elevated WBC count, in the range of 15,000-40,000/mm^3, and a predominance of granulocytes.[25] Whereas, the WBC and differential counts are usually normal in bronchiolitis.[26]

Independent "*t*" test done for the laboratory parameter in relation with iron deficiency anemia among ALRTI showed mean of hb, total RBC count, hematocrit, MCV, MCH, MCHC, RDW, serum ferritin to be significantly different among the iron deficiency positive group and iron deficiency negative group with highly significant p-value < 0.01 whereas TLC, differential counts and platelets were statistically insignificant between iron deficiency positive and negative group.

In this study Hb<11gm/dl was considered as anemia. Out of 82 cases, 64 (78%)patients had hemoglobin level <11gm/dl and 18 (22%) with Hb≥11gm/dl. Out of 64 patients with Hb<11gm/dl, 55 patients (86%) had macrocytic hypochromic RBC in PBS and 9 with normocytic normochromic RBC. Anemia with normocytic normochromic RBC may be due to other factors such as worm infestations, occult gastrointestinal bleeding due to milk proteinallergy, etc. The mean value for MCV in microcytic hypochromic and normocytic normochromic anemia was 67.73±6.87 and 82.52±2.15 fl respectively. Similarly, MCH, MCHC and serum ferritin for the two groups were 21.36±2.74 and 27.75±0.98pg, 31.58±1.69 and 32.7±1.12 gm/dl, and 50.19±45.66 and 99.79±32.07ng/ml respectively. In previous study done by Malla T et al[1], considered Hb<10 gm/dl as anemic with 68.6% of patient with Hb<10 gm/dl and 31.4% with Hb>10 gm/dl. Out of total anemic patient 82.3% had macrocytic hypochromic RBC and remaining 17.7% with normocytic normochromic RBC. Mean MCV, MCH and MCHC was 64 fl, 17pg and 25 gm/dl respectively inmicrocytic hypochromic anemia and 80fl, 25pg and 32gm/dl in normocytic normochromic anemia. In other studies done by Hussain SQ et al[17] had 64.4% of anemic patient with 78.9% having microcytic hypochromic picture of RBC morphology, Ramakrishnan K et al[20] 74% hadanemia, and Savitha MR et al[21] 76.92% had anemia; However, study done by MouradS et al[27] had only 32% of cases with anemia.

In this study, chi square test of association showed that among ALRTI cases, chances of IDA was 3 times more among the respondent with Hb<11 gm/dl as compared to respondent with Hb>11 gm/dl [OR 3 (2.03-4.42) and p-value 0.00]. Similar results were observed with MCV <76 fl as compared to MCV ≥76fl with OR 3.42 (2.2-5.32 and p-value 0.00, MCH <24pg as compared to MCH ≥24pg with OR 12.33 (4.60-36.49 and p-value 0.00, and MCHC <30gm/dl as compared to MCHC ≥30gm/dl with OR 14.46 (1.71-122.09) and p-value 0.002. With RDW >14.5%, chances of IDA was 2.7 times more than those with RDW<14.5% [OR 2.7 (1.9-3.82) and p-value 0.00] in ALRTI cases. For serum ferritin with value <30ng/ml as compared to >30ng/ml had an OR 5.5 (2.1-14.36) and p-value 0.00. Finally, there was 2.61 times more chances of having IDA with macrocytic hypochromic RBC as compared to normocytic normochromic RBC in PBS [OR 2.61(1.87-3.66) and p-value 0.00]. No relevant literature and similar analysis was available to compare this result.

In multivariate linear regression analysis, among the laboratory parameters, MCV and MCH were statistically significant predictors of iron deficiency with OR [-0.01(-0.03-0.01)], p-value of 0.02 and OR [-0.07(-0.13—0.003)], p value of 0.04 respectively in ALRTI.

CONCLUSION

In this study, IDA had strong association with ALRTI infections. So, iron supplementation can be used as an indirect measure for reduction of incidence of ALRTI in children more than 6 months of age, especially in all developing countries.

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