

## A Clinical Study on the Incidence, Clinical Course and Prognosis of Community-Acquired Pneumonia in Children below 05 Years in Deficiency of Vitamin D, Serum Zinc, Ig G, Ig M and Serum Iron

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Conflict of interest: Nil

### Abstract:

**Background:** Community Acquired Pneumonia (CAP) accounts for mortality of less than five years children all over the World. Immunity among them is disrupted by malnutrition and deficiency of Vitamin D, Zinc and Iron which play vital role. This prospective study was aimed at understanding the relation between serum levels of these three elements in under five children suffering from Acquired Pneumonia (CAP).

**Aim of the Study:** To correlate the serum levels of Vitamin D, Zinc and Iron and the severity of Community acquired Pneumonias in the children aged below 5 years.

**Materials:** A clinical and laboratory based study was conducted KMCT, Kozhikode in the department of pediatrics with 57 children in the study group and 55 children in the control group aged below 05 years. Children diagnosed with CAP and severe CAP was included in the study group. British Thoracic Society (BTS) criteria were considered to classify the grading of CAP in this study.

**Mild to moderate:** Children with temperature less than 38.5 °C, respiratory rate less than 50 breaths/min, and mild breathlessness.

**Severe cases:** Children who had temperature less than 38.5 °C, respiratory rate more than 50 breaths/min, and severe degree of difficulty in breathing showing nasal flaring, cyanosis, and tachycardia. Biochemical investigations included serum calcium, phosphate, alkaline phosphatase, vitamin D3 levels, Serum zinc level, Albumin globulin ratio and Iron using conventional and high-performance liquid chromatography (HPLC). Immunological tests to estimate total IgG and Ig E levels were conducted.

**Results:** The CAP group of 57 children and the control group of 55 healthy children had 34: 24 and 35:20 male to female ratio. The mean ages were 03.45±0.85 and 03.80± 0.34 years in the CAP and control groups respectively. There was no statistical significant difference between the two groups in regards to their age, gender and type of feeding. (P values > 0.05) There was a statistical significance between the CAP children and control group children in terms of these levels of serum Vit.D and serum Zinc, (p value less than 0.05). Inadequate Vit. D, Zinc and TIBC values were noted in relation to the severity of the CAP.

**Conclusions:** Adequate dietary Zinc, vitamin D and Iron are protective in nature to the children below 05 years in preventing infection with community-acquired pneumonia. But the study showed no correlation between adequate serum iron levels and CAP. Watchful supplements of zinc, vitamin D, and iron helped to develop the immune system in children which prevents CAP.

**Keywords:** Vitamin D, Zinc, Iron, Community acquired Pneumonia.

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### Introduction

Vitamin D is important in maintaining the Phosphate and calcium ratio in the bone but also to exert its function on immunity. The cofactors like zinc are essential to get optimal vitamin D functionality. Being trace mineral zinc is available in abundant in the body and also as a part of more than 600 enzymes, numerous proteins, and over 2500 transcription factors. [1, 2] Zinc is also useful in cellular apoptosis, immune function, brain maturation and development, taste and smell

regulation, skin and mucosal integrity, and metabolic function. [3, 4] Zinc is also used as a ion signaling, to regulate gene expression, Protein, DNA synthesis and cell division. [5] Zinc is also necessary for Vitamin D regulation and its functioning. [6] When a child develops an acute infection of the parenchyma of the lungs in a previously status, and not resided preceding 15 days in a Hospital, it is defined as Community-acquired pneumonia (CAP). [7] Community

acquired pneumonia (CAP) still remains the major cause of mortality in less than 5 years children in India and developing countries. [8] 151.8 million new cases of CAP are reported all over the world as on 2020 reports. (9) Among them 08.95% children require hospital admission for intensive care. [10] India is among the top 05 countries contributing to the world's total number cases of CAP [11].

According to WHO guidelines, CAP can be classified as those children with rapid respiratory rate above a cut off rate; for infants of less than 02 months of age it is 60 or more per minute, for 2–11 months of age 50 or more breaths per minute and 12–59 months of age is 40 or more breaths per minute. [12] It also defined severe CAP as presence of certain vital signs like inability to drink, repeated vomiting, convulsions, marked weakness and lethargy, unconsciousness, stridor in an otherwise calm child with severe malnutrition. [13] To simplify the two categories of CAP are: "Pneumonia": A child with rapid respiratory rate with or without chest in-drawing. "Severe Pneumonia": In addition to the above any other danger signs described above. [14] Iron is essential mineral in the body concerned with immune integrity, oxygen carrying capacity and also acts as co-enzymatic reactions against pathogens. [15]

The deficiency of Iron results in CAP in many children. [16] Similarly Zinc is used in the body for maintaining the integrity of the immune system by helping in the maturation of immune cells. [17] Children develop zinc deficiency as they absorb zinc at low levels and many of them might have received insufficient amounts from their mothers. [18] The present study was aimed to assess the serum levels of Calcium, Zinc and Iron and verify their relation to the incidence and severity of CAP among the children of below 05 years of age and also identify the most related nutrient deficiency to infection development and progression.

#### **Materials:**

##### **Type of Study: Prospective Case Control Study**

**Institute of Study:** KMCT College, Kozhikode, Kerala.

**Period of Study:** March 2020 to February 2021.

A study was conducted KMCT, Kozhikode in the department of pediatrics wherein 57 children aged less than 05 years and above 02 months diagnosed with CAP were included.

An Institutional ethics committee approval was taken before the commencement of the study. An approved consent form and proforma was used to collect the data for analysis.

#### **Inclusion Criteria:**

Children aged less than 05 years and more than 02 months were included. Children diagnosed with CAP and severe CAP was included.

#### **Exclusion criteria:**

1. Children aged above 05 years and below 02 months were excluded.
2. Children with co-morbidities like, diabetes, renal diseases and immunosuppressive drugs were excluded.
3. Children with nosocomial infections causing pneumonia, cardiac, neurological, musculoskeletal, hepatic diseases were excluded.

55 children were considered as control group who were healthy and aged less than 05 years age. British Thoracic Society (BTS) criteria (19) were considered to classify the grading of CAP in this study.

**Mild to moderate:** Children with temperature less than 38.5 °C, respiratory rate less than 50 breaths/min, and mild breathlessness.

**Severe cases:** Children who had temperature less than 38.5 °C, respiratory rate more than 50 breaths/min, and severe degree of difficulty in breathing showing nasal flaring, cyanosis, and tachycardia. All the children were subjected to thorough history taking, history of breastfeeding. All the children were subjected to thorough clinical examination, radiological examination (X-Ray AP and Lateral views) and hematological investigations (complete blood counts, Hemoglobin). C-reactive protein was estimated. Biochemical investigations included serum calcium, phosphate, alkaline phosphatase, vitamin D3 levels, Serum zinc level, Albumin globulin ratio and Iron using conventional and high-performance liquid chromatography (HPLC). Serum iron assay analysis was done on a 5010- spectrophotometer. Transferrin saturation percentage was calculated as the value of serum iron divided by the total iron-binding capacity of the available transferrin. Serum ferritin levels were estimated in spite of the risk that its levels may be elevated under certain conditions such as infection and inflammation. Immunological tests to estimate total IgG and Ig E levels were conducted.

**Statistical analysis:** All the data was analyzed using standard statistical methods using Statistical Package for Social Science (IBM SPSS) version 15. Data was shown as percentage, mean, standard deviation. For quantitative data with parametric distribution, an independent t test and one-way analysis of variance (ANOVA) were employed. For non-parametric data, the Mann Whitney test was used. Categorical variables were compared using the Chi-square test.

**Results**

In the present study subjects were considered in two groups. In the CAP group 57 children were included and in the control group 55 healthy children were included. There were 34 male children and 23 female children in the CAP group. There were 35 male children and 20 female children in the control group. The mean age in the CAP group was 03.45±0.85 years and in the control group it was 03.80± 0.34 years.

The youngest child in the CAP group was 09 months old and the eldest was 4.9 years old. The youngest child in the control group was 12 months

old and the eldest was aged 4.8 years. 79% of the children in the CAP group were breast fed and 83% of the control group was breast fed. There was no statistical significant difference between the two groups in regards to their age, gender and type of feeding. (P values > 0.05), (Table 1). The mean weight and height of the children in relation to their age groups in months was tabulated in the Table 1 for both the groups of the study.

It was observed that there was significant statistical difference between the two groups in regards to mean height and weight of the CAP group which showed significantly lower values compared to the control group (Table 1).

**Table 1: Showing the Age, gender, mean height and weights of the two groups and their correlation (n-CAP- 57; Control-55).**

Observation	Mean weight		Mean height in Cms		Mean Age	
	CAP	Control	CAP	Control	CAP	Control
<b>Age</b>						
03 m to 10 m	04.10	06.24	51.23	55.36	03.45±0.85	03.80± 0.34
11 m to 20 m	08.21	11.27	61.55	65.21		
21 m to 30 m	11.54	14.52	72.30	86.44		
31 m to 40 m	18.61	21.32	90.81	96.76		
41 m to 50 m	22.31	24.56	98.61	102.38		
<b>Gender</b>	Number	Percentage	Number	Percentage	--	--
<b>Male</b>	34	59.64	35	61.40	03.45±0.85	03.80± 0.34
<b>Female</b>	23	40.35	20	35.08		

Table 2 showed the morbidity, mortality and final outcome of the children treated for CAP after admission in the study. There were 02 (03.50%) deaths in the study, re-admission in 11/57 (19.29%) children, prolonged hospitalization in 08/57 children (14.03%), post discharge lung sequelae in

05.57 (08.77%) of the children. Overall 50/57 children recovered initially after treatment in the study. There was statistical significant observation in regards to the number of re-admitted children, prolonged hospitalization and those recovered totally (p value less than 0.05), (Table 2).

**Table 2: Showing the severity of CAP and their outcome in the study subjects (n-57)**

Observation	Number	Percentage	P value
<b>Mortality</b>			
Number of deaths	<b>02</b>	<b>03.50</b>	0.062
<b>Morbidity</b>			
Re-admitted	<b>11</b>	<b>19.29</b>	<b>0.038</b>
Prolonged Hospitalization	<b>08</b>	<b>14.03</b>	<b>0.021</b>
<b>Final Outcome</b>			
Recovered totally	<b>50</b>	<b>87.71</b>	<b>0.001</b>
Post discharge Sequelae	<b>05</b>	<b>08.77</b>	0.151

Serum iron level, mean value of TIBC (Total Iron Binding capacity) and adequacy of TIBC were observed to be having a significant difference between the CAP group and the control group (p value less than 0.05). However, the serum Transferrin levels saturations were similar in both

the groups (p value more than 0.05), (Table 3). Similarly the serum Ig G and Ig M levels in the children in the CAP group were comparatively lower than the values in the control group; there was statistical significance between the two groups (p value was less than 0.05), (Table 3).

**Table 3: Showing the Iron biding capacity and transferrin levels in the subjects both groups (n: CAP-57, control-55)**

Observation	CAP	Control	P value
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<b>Serum Iron Mean value</b>	125.42±5.68	134.51±6.31	<b>0.001</b>
<b>TIBC Mean value</b>	586.12±14.21	519.81±10.31	<b>0.001</b>
<b>TIBC Adequacy</b>			<b>0.001</b>
Adequate	06 (%)	47 (%)	
Inadequate	51 (%)	03 (%)	
<b>Transferrin Saturation</b>	0.27±0.10	0.26±0.07	0.211
<b>Mean Ig G levels</b>	536.79±102.38	827.59±124.79	<b>0.014</b>
<b>Mean Ig E levels</b>	102.65±29.55	119.38±28.32	<b>0.301</b>

Both the serum Vitamin D and serum zinc levels were inadequate in the CAP group when compared to the control group in this study. There was a statistical significance between the CAP children and control group children in terms of these levels of serum Vit.D and serum Zinc, (p value less than 0.05), (Table 4)

**Table 4: Showing the serum Vit. D and serum Zinc values in both the groups (n-CAP-576, Control-55).**

Observation- Mean values	CAP group	Control group	P value
<b>Vit. D (n mol/L)</b>	35.74±4.61	85.34±7.66	0.001
<b>Adequacy of Vit. D</b>			
Adequate	08 (14.03%)	52 (94.54%)	0.001
Inadequate	49 (85.96%)	03 (05.45%)	
<b>Serum Zinc (µg/dL)</b>	117.85±9.34	148.91±5.33	0.001
<b>Adequacy of serum Zinc</b>			
Adequate	06 (10.52%)	50 (90.90%)	0.001
Inadequate	51 (89.47%)	05 (09.09%)	

Within the CAP group bio-chemical and immunological tests values were compared depending upon the severity of the CAP disease whether it was mild, moderate or severe. It was observed that Vit. D levels, Mean Ig G levels and mean Ig M levels were associated with the severity of the disease. (p values less than 0.05). All the

other values like, Hemoglobin, Total serum Iron, Transferrin saturation, Serum calcium, serum Phosphate, serum Alkaline phosphatase, serum Zinc and mean values of TIBC were not related to the severity of the CAP disease in the study group (Table 5). Children with severe degree CAP had Vit. D deficiency in this study.

**Table 5: Showing the comparative values of Hemoglobin, Vit. D, Zinc, Ig G, IG M, Calcium, A/G ratio, Phosphate and Alkaline Phosphatase in all the severity degrees of CAP (n- 57)**

Observation	CAP group			P value
	Mild	Moderate	Severe	
<b>Mean Hemoglobin</b>	10.5Gm/dL	09.81 Gm/dL	08.54 Gm/dL	0.081
<b>Mean Total serum Iron</b>	127.80±6.10	120.58±4.85	110.90±5.50	0.611
<b>Mean Transferrin saturation</b>	23.30±1.25	22.81±4.10	20.54±3.41	0.154
<b>Mean value of TIBC</b>	576.22±13.57	570.81±5.21	566.21±6.14	0.288
<b>Mean Serum Vit. D</b>	34.11±5.10	23.50±3.44	20.54±2.10	<b>0.025</b>
<b>Mean Serum calcium</b>	08.29±1.20	08.86±1.44	09.88±1.54	0.423
<b>Mean Serum Phosphate</b>	04.58±0.85	04.11±1.01	03.85±1.33	0.235
<b>Mean Serum Zinc</b>	137.27±11.	122.38±09.65	107.64±08.44	0.147
<b>Mean Serum Alkaline phosphatase</b>	317.12±110.2	299.87±118.7	224.55±96.57	0.511
<b>Mean Ig G</b>	538.25±27.84	497.88±29.67	421.86±35.41	<b>0.042</b>
<b>Mean Ig M</b>	94.55±3.66	79.35±5.87	69.36±7.12	<b>0.024</b>
<b>Mean A/G ratio</b>	1.12±0.04	1.10±0.01	1.11±0.00	0.557

Inadequacy of Vit. D, Zinc and TIBC was observed and noted in the tables 3, 4 and 5, in relation to the severity of the CAP, it showed a significant relation when compared with other degrees of CAP in this study (Table 6). The combined inadequacy of vitamin D, Zinc and TIBC was significantly low in the patient group suggesting their strong association in pneumonia development (p values less than 0.05).

**Table 6: Showing the significance of the serum values of Vit. D, TIBC and Zinc in relation to the severity of the CAP in the subjects (n-57).**

Observation	Mild	Moderate	Severe	P value
<b>Vit. D</b>	34.11±5.10	23.50±3.44	20.54±2.10	<b>0.021</b>

<b>TIBC</b>	576.22±13.57	570.81±5.21	566.21±6.14	<b>0.047</b>
<b>Serum Zinc</b>	137.27±11.	122.38±09.65	107.64±08.44	<b>0.050</b>

### Discussion

A great degree of Childhood morbidity and mortality are caused by community acquired Pneumonias and requiring 08.95% children a Hospital admission for intensive care. Among them 0.2% are lost in spite of timely treatment (9) There many risk factors and community related problems in their management which change the course of CAP. [10] In the present study the risk factors were evaluated in the children aged below 05 years with the clinical diagnosis of CAP. The risk factors studied were serum iron, vitamin D, Ig G, Ig M and zinc values assessed by laboratory investigations. The effect of deficiency of these factors on the severity and course of the disease were analyzed. The role of Iron and its impact was assessed by estimating the Iron profile (Serum Iron, Serum Transferrin and Total Iron Binding capacity, and the adequacy of these values in the subjects) in the CAP group. It was observed that, there was a possible risk of children with low hemoglobin acquiring CAP and succumbing due to the disease. The mean Hemoglobin value was 08.54 Gm/dL in children with the severe form of CAP (Table 4).

This finding might show that there was a strong association between iron deficiency anemia and the CAP. In a similar study by El-Sakka et al. [20] they found that low hemoglobin levels in children aged below 05 years stand every chance to develop acute lower respiratory infections; it was shown as 62.5% of pneumonia patients of their study. Another study by Hussain et al. [21] showed among their hospitalized children 64.5% had anemia when compared to 28.2% of their healthy children. The former were more prone to CAP by 4.6 times. In the present study there was no statistical significant relation between anemia and CAP even though the children with low hemoglobin were observed in the severe type of CAP (Table 5). But studies by Malla [22], Coles [23] and Shallans' [24] showed a close relation between low hemoglobin levels and CAP severity. In the present study the TIBC was more in the CAP when compared to the control group (Table 3). But the results could not be taken in the face value as the role of infection and other physiological factors were also at play on this CAP group.

It was observed that Vit. D levels, Mean Ig G levels and mean Ig M levels were associated with the severity of the disease. (p values less than 0.05), (Table 5). But in this study inadequacy of Vit. D, Zinc and TIBC was also observed and noted in the tables 3, 4 and 5, in relation to the severity of the CAP, it showed a significant relation when compared with other degrees of CAP in this study (Table 6). Kulkarni and Chougule [25] and

Jovanovich et al. [26] commented that a high association existed between vitamin D deficiency and CAP children aged below 05 years. A group of authors; Haider N, Nagi AG, Khan et al [27] noted that their children in the study 74% showed clinical features of Rickets in addition to CAP. They showed low or normal calcium, low phosphorous and high serum alkaline phosphatase. Some authors showed that a subclinical vitamin D deficiency also can predispose to CAP in children below 05 years. [28] In this study low serum levels of Zinc were observed in severe type of CAP (Table 6) and this study was comparable to another study by Yuan X, Qian SY et al [29] wherein the zinc level in peripheral blood was reduced in 76% of critically ill infants with CAP.

It was shown that there was a close relation of susceptibility to CAP in children aged between 0 to 24 months, and their serum Zinc values by Arica et al. [30] An unique study exclusively on correlation between serum Zinc levels and acquiring Pneumonia in children the incidence of y Zhou W, Zuo X, Li J et al proved that the incidence of pneumonia, days of hospitalization, rapid improvement after acquiring Pneumonia were dependent upon the Zinc levels.

### Conclusions

Adequate dietary Zinc, vitamin D and Iron are protective in nature to the children below 05 years in preventing infection with community-acquired pneumonia. But the study showed no correlation between adequate serum iron levels and CAP. Watchful supplements of zinc, vitamin D, and iron helped to develop the immune system in children which prevents CAP.

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