

Association between Serum Concentration of 25-Hydroxyvitamin D and Community-Acquired Pneumonia**Chandan Gupta¹, Sunita Khandelwal², Ahmed Zuber³, Amit Kumar Saini⁴, Hardik Kabra⁵**¹Resident 3rd Year, Department of Paediatrics, Government Medical College Kota, Rajasthan²Associate Professor, Department of Paediatrics, Government Medical College Kota, Rajasthan³Resident 3rd Year, Department of Paediatrics, Government Medical College Kota, Rajasthan⁴Resident 2nd Year Department of Paediatrics, Government Medical College Kota, Rajasthan⁵Resident 2nd Year Department of Paediatrics, Government Medical College Kota, Rajasthan

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Conflict of interest: Nil

Abstract:

Background: Pneumonia is an acute respiratory tract infection (RTI) which is classified according to age and specific causative organism. Pneumonia can be caused by bacteria, viruses or fungi. Vitamin A and zinc supplementation is used for the prevention of respiratory infections in developed countries. Recent research suggested the role of vitamin D in the prevention of pneumonia and increasing the individual's immunity. Vitamin D also has antimicrobial properties and according to recent studies, its deficiency may be correlated to an increased frequency of respiratory infections. Vitamin D deficiency can positively affect a wide variety of microbial infections such as Gram-positive and Gram-negative bacteria, fungi, mycobacteria, and viruses.¹² Given the importance of pneumonia and because vitamin D deficiency is one of the possible factors involved in susceptibility to pneumonia, further studies on the possible role of vitamin D deficiency in the prevalence or severity of the disease can be useful.

Objectives: (1) To study the correlation of serum calcium and vitamin D3 level in community acquired pneumonia in children upto 18-year age admitted in JK lone hospital Kota. (2) To know the association of serum calcium and vitamin D3 in community acquired pneumonia in children upto 18-year age and to compare the association in number of episodes of disease.

Methods: Children admitted in JK lone hospital Kota who full field the criteria of community acquired pneumonia. exclusion criteria were excluded. The following parameters, recorded on admission, were evaluated: date of presentation (month, year), age, sex, co-morbidity, duration of symptoms, clinical symptoms (body temperature, respiratory rate, heart rate, and arterial systolic and diastolic blood pressure), pneumonia-associated confusion, and relevant investigation sent on day of admission (CBC, RFT, LFT, serum calcium, vitamin d3) and report collected. Then reports were analyzed and the serum levels of 25-hydroxyvitamin D were determined by electrochemiluminescence binding assay in Roche Cobas 601 immunoassay analyzer and mean serum levels of 25-hydroxyvitamin D in each risk class were calculated. Then find Correlation between serum calcium and vitamin D3 level in pneumonia patients.

Results: In our study it was stated that majority of pediatric patients who had pneumonia belonged to 0–1-year age group i.e. 54%, followed by 21% in 1–3-year age group, 11% in 3–5-year age group, 9% in 5–10-year age group and 5% in >10-year age group. Percentage distribution showed that insufficiency (20-30 ng/ml) was maximum seen in 0–1-year age group, followed by 1–3-year age group. Vit D deficiency was maximum seen in >10-year age group, followed by 3-5 year and 0-1 year.

Conclusions: The study shows a significant correlation between low Hb levels and low Ca levels and with increased episodes of pneumonia. Severity of pneumonia is inversely related to Vitamin D levels and Ca, Hemoglobin levels.

Keywords: Pneumonia, Vit D Level, Episodes.

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Introduction

The World Health Organization (WHO) defines pneumonia in children as presence of cough or difficulty in breathing associated with fast

breathing or chest in drawing in children of 2-59 months of age. Pneumonia is the single largest infectious cause of death in children worldwide.

Pneumonia is an acute respiratory tract infection (RTI) which is classified according to age and specific causative organism. Based on source, pneumonia is classified as community acquired pneumonia (CAP) or nosocomial pneumonia and based on pathology it is classified as bronchopneumonia, lobar pneumonia or interstitial pneumonia. Pneumonia can be caused by bacteria, viruses or fungi. Common bacterial agents causing pneumonia in the first 2 months of life are pneumococci and staphylococci (gram positive) or Klebsiella and Escherichia coli (gram negative). In age group 3 months to 3 years, the chief organisms are pneumococci, Haemophilus influenzae and staphylococci. After 3 years, common pathogens are pneumococci and staphylococci. Chlamydia and mycoplasma may cause CAP in adolescents. Common viral aetiology accounting for pneumonia among children includes respiratory syncytial virus (RSV), influenza, parainfluenza and adenovirus. [1,2]

Vitamin A and zinc supplementation is used for the prevention of respiratory infections in developed countries. Moreover, vitamin C is used despite the little knowledge about its efficacy on respiratory infections. [3,4,5]

Recent research suggested the role of vitamin D in the prevention of pneumonia and increasing the individual's immunity. [6,7] Vitamin D is a fat-soluble vitamin, essential for calcium and phosphate homeostasis. Vitamin D obtained from sun exposure, food, and dietary supplements are biologically inert and undergo two hydroxylations for activation. The first hydroxylation occurs in the liver and converts vitamin D to 25-hydroxyvitamin D (25(OH)D), also known as calcidiol, calcifediol, or 25-hydroxyvitamin D₃. The second hydroxylation takes place mainly in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D (1,25(OH)₂D), additionally called calcitriol. [8] Vitamin D also has antimicrobial properties and according to recent studies, its deficiency may be correlated to an increased frequency of respiratory infections. [9] The serum concentration of 25-hydroxyvitamin D (25(OH)D) is the best vitamin D status index reflecting vitamin D produced in the skin and offered from food and dietary supplements. Vitamin D is important for the normal activity of skeletal and nonskeletal tissues, immune cells and immunity, bone calcification, and brain processes. [10]

Further, vitamin D metabolites play an important role in the body's immunity by induction of phagocyte migration, modulation of the Th1–Th2-cell balance, and the differentiation of T regulatory cells. Some studies showed that vitamin D may be helpful in the treatment of tuberculosis, psoriasis, and multiple sclerosis, as well as for prevention of

cancers. Some studies showed that vitamin D may be helpful in the treatment of tuberculosis, psoriasis, and multiple sclerosis, as well as for prevention of cancers. [11] It is shown that vitamin D deficiency (<20 ng/mL) is a prevalent condition and may be a key contributor to both acute and chronic infectious diseases including sepsis, pneumonia, urinary tract infections, and surgical site infections. Most cells, such as B and T lymphocytes, monocytes, and dendritic cells have specific vitamin D receptors (VDRs). Vitamin D demonstrates its immunomodulatory effects on these cell lines through its effects on the VDR. Deficiency is associated with reduced innate immunity and an increased risk for infections. Vitamin D deficiency can positively affect a wide variety of microbial infections such as Gram-positive and Gram-negative bacteria, fungi, mycobacteria, and viruses. [12] Given the importance of pneumonia and because vitamin D deficiency is one of the possible factors involved in susceptibility to pneumonia, further studies on the possible role of vitamin D deficiency in the prevalence or severity of the disease can be useful. High prevalence of vitamin D deficiency is reported among Iranian population in several studies. Considering the high incidence of pneumonia in Iran, we aimed to investigate the association between serum concentration of 25-hydroxyvitamin D (25[OH]D).

Aims and Objectives

Aim: To study the correlation of serum calcium and vitamin D₃ level in community acquired pneumonia in children upto 18-year age admitted in JK lone hospital Kota.

Primary Objective: To know the association of serum calcium and vitamin D₃ in community acquired pneumonia in children upto 18-year age and to compare the association in number of episodes of disease.

Methodology

Inclusion Criteria: Children upto 18 years of age admitted in JK lone hospital Kota for pneumonia.

Exclusion Criteria:

- Severely immunocompromised patients,
- patients with tuberculosis
- patients with malabsorption disorder
- patients with a history of malignancy
- chronic renal or liver disease, patients with congestive health failure or cerebrovascular disease,
- Children admitted for pneumonia with seizure disorder.
- Children on any drug intake history like furosemide, NSAIDs and antiepileptics etc.,

Material and Methods

Children admitted in JK lone hospital Kota who full fields the criteria of community acquired pneumonia. Exclusion criteria were excluded. The following parameters, recorded on admission, were evaluated: date of presentation (month, year), age, sex, co-morbidity, duration of symptoms, clinical symptoms (body temperature, respiratory rate, heart rate, and arterial systolic and diastolic blood pressure), pneumonia-associated confusion, and relevant investigation sent on day of admission (CBC, RFT, LFT, serum calcium, vitamin d3) and report collected.

Then reports were analysed and the serum levels of 25-hydroxyvitamin D were determined by electrochemiluminescence binding assay in Roche Cobas 601 immunoassay analyser and mean serum levels of 25-hydroxyvitamin D in each risk class were calculated.

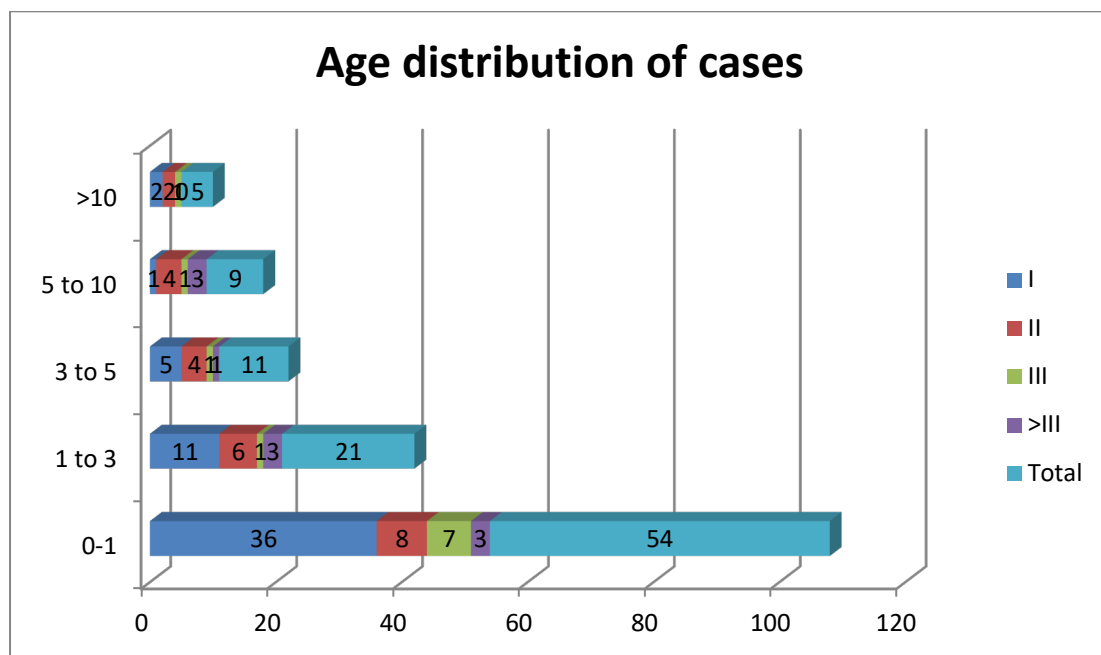
Vitamin D severe deficiency was defined as 25(OH)D levels <10 ng/ml, moderate deficiency as 25(OH)D levels between 10-20 ng/ml, and insufficiency as 25(OH)D levels between 20-29 ng/m. Then find Correlation between serum calcium and vitamin D3 level in pneumonia patients.

Results

Table 1: Age distribution of cases

Episode	0-1	1-3	3-5	5-10	>10	P value
I	36	11	05	01	02	0.06
II	08	06	04	04	02	0.46
III	07	01	01	01	01	0.80
>III	03	03	01	03	00	0.17
Total	54	21	11	09	05	100

Chi square= 16.39

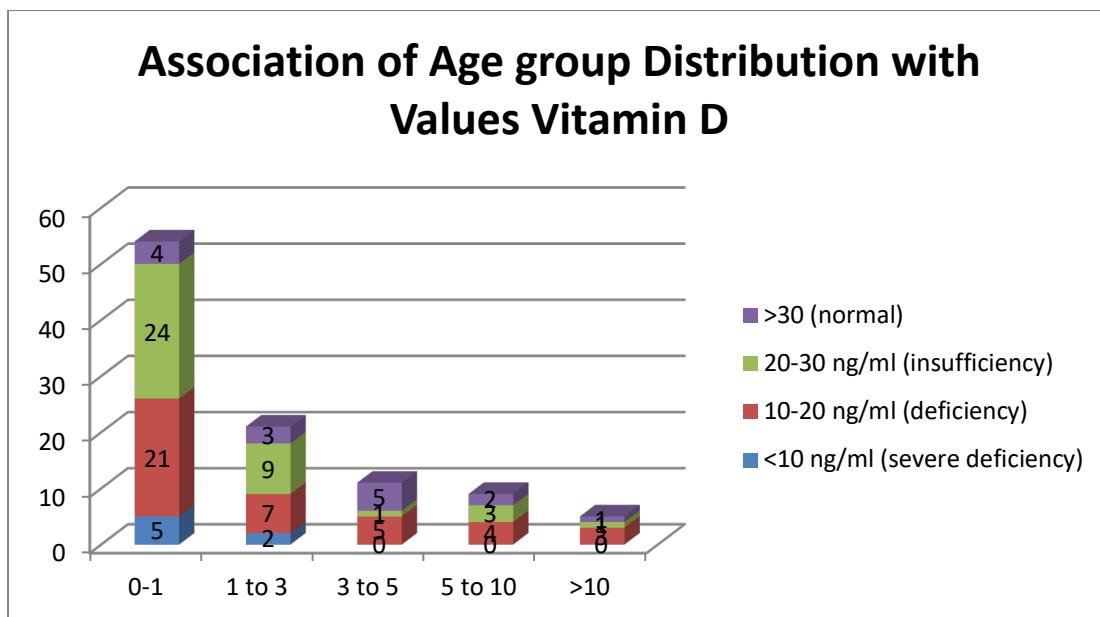


Graph 1: Age distribution of cases

Above table stated that majority of pediatric patients who had pneumonia belonged to 0–1-year age group i.e. 54%, followed by 21% in 1–3-year age group, 11% in 3–5-year age group, 9% in 5–10-year age group and 5% in >10-year age group.

Table 2: Association of Age group Distribution with Values Vitamin D

AGE (in years)	<10 ng/ml (severe deficiency)	10-20 ng/ml (deficiency)	20-30 ng/ml (insufficiency)	>30 (normal)	Total	P value
0-1	5(9.8%)	21(39.2%)	24(45%)	4(5.9%)	54	0.51
1-3	2(10%)	7(35%)	9(40%)	3(15%)	21	0.55
3-5	0	5(50%)	1(16.7%)	5(33.3%)	11	0.8
5-10	0	4(40%)	3(40%)	2(20%)	9	0.74
>10	0	3(60%)	1(20%)	1(20%)	5	0.83
TOTAL	7	40	38	15	85	



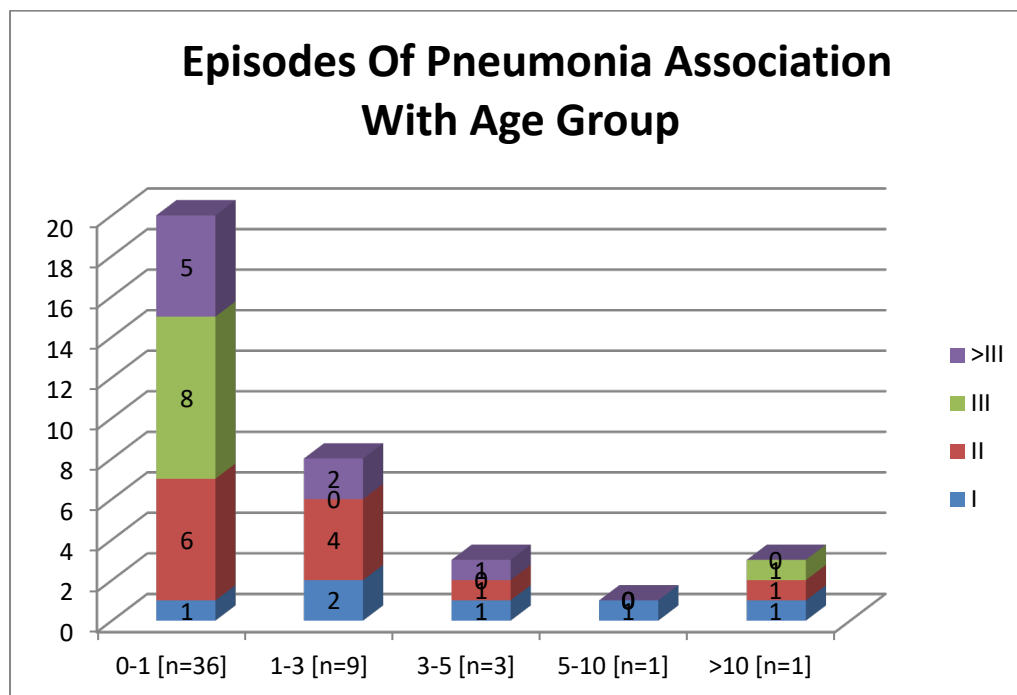
Graph 2: Association of Age group Distribution with Values Vitamin D

Above table and chart stated that there is no significant effect of age group on Vitamin D values. But percentage distribution showed that insufficiency (20-30 ng/ml) was maximum seen in 0–1-year age group, followed by 1–3-year age group. Vit D deficiency was maximum seen in >10-year age group, followed by 3-5 year and 0-1 year.

Table 3: Episodes of Pneumonia Association with Age Group

Episode	0-1 [n=36]	1-3 [n=9]	3-5 [n=3]	5-10 [n=1]	>10 [n=1]	P value
I	01	02	01	01	01	0.29
II	06	04	01	00	01	0.02
III	08	00	00	00	01	0.02
>III	05	02	01	00	00	0.00

Chi square= 5.05



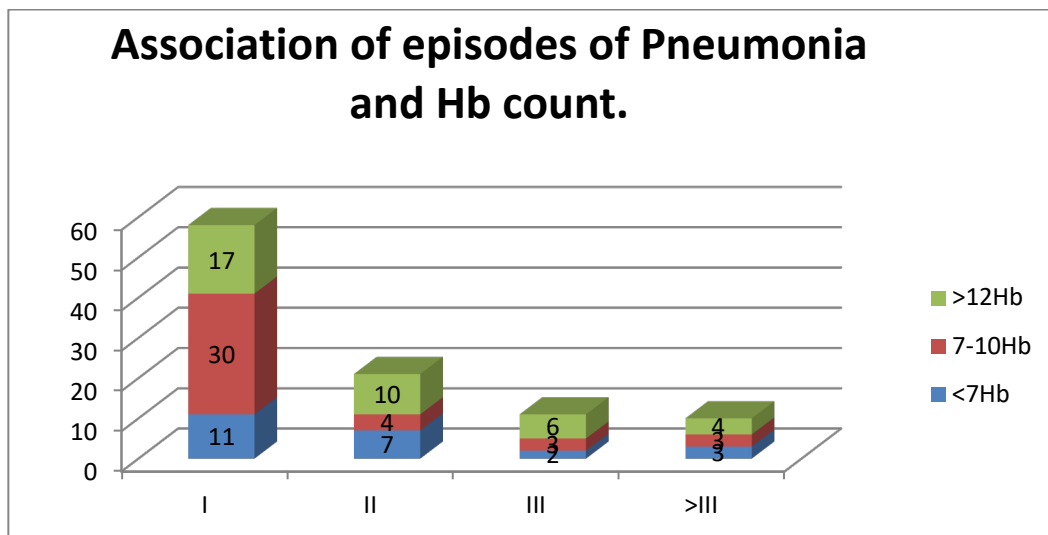
Graph 3: Episodes Of Pneumonia Association with Age Group

Above table and graph showed that episodes of pneumonia had association with age group distribution. Maximum episodes of pneumonia were seen in 0–1-year age group, followed by 1–3-year age group. In 0–1-year, age group 3 episodes were seen in 8 neonates, 2 episodes were seen in 6 neonates, >3episodes were seen in 5 neonates. P value showed that >1 episodes had significant relation age group distribution.

Table 4: Association of Episodes of Pneumonia and Hb Count

Episode	<7Hb	7-10Hb	>12Hb	P value
I	11	30	17	0.035
II	07	04	10	0.004
III	02	03	06	0.001
>III	03	03	04	0.07

Chi square= 18.71



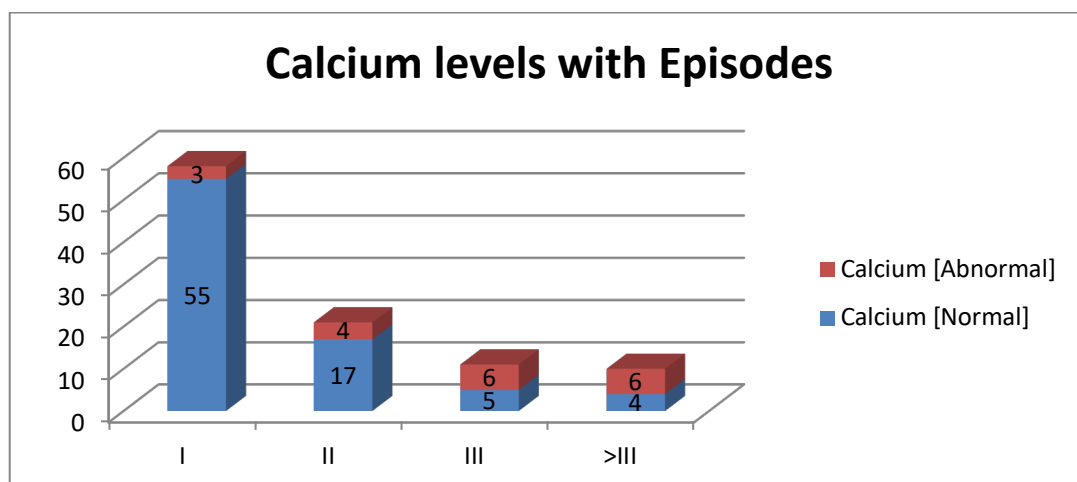
Graph 4: Association of episodes of Pneumonia and Hb count.

There was significant association of episodes of pneumonia and Hb count.

Table 5: Calcium levels with Episodes

Episode	Calcium [Normal]	Calcium [Abnormal]	P value
I	55	03	0.0001
II	17	04	0.002
III	05	06	0.04
>III	04	06	0.02

Chi square= 4.48



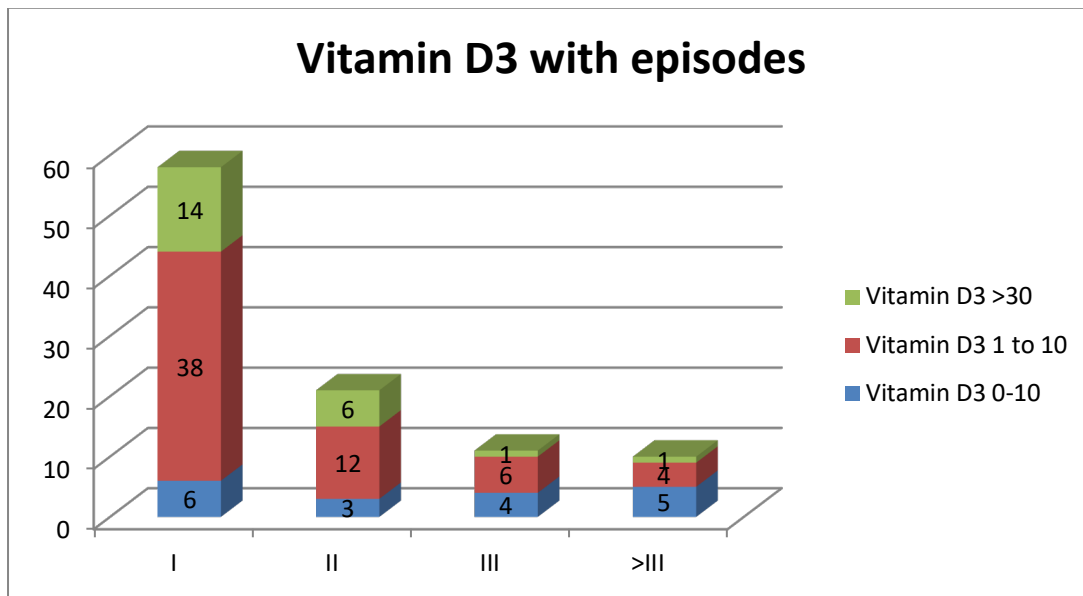
Graph 5: Calcium levels with Episodes

There was significant association of calcium level with episodes of pneumonia. No of patients in which episodes of pneumonia was more than one were more than those pts who had normal Ca level.

Table 6: Vitamin D3 with episodes

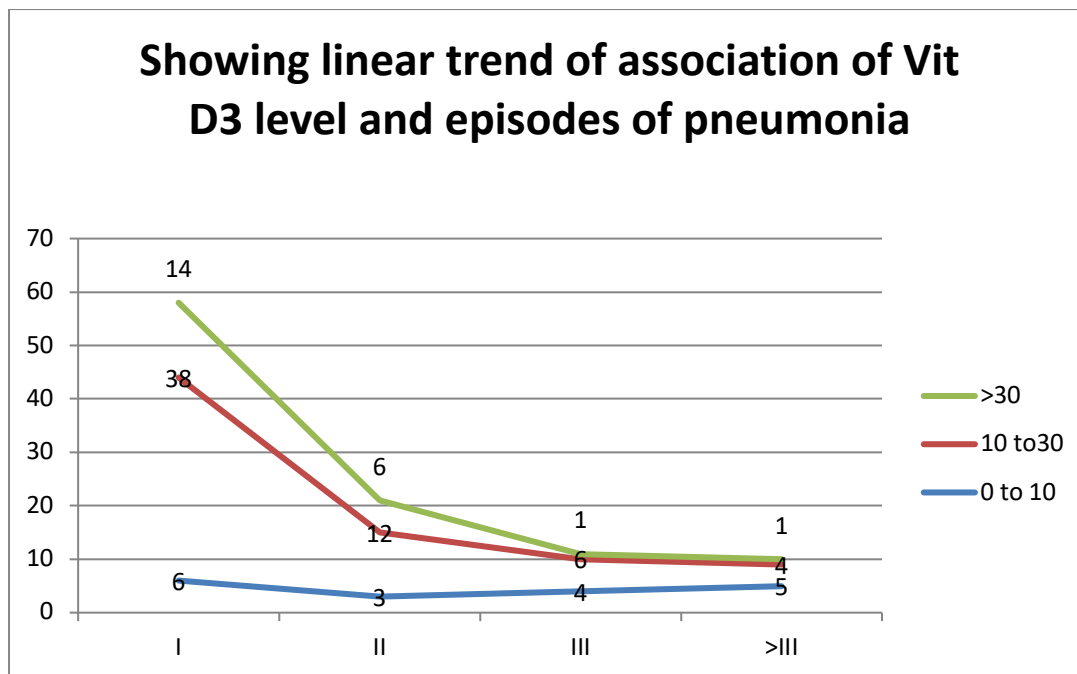
Episode	Vitamin D ₃ 0-10	Vitamin D ₃ 10-30	Vitamin D ₃ >30	P value
I	06	38	14	0.04
II	03	12	06	0.01
III	04	06	01	0.11
>III	05	04	01	0.67

Chi square= 5.30.



Graph 6: Vitamin D3 with episodes

Above table and graph explain that no. of patients who had severe Vit D3 deficiency had more episodes of pneumonia.

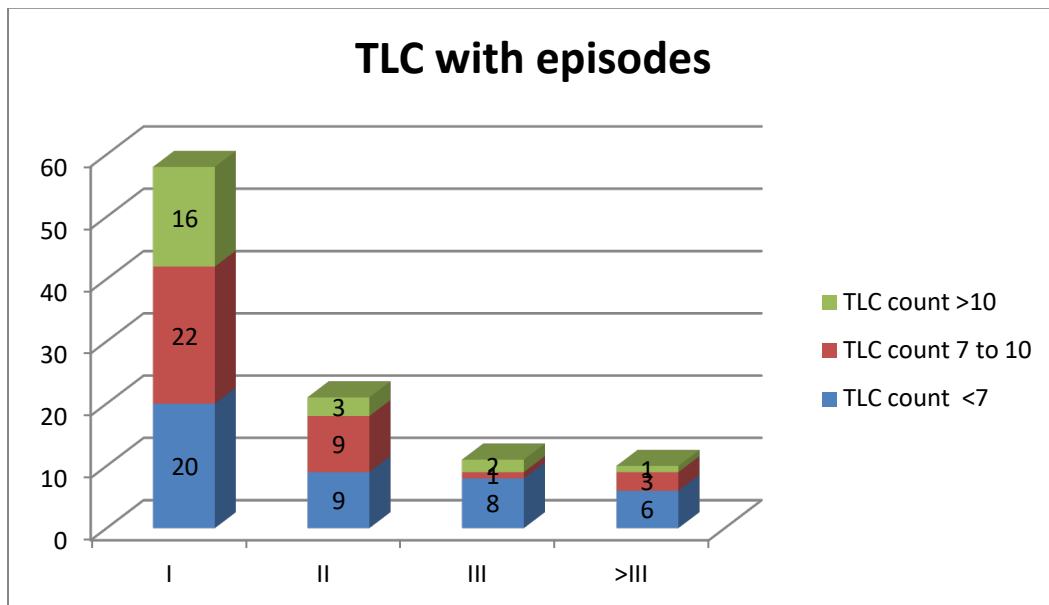


Graph 7: Showing linear trend of association of Vit D3 level and episodes of pneumonia

Table 7: TLC with episodes

Episode	TLC count <7	TLC count 7-10	TLC count >10	P value
I	20	22	16	0.24
II	09	09	03	0.52
III	08	01	02	0.49
>III	06	03	01	0.18

Chi square= 3.44



Graph 9: TLC with episodes

There was no significant association of TLC Count with episodes of pneumonia. Yet no of patients with >I episodes of pneumonia with TLC <7 were comparatively more than those patients who had normal level of TLC.

Table 8: Oxygen requirement in relation to age in community acquired pneumonia

AGE (Years)	0-1	1-3	3-5	5-10	>10	P value
Oxygen Given	19	4	1	2	0	0.0001
Without Oxygen	35	17	8	5	3	0.003
Total	54	21	9	7	3	

Chi square= 3.47

Discussion:

Above study was conducted to study the association of serum calcium and vitamin D3 in community acquired pneumonia in children upto 18-year age admitted in Jk Lone Hospital Kota.

In our study it was stated that majority of pediatric patients who had pneumonia belonged to 0-1-year age group i.e. 54%, followed by 21% in 1-3-year age group, 11% in 3-5-year age group, 9% in 5-10-year age group and 5% in >10-year age group. There are an estimated 120 million cases of pneumonia annually worldwide, resulting in as many as 1.3 million deaths.

Our findings are similar to findings of Garenne et al who stated that younger children under the age of 2 in the developing world account for nearly 80% of paediatric deaths secondary to pneumonia. In our study there was no significant effect of age group on Vitamin D values. But percentage distribution showed that insufficiency (20-30 ng/ml) was

maximum seen in 0-1-year age group, followed by 1-3-year age group. Vit D deficiency was maximum seen in >10-year age group, followed by 3-5 year and 0-1 year. Similarly, studies on children with asthma reported no association between vitamin D and age. [15,16,17] Albar et al. reported a trend for higher vitamin D level with younger age, but this did not reach statistical significance. [18] However, our findings are in line with those of Brehm et al. who reported that lower age and BMI were prevalent in the highest quartile of vitamin D level. [19]

In our study there is no significant relation of Vit D deficiency and episodes of pneumonia, but no. of patients who had severe Vit D3 deficiency had more episodes of pneumonia. There is a growing health concern regarding low vitamin D status in children, particularly those with persistent pulmonary illnesses, including asthma. [20,21] This is because a low level of serum vitamin D was found to have an impact on asthma control and its

severity. [22,23,24] According to Benner, a vitamin D level of 50 nmol/L (20 ng/ml) was adequate for improvement in asthma outcome. [25]

In a hospital-based case control study by Wayse et al on 150 Indian children under 5 years of age, one of factors associated with significantly higher OR for having severe acute lower respiratory infection was serum 25(OH)D less than 10 ng/mL (OR =11).[26] Aregbesola et al investigated the effect of 25(OH)D on the risk of incident hospitalized pneumonia in an aging general population in eastern Finland. They found that the subjects with the lowest level of serum 25(OH)D had a significant 2.6-fold (95% CI: 1.4, 5.0) higher risk of developing pneumonia compared to the subjects with the highest levels.[27] They concluded that there was an inverse effect of serum 25(OH)D concentration on the risk of incident pneumonia in the aging population.

Quraishi et al reported the result of the third National Health and Nutrition Examination Survey in a large nationally representative cohort of non-institutionalized adults in the United States. They showed that after adjusting for demographic factors, clinical data, and season, 25(OH)D levels less than 30 ng/mL were associated with 56% higher risk for CAP. [28]

Holter et al investigated the vitamin D status and long-term mortality in CAP. They showed that high prevalence of vitamin D deficiency and inadequacy among hospitalized adults with CAP and patients with vitamin D deficiency at hospital admission resulted in a 91% increase in risk of death during long-term follow-up after discharge, but no significant difference in survival was observed in patients with vitamin D inadequacy, compared to patients with vitamin D sufficiency.[29]

There was significant association of calcium level with episodes of pneumonia in our study. No of patients in which episodes of pneumonia was more than one were more than those pts who had normal Ca level. The study by Johnson AW [30] showed similar results that children with pneumonia had lower levels of plasma calcium and phosphate when compared with the controls. Haider et al. [31] showed that hypophosphatemia with low plasma calcium levels was common in children with pneumonia.

In contrast, a study by Oduwole et al. [32] showed that children with pneumonia had higher plasma calcium and phosphate levels than ill patients, with other diagnoses other than pneumonia, with whom they were compared. Reduced dietary intake in children with pneumonia could reduce calcium or phosphate levels, and this may occur even when serum vitamin D levels are normal.

The depletion of plasma calcium and phosphate in pneumonia may, therefore, be due to impairment in any of the multi-systemic homeostatic mechanisms regulating the levels of the elements in the blood. Ill children, including those with pneumonia, may have reduced blood levels of calcium and phosphate regardless of their vitamin D levels. Further our study also showed significant association of Hb level and pneumonia episodes, but there is no association was seen with TLC values. Anaemia is the commonest ailment affecting human's health, socio-economic development and overall betterment of the mankind.

Most common cause for anaemia is nutritional deprivation, particularly iron deficiency. According to world health organization more than half of children in the South-East Asia and African Regions (53.8% or more) are classified as having anaemia [33]. 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 acute lower respiratory tract Infection (ALRI). In a similar study of 43 children between 3-5 years found 83% with pneumonia had Haemoglobin less than 11 g/dL [34]. De-Silva et al. [35] studied 366 children in Sri Lanka and observed that Iron supplementation significantly improves iron status and reduces morbidity from URTIs in children with or without infection. Mourad et al. [36] in a study involving 200 children found that Anaemic children were two times more susceptible to lower respiratory tract infection compared to the control and Ramakrishna et al. [37] in a study of 100 children with ALRI found that Anaemic children were 5.75 times more susceptible to LRTI compared to the control group.

Thus, the study shows a significant correlation between low Hb levels and low Ca levels and with increased episodes of pneumonia. Severity of pneumonia is inversely related to Vitamin D levels and Ca, Haemoglobin levels.

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