A DISSERTATION ON

SERUM ZINC LEVEL IN CHILDREN ADMITTED WITH PNEUMONIA IN A TERTIARY CARE HOSPITAL

M.D (BRANCH VII)

PAEDIATRIC MEDICINE

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INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN,
MADRAS MEDICAL COLLEGE, CHENNAI.

CERTIFICATE

This is to certify that the dissertation entitled "**Serum zinc level in children admitted with pneumonia in a tertiary care hospital"** submitted by **Dr.P.Reghupathy** to the faculty of Paediatrics, The Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of M.D. Degree Branch VII (Paediatrics) is a bonafide research work carried out by him under our direct supervision and guidance.

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This is submitted to the **Tamilnadu Dr.M.G.R.Medical University**, Chennai in partial fulfilment of the rules and regulations for the M.D.Degree Examination in Paediatrics.

Place: Chennai

Date: **Dr. P.REGHUPATHY**

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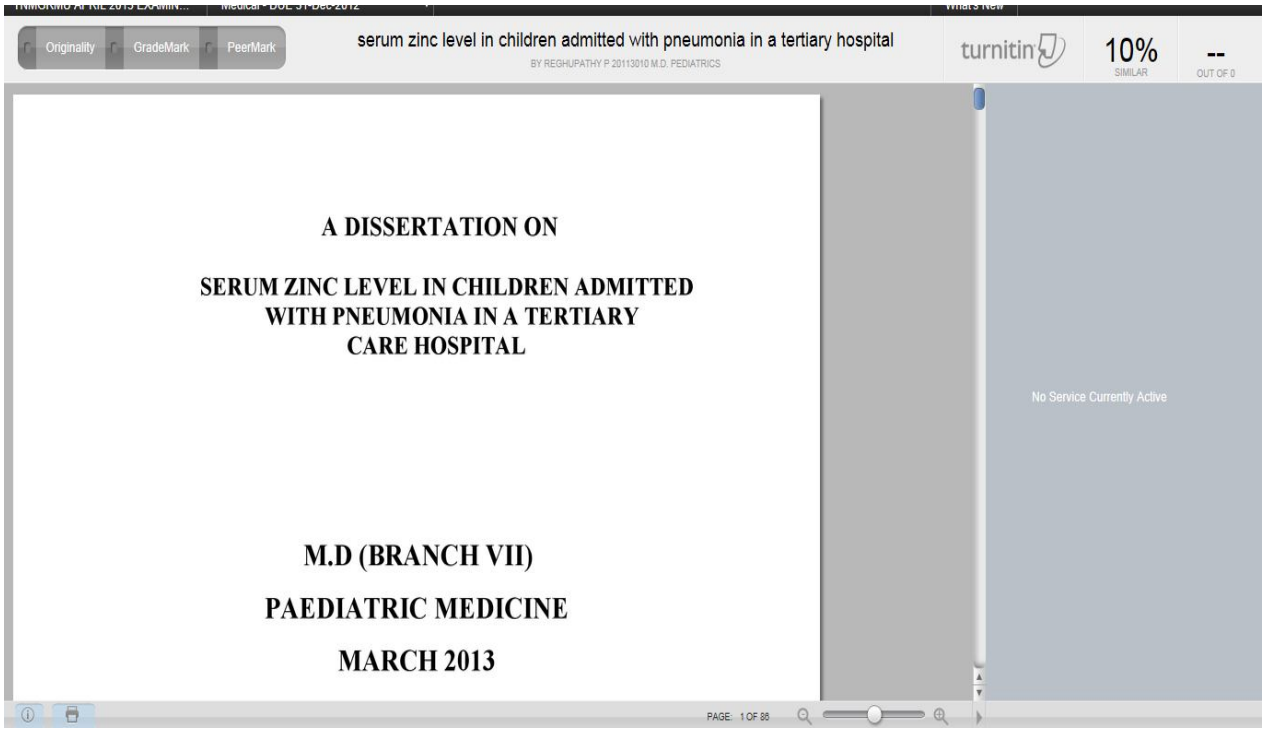
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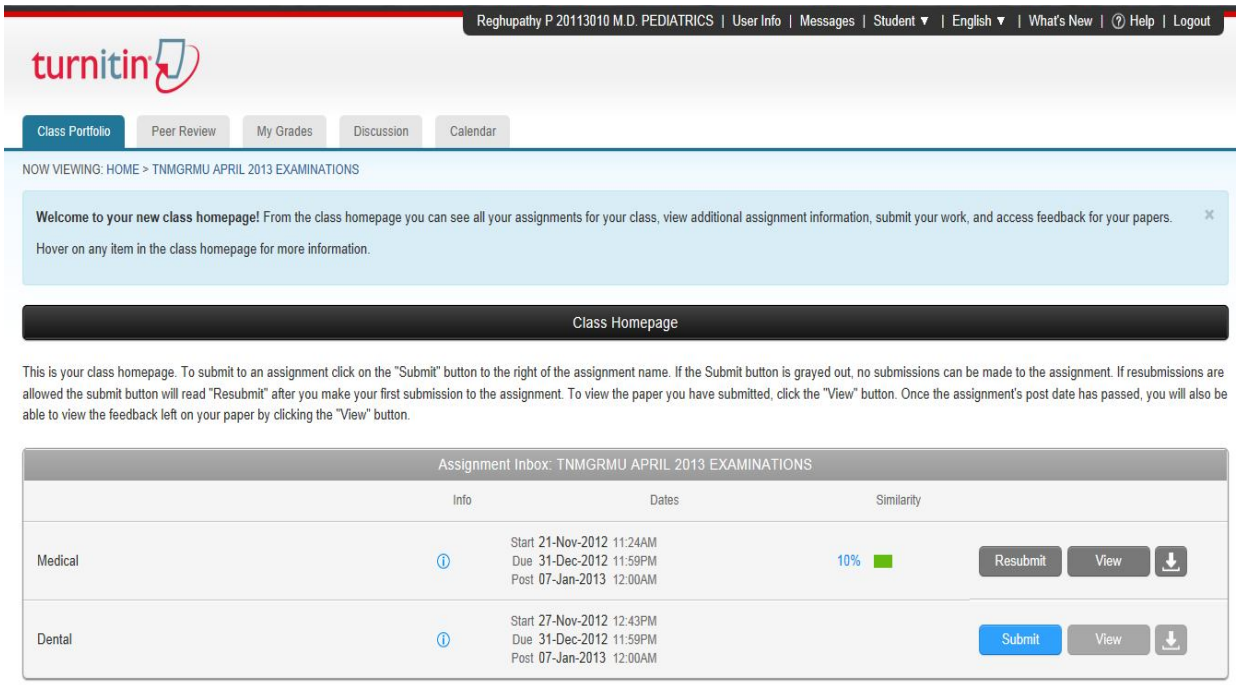
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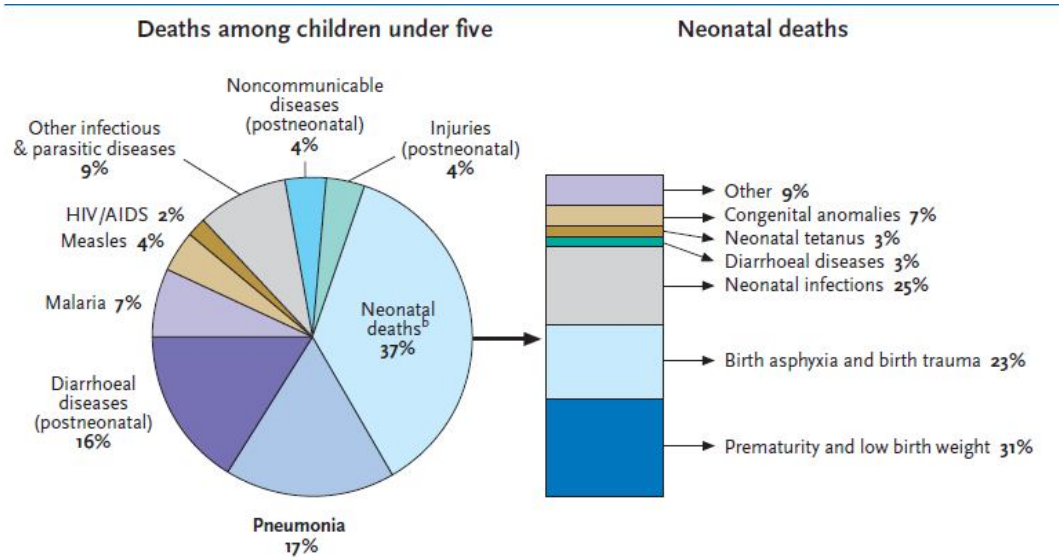
INTRODUCTION

In the past thirty years the total number of children dying within five years of life has come down by almost one third. But this decrease in mortality rate has not been the same throughout the globe. Infectious diseases still kill huge number of children in low income countries. This problem is augmented by co existing malnutrition, both forming a deadly combination kill considerable number of children in the young age. Each year greater than ten million children loss their life within five years of age in developing countries.(1)

Pneumonia is defined as an inflammation of the lung parenchyma. Pneumonia is the most common cause of death in children worldwide and every year around 1.2 million under five children die because of pneumonia.(1)It accounts for eighteen percent of all under five years deaths including non infectious cause

Pneumonia is more common in south Asia and sub-Saharan Africa (1) Incidence of pneumonia in south Asia is 0.36 episodes per Child per year as compared to 0.26 for world and 0.03 for industrialized countries. (3). This illustrates the prevalence of organisms and risk factors for pneumonia such as over crowding and malnutrition

Figure-1.CAUSES OF UNDERFIVE MORTALITY



Reference: World Health Organisation. The Global burden of disease.update.WHO.2008

ETIOLOGY

Pneumonia may be infectious or non-infectious. Infectious pneumonia is of concern, as it is a killer disease in children. It may be caused by any microorganism such as virus, bacteria or fungus .viral pneumonia is more prevalent but the bacterial ones left untreated becomes serious life threatening disease and the picture is even more worse in the children less than five year of age

The most common organisms causing pneumonia according to world health organism recent update are.(1) Streptococcus pneumoniae (pneumococci) is the leading cause of bacterial pneumonia in children; There are many strain with in this group causing pneumonia. they have a polysaccharide capsule and this encapsulated variety cause serious disease in children. It is not only the leading cause of life threatening bacterial pneumonia but also an important cause of bacteraemia and meningitis in children (1,3) This organism alone kills around one million children in a year worldwide

- Haemophilic influenzae type b (Hib) is the next common bacterial cause of pneumonia in children. It is a gram negative cocco-bacilli. Though invasive disease caused by this organism is decreased by effective vaccination , it still remains a common pathogen causing pneumonia and meningitis worldwide(1,3)

- Among viruses respiratory syncytial virus (RSV) forms the leading cause in this age group. Bronchiolitis and viral pneumonia are the two major respiratory illness caused by respiratory syncytial virus in infants. It is responsible for fifteen to forty percent of childhood pneumonia (1,3)

ETIOLOGIC AGENTS GROUPED BY AGE OF THE

PATIENT

AGE GROUP	COMMON PATHOGENS IN CHILDREN
Neonates (<3 wk)	Group B streptococcus, E.coli, gram-ve bacilli followed by pneumococci, H. influenzae (type b,* nontypable)
3 wk-3 mo	Viruses form most common cause of that RSV being the most common, followed by parainfluenza , influenza and adenovirus). Of bacterial pneumococci and H. influenzae are common in that order, if patient is afebrile, consider Chlamydia trachomatis
4 mo-4 yr	RSV followed by parainfluenza , influenza and adenovirus), pneumococci followed by Hemophilus influenzae, Mycoplasma and group A streptococcus form the bacterial cause
≥5 yr	Mycoplasma pneumoniae takes lead in this age group followed by pneumococci, Chlamydophila neumoniae, H.influenzae. Viruses include influenza viruses, adenovirus Legionella pneumophila

From Kliegman RM, Marcdante KJ, Jenson HJ, et al: Nelson essentials of paediatrics E.coli- escherichia coli, H.influenzae- hemophilus influenzae, RSV respiratory syncytial virus.

PATHOGENISIS

Physiologic defence mechanisms such as mucociliary clearance, secretary immunoglobulin A (IgA) the component of normal secretions and airway clearing by coughing keeps the lower respiratory tract sterile.(3)This pushes most of the organism away from the lower respiratory tract Macrophages present in alveoli and bronchioles, secretary IgA, and other immunoglobulins are the immunologic defence mechanisms of the lung that limit pathogenic organisms invasion. Immunoglobulins bind and macrophages engulf the organisms making them avirulent . Pneumonia occurs when the invading organisms breech or overcome these defence mechanisms

Pneumonia caused by viral organisms results from direct spread of infection along the respiratory tract causing direct injury to the epithelium of respiratory tract, Which results in airway obstruction from swelling, abnormal secretions, and cellular debris. young infants have small airways making them susceptible to more severe infection.(3) Airway obstruction in association with atelectasis, interstitial edema, and mismatch of ventilation-perfusion cause more hypoxemia. Viral respiratory tract infection by altering host defence

mechanisms, viscosity of secretions, and altering the bacterial flora predispose to bacterial infection

Bacteria affects the respiratory tract mostly by colonizing the trachea and then gaining access to the lungs, but pneumonia can also occur by seeding of lung parenchyma after systemic bacteraemia. After bacterial infection of the lung tissue, the pathology differs for different organisms.

Pneumococci causes local edema helping the organisms to proliferate and spreads to nearby areas of lung. It causes the characteristic focal lobar involvement in the pneumococcal pneumonia.

Mycoplasma get attaches itself to the epithelium of the respiratory tract. It inhibits ciliary action causing destruction of cells and an inflammatory response in the submucosa. As the disease process progresses, sloughed cell debris, cells of inflammation and accumulated mucus leads to airway obstruction and spreading of infection along the bronchial tree, as in viral pneumonia.(3)

CLINICAL MANIFESTATIONS

The presentation of pneumonia in children are (1)

Fast breathing

Chest indrawing

The above two are sensitive indicators for pneumonia in this age group and chest indrawing indicates severity of pneumonia. It is noted in lower chest wall of children. here during inspiration chest wall moves inwards or retracts.(normally there will be expansion in inspiration) other common complaints are cough, fever, chills, loss of appetite. In viral pneumonia wheezing is more common as airway obstruction forms common pathogenesis in viral pneumonia When severity of illness increases children are not able to drink or feed and may also have altered level of consciousness, and convulsions.

WHO CLASSIFICATION

World health organisation classified acute respiratory infection in children presenting with respiratory symptoms in the following way. In children two months to five years they classified acute respiratory infections as NO PNEUMONIA, PNEUMONIA, SEVERE PNEUMONIA and VERY SEVERE DISEASE.

According to them when a child with respiratory symptom is not able to drink, having convulsions, when chid is abnormally sleepy (lethargy) or difficult to arouse, when there is stridor in calm child or child is having severe malnutrition it is classified as **very severe disease**.

When a child presenting with respiratory infection has chest indrawing it is classified as **severe pneumonia.**

When a child presenting with respiratory infection has only fast breathing and there is no indrawing of chest it is classified as **pneumonia** (fast breathing –respiratory rate-50 per minute or more if child 2months up to 12 months. respiratory rate 40 per minute or more if child 12 months up to 5 years).

When a child presenting with respiratory infection has no fast breathing, no chest indrawing and have no signs of very severe disease it is classified as **no pneumonia, cough or cold.**

Host immune factors oppose the invading organism effectively in healthy hosts, but children with compromised immunity have increased risk to progress in to pneumonia. Undernutrition makes the immunity weak. adequate and balanced diet is essential for development and improvement of natural defences. Good nutritional

status not only prevent pneumonia but also decrease the duration of pneumonia

Global action plan for prevention and control of pneumonia (GAPP) has following important strategies to treat, prevent and protect from pneumonia(2).

--- treatment of pneumonia at all health care level

--- effectively vaccinate vulnerable population

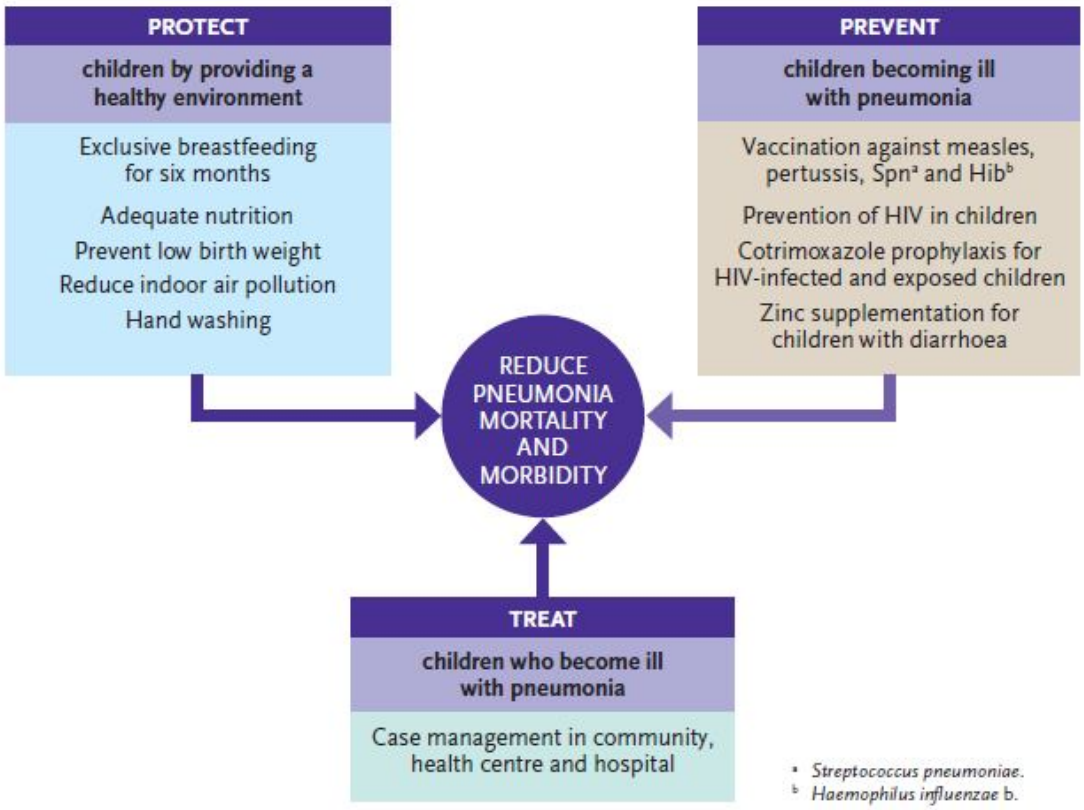
--- To Prevent and manage the Human immunodeficiency virus infection

--- To improve the nutrition and reduce the occurrence of low birth weight

--- adequate measures to control indoor pollution

Death occurring in pneumonia in children is strongly associated with Under nutrition, poverty and difficulty in health care facility accessibility

Framework for pneumonia control (GPAP -WHO)



In these strategies, for improvement of nutrition technical consensus states " to promote the habit of exclusive breastfeeding and to supplement zinc are important strategies to prevent pneumonia "

ROLE OF ZINC

In 1509 zinc was first recognized as element .It was first essentiality demonstrated in Plants by Raulin in 1869 and in animals in 1934 . In human being zinc is 2nd only to iron in quantity (11). In

aqueous solutions it has an oxidative state, known as Zinc2+ and it usually occurs in tetrahedral complex .It acts as a Lewis acid. It is not a redox active metal and easily forms complexes with body substances such as aminoacids, peptides, proteins and nucleotides. It easily combines nitrogen donors which are electron rich.

Zinc is an essential micronutrient in humans. According to cotzias 1955 an element is said to be essential only if the element obeys the following criteria

* Concentration from one animal is fairly constant

*To withdrawl the body produces the same functional and structural abnormality whatever the species studied and it should be reproducible

*The inclusion of element will reduce or prevent the above mentioned abnormalities

*There should be biochemical changes along with this abnormalities

*These changes doesn't occur or get corrected when this deficiency is prevented or corrected. Zinc fulfils this criteria and forms an essential trace element in human body.

The amount of zinc in human body is distributed as follows

Whole body	:	1.50-2.50 grams
Organ	:	Percentage
Skeletal Muscle	:	Fifty seven
Bone	:	Twenty nine
Skin	:	Six
Liver	:	Five
Brain	:	Two

Kidneys and Heart have less than one percent Hair and Blood Plasma have only 0.1%

SOURCES

Zinc is present in variety of foods.

Sea food especially shellfish is rich in zinc.

Beef, red meats are also found to be rich sources of zinc.

Though zinc is found in large quantities in whole grains, they are concentrated in the bran, germ part of the grain .They are vulnerable to get lost and get easily removed around eighty percent by

milling. Even the available amount not gets fully absorbed due to coexisting phytates.

Zinc is also found in good amount in nuts and legumes Diet having increased meat increases the amount of zinc getting absorbed.

AMOUNT 0F ZINC IN ZINC RICH FOODS

Food Items*	Zinc**
Oysters	>Twenty Five
Shellfish	Twenty
Brewers Yeast	Seventeen
Wheat Germ	Seventeen
Wheat Bran	Sixteen
Low Fat Roast Beef	Ten
Pine Nuts	Six
Pecans	Six
Cashews	Six
Roasted Pumpkin Seeds	Ten
Veal Liver	Ten
Lamb	Four-Eight

*for hundred gram of food item

** zinc expressed in milligrams

ABSORBTION

Absorption of zinc takes place throughout the intestine (25)

- Absorption of zinc occurs primarily in the jejunum

-there is no absorption of zinc in stomach and large intestine

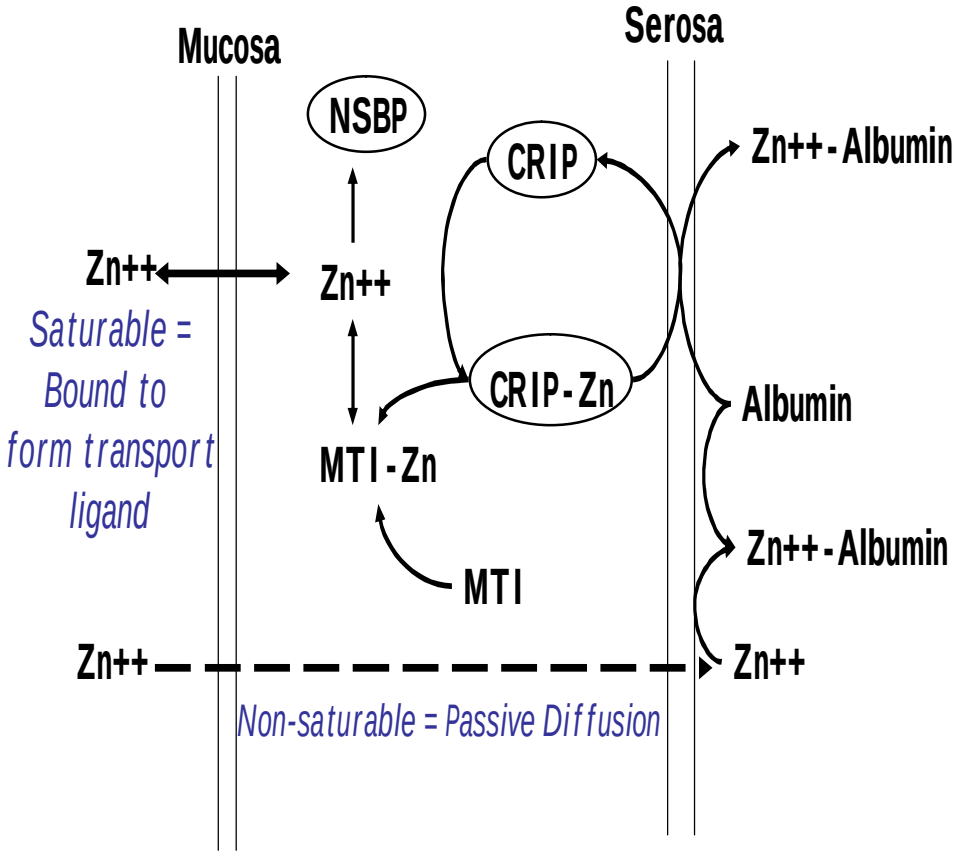
- In jejunum

  There are two processes that occur in jejunum

  - ❖ One is a Non mediated process.
  - ❖ It doesn't gets saturated
  - ❖ Zinc content of the food doesn't affects this.
  - ❖ Next is a mediated one, It gets saturated.
  - ❖ This process can be increased by zinc deficiency.

The first process is unsaturable as it is not ligand mediated and the absorption occurs by the process of passive diffusion. The second one is ligand mediated and hence saturable

Absorption



CRIP=cysteine-rich intestinal protein; MTI=metallothionine;
NSBP, non-specfic binding protein

Bioavailability :

Low calcium and high protein intake promote absorption and retention of zinc. Animal protein including milk appear to promote zinc release and bioavailability from its phytate complex. Phytate (present in bran, whole grain cereals , and legumes) and high iron intake inhibit zinc absorption. Iron has little effect on zinc absorption from a complex meal. Fats tend to dilute zinc from the total diet.

Average adult Indian vegetarian diet usually contain 16mg of zinc so that 10% of this (1.6 mg) is available.

Food sources of zinc for infants

The feasibility and potential of a local non fortified food – based approach for preventing onset of zinc deficiency in mid-infancy are challenging. An infant of 6-8 months is in the critical transition period of infant feeding. Breast milk, perhaps augmented by the release of modest neonatal stores in early infancy (25), Provides sufficient zinc for the first few months of life. However, as lactation progresses, the physiologic decline in breast milk zinc concentration is notable.

By 7 months –postpartum, the zinc concentration in human milk is <1 mg/L and the intake of Zinc from breast milk by the exclusively breast – fed 7 – months infant is only 0.5 – 0.6 mg regardless of mother's zinc status.

Complementary foods in developing countries are typically limited almost entirely to plant foods, The amount of zinc present in plants which are thought to be most favorable itself are not adequate for the requirement of the children(19)

This problem is further increased due to unfavourable bio availability caused by the phytates.

Plant foods with the most favourable Zinc concentrations notably grains and legumes also have the highest phytate concentrations challenging research is now being directed to bio fortification of grains with Zn and to lowering phytate. (11).

Micronutrient fortification of food staples provided a partial solution to achieving adequate Zn in plant foods. However, these fortified foods will not reach all older infant/ toddlers especially the millions of rural poor. (20) similar constraints are encountered with the availability of sprinkles yet to be shown efficacious in preventing or managing Zn absorption/ deficiency. There remains a compelling current and long term need for locally produced non fortified

complementary foods providing adequate Zn. Animal source foods, especially meats including organ meats, not only contain the highest concentrations of Zn but provide zinc in a bioavailable form

EXCRETION

- Zinc is lost via hair, sweat, desquamation, bile pancreatic secretions, seminal fluid, urine, feces
- Main endogenous loss is by

  -Secretions into gut

    - Bile and pancreas

  -Mucosal cells
- Urinary and integumental losses

  < 20% under normal conditions

    – Losses increase with trauma, muscle catabolism, and administration of chelating agents (EDTA)
- Primarily in fecal material

  It contains unabsorbed zinc and secreted zinc. (endogenous sources) from pancreatic and intestinal sources

REGULATION OF ZINC

Metallothionein is primarily involved in zinc metabolism (25). It is concentrated in liver, kidney, pancreas, intestine. It acts as a Zn2+ buffer and controls free Zn2+ level. It controls intracellular zinc pool responsive to both hormones and diet

- Zinc-binding protein, metallothionein (MT), is involved in the regulation of zinc metabolism

MT is inducible by dietary zinc via the metal response element (MRE) and MTF-1 mechanism of transcriptional regulation

Increase in cellular MT → ↑ Zinc binding within cells -Acute infections associated with proinflammatory cytokines increases zinc uptake into liver, bone marrow and thymus and reduces the amount going to bone, skin and intestine

FUNCTIONS OF ZINC

ZINC IN ENZYMES

There are more than 70 zinc-containing enzymes in human being. Zinc is found in metal stabilized active sites forming Secondary & tertiary protein structures Examples of general types

1. Carbonic anhydrase
2. Dehydrogenases
3. Phosphatases
4. Peptidases
5. Kinases
6. Deaminases.

Zinc is first demonstrated in carbonic anhydrase. Carbonic anhydrase found primarily in red blood cells but also in tubular structure in kidney. It is needed for the following reaction, from which carbon di oxide is rapidly disposed.

Carbonic anhydrase Zn 2+

$CO_2 + H_2 \rightarrow H_2CO_3 \rightarrow H + HCO_3$

The amount of zinc that is associated with carbonic anhydrase and carried by Red blood cells is eight to nine times than in tissues and plasma. Carbonic anhydrase has increased affinity for zinc and even in mild deficiency of zinc break down of this enzyme doesn't occur.

Alkaline phosphatase contains four zinc ions in one enzyme molecule, two of the ions are used for enzymayic activity and two of

the ions are used for structural integrity. Similarly Alcohol dehydrogenase also contains four zinc ions two for enzymatic activity and two for structural maintanence.

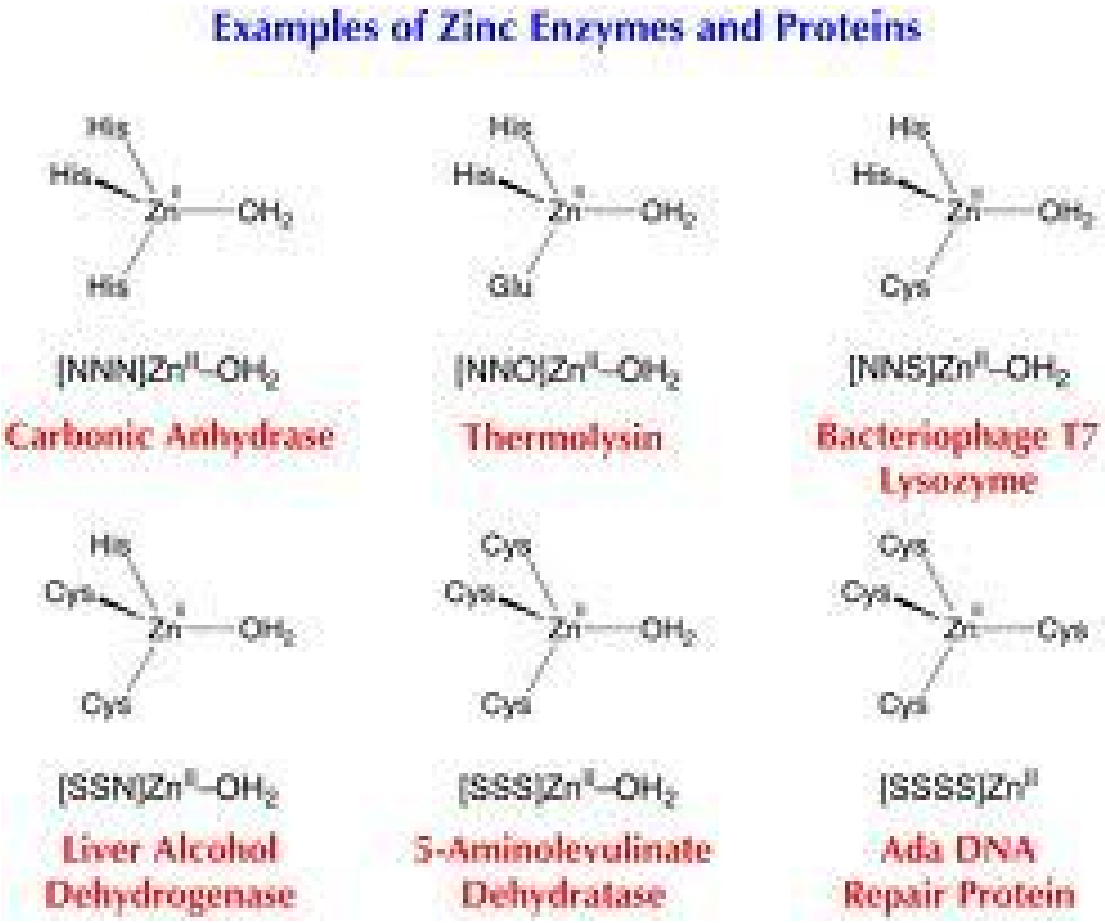
Carboxy peptidase and aminopeptidase are the protein digesting enzyme having zinc in their structure. Superoxide dismutase needs both zinc and copper for its structural maintanence. This is essential for removal of free radical removal. Role of zinc in the integrity of this enzyme is postulated to have its protection role in infections as it forms the basis for antioxidant action of zinc.

Phospholipase C requires zinc for enzymatic activity, this enzyme hydrolases the phosphodiester bond in phospholipid Polymaerase, kinase, transferase, phosphorylase and transciptase all require zinc, Zinc metalloenzymes DNA and RNA polymerase are important in nucleic acid synthesis.

Zinc forms both catalytic and structural unit of enzymes. Plasma alkaline phosphatase and dehydrogenase are found to de low in deficiency of zinc.

Zinc as a constituent of these enzymes quotes the importance of zinc in body functions, management of oxidative stress and integrity

of cells. In zinc deficiency alteration of these equilibrium leads to disease manifestations and suscebtiability to infections.

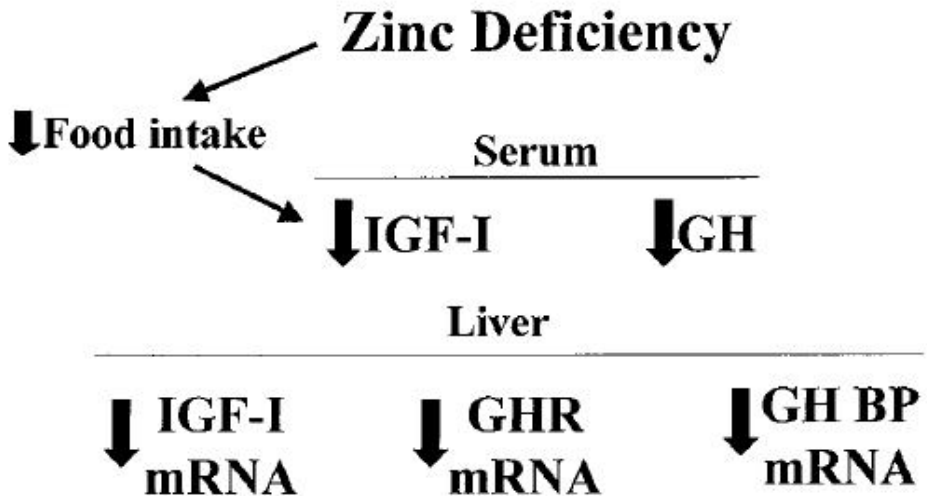


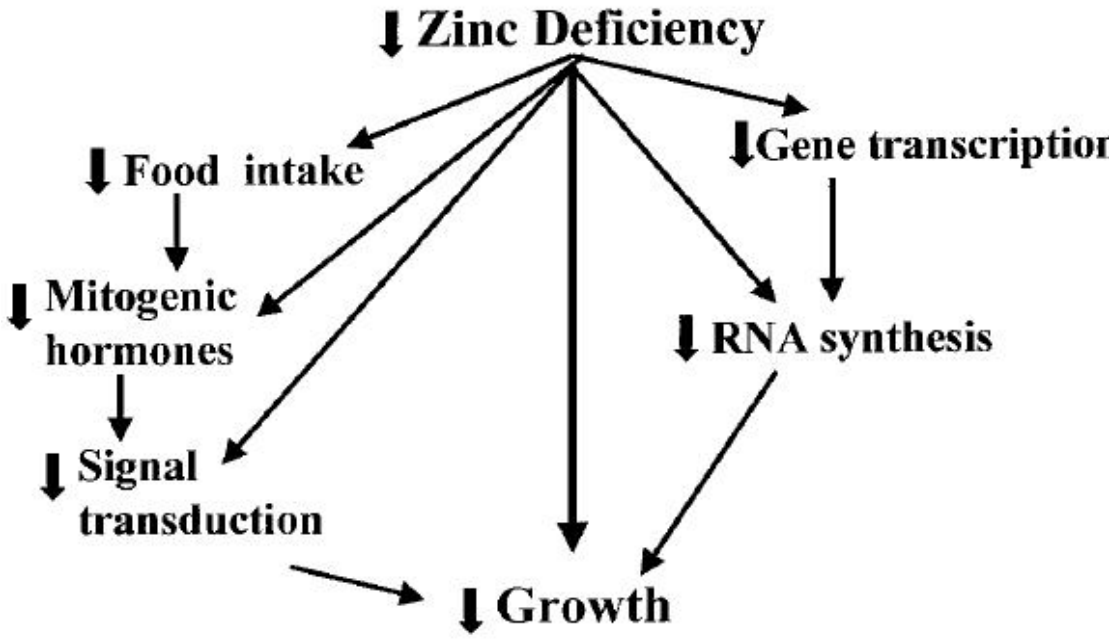
ZINC IN HORMONES

Zinc plays important role in the synthesis,storage and release of many hormones. It is important in testosterone,insulin and steroids. Zinc deficiency is associated with hypogonadism

ZINC IN GROWTH

Being one of the abundant element in human body, it plays vital role in growth. Zinc is involved in all aspects of growth. It is involved in transcription, cellular differentiation, enzymes and structural units of cartilage and bones. Growth failure is an important manifestation of zinc insufficiency. Animal studies shows that zinc is essential for food intake itself. Even with adequate feeding when it was not having adequate zinc growth failure was documented.(8) It is evident that zinc acts by separate mechanisms in controlling food intake and growth. Both growth hormone level and action of growth hormone are dependent on zinc. Intra cellular mechanisms responsible for growth signaling in response to IGF is affected by zinc(23).



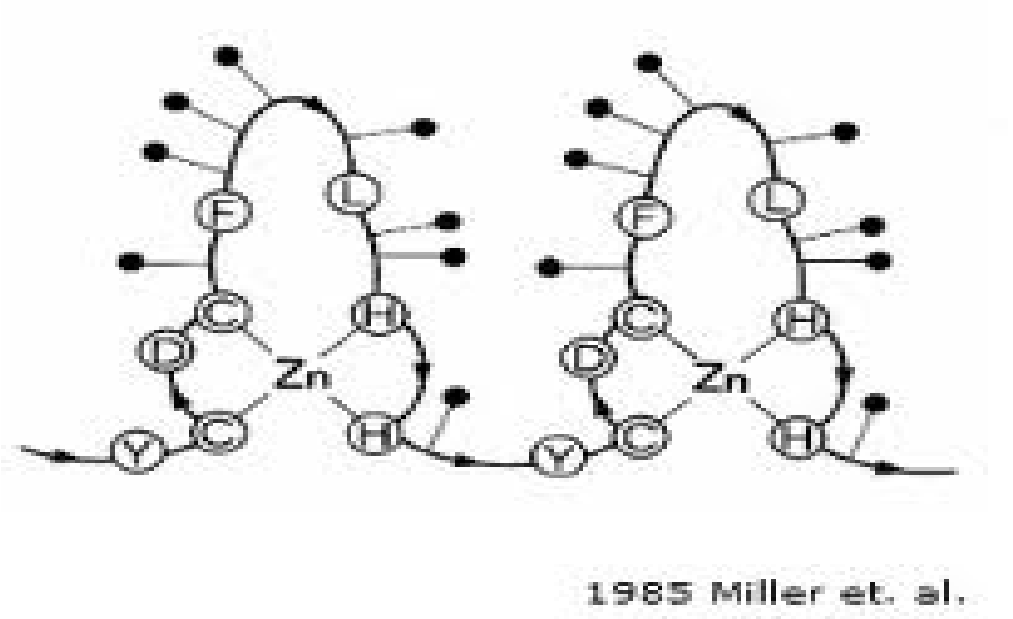


ROLE IN TRANSCRIPTION

Ions of zinc present in the Zinc finger structures are important for the process of transcription. C two H two zinc finger binding motif is a predominant motif in eukaryotic transcription. It is involved in skeletal differentiation. There are 2 cysteine and 2 histidine residues. They together form in to 4 residues and bind with single ion of zinc. (25) This combination is known as zinc binding motif..It binds to response structures in the upstream promoters of genes coded by RNA poly 2.It also binds to five S ribosomal Ribo nucleic acid gene, 5S Ribo nucleic acid , & activates transcription by RNA polymerase 3.Gene expression is controlled by specific proteins call transcription factors. Zinc containing transcription factors account for 1% of

genome. Zinc plays key structural role in transcription factor protein. Zinc influences cell division, growth, DNA and RNA metabolism (9), growth, development, sexual protein. As already mentioned zinc containing metallo enzymes are involved in every step of transcription and in nucleic acid synthesis.

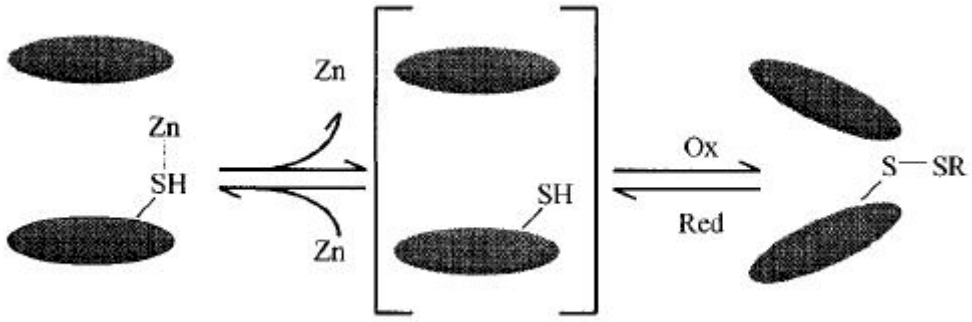
STRUCTURE OF ZINC FINGER



In the figure it is evident of zinc binding with C2H2

ZINC IN CELL MEMBRANE

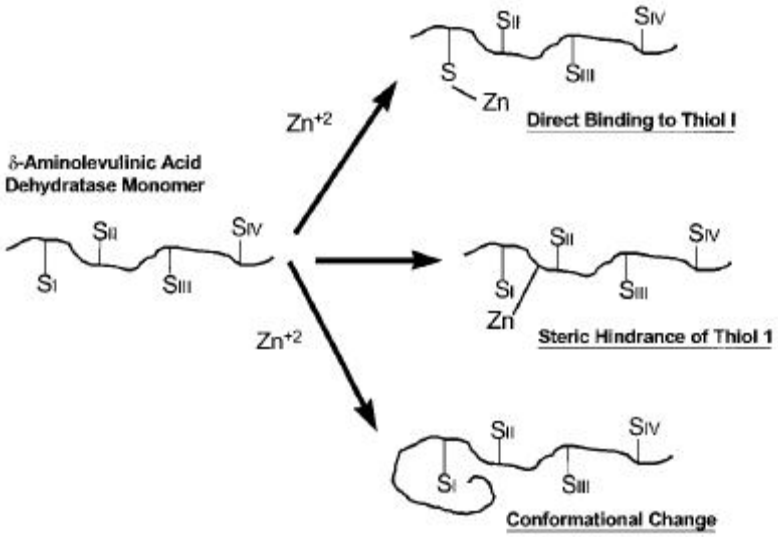
Zinc is critical for functioning of biomembranes. Cell membrane fractions contain high concentrations of zinc. Many finding in zinc deficiency is said to be because of plasma membrane abnormality. Impaired platelet function, altered osmotic fragility in RBC and signs of peripheral neuropathy are all attributed to membrane dysfunction seen in zinc deficiency. Zinc affects membrane function by its effect on calcium channel in the membranes.



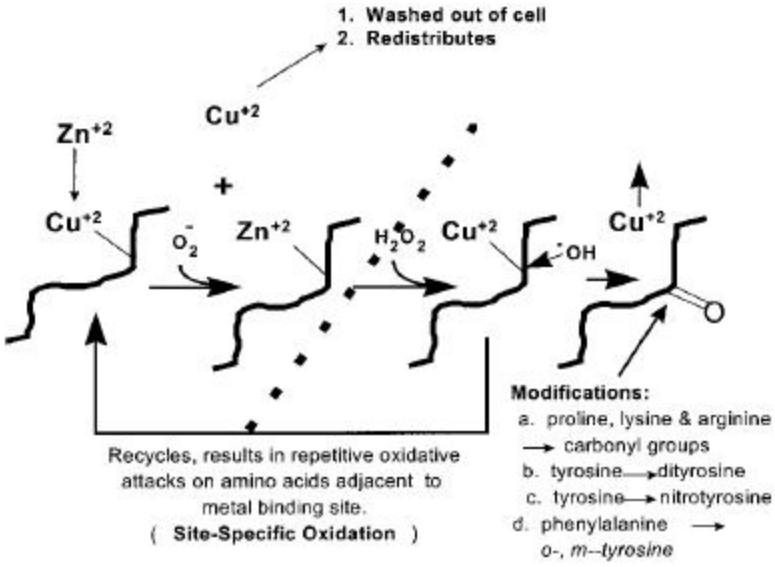
In the figure zinc binds to sulphidryl group and keeps it active and open, when zinc is not available disulphide bond forms and channel get inactivated

ANTIOXIDANT ACTION

Zinc protects from the oxidative damage by competing for binding sites with redox metals. Zinc has both acute and chronic antioxidant action. Acute action is helpful immediately after administration and due to stabilization of sulfhydryl group. Chronic antioxidant property is due to metallothionin formation. This anti oxidant action of zinc is one of the main proposed mechanism (5, 25) by which zinc acts against infectious organisms and decreasing the severity of diseases caused by them.



Above figure shows stabilization of sulfhydryl group



Here it is shown that copper recycles and continues the process of oxidation and zinc stabilizes the metal binding site and acts as an antioxidant

IMMUNE FUNCTION

Zinc plays important role in immunity and its regulation. All cell lines in the immune system such as lymphocytes, neutrophils, macrophages, mastocytes & thrombocytes. Zinc is essential for the expression of action of thymulin. It is a specific hormone for the thymus gland. (5).

Thymulin is needed by T cells for induction of T cell markers, promotion of cytotoxic, suppressing and productive (interleukin 2) functions (5,6).

T helper cells have two subsets Th_1 and Th2. Zinc is essential for the maintenance of balance between these two subsets, cytotoxic T cells also need zinc for their subset maintenance and expression.

Zinc is needed for thymulin, It is possible zinc is involved in genesis of haematopoietic stem cells in the thymus micro environment (5,25)

Deficiency of zinc produced following abnormalities in the immune system of human beings.

1. Decreased thymulin activity observed is corrected by addition of zinc T – cell subpopulation studies. CD_4 + to CD8 + Ratio decreased.

   CD_4 + $CD_4$5RA+ to CD + $CD_4$5RO + Borderline

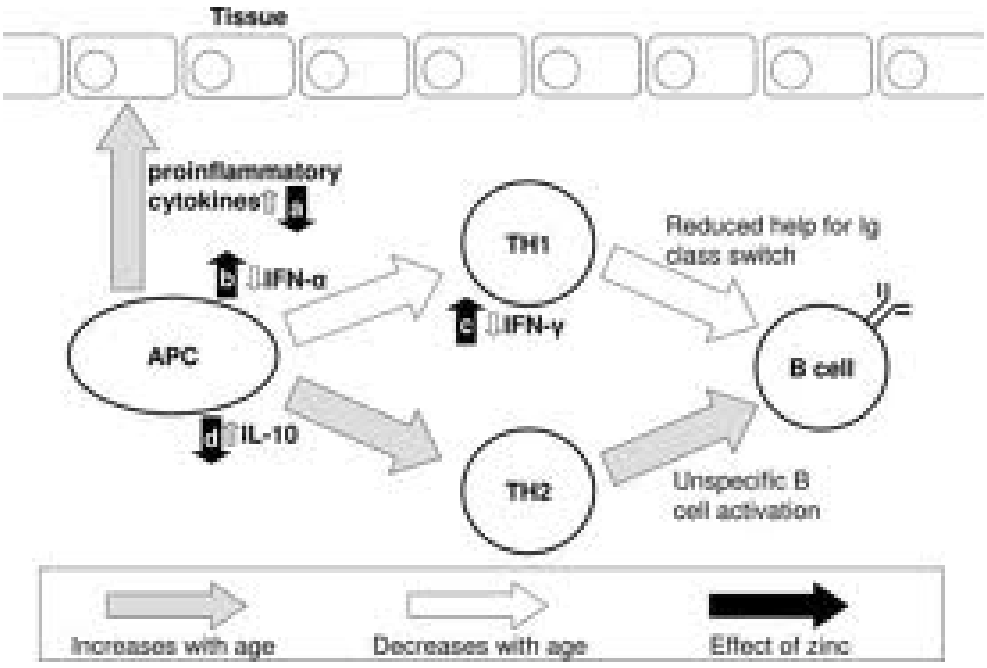
2. Th_1 cytokines both cytokines decreased.

   IL – 1, IFN gamma

3. Th_2 cytokines No change

   Interluekin – 4, Interluekin – 6, Interleukin– 10.

4. Natural killer cells activity gets reduced Precursors in cytotoxic T lymphocytes CD8 + CD73 + Decreased.



EFFECT OF ZINC IN IMMUNE CELLS

ZINC DEFICIENCY

Zinc concentrations of plasma, blood cells, hair and urine decrease in severe deficiency states. In deficient animals following observations made (6).

Failure of platelet aggregation

Impaired Calcium uptake

Peripheral neuropathy

Central nervous system synaptic vesicles showed decreased calcium uptake

Reduced cell membrane sulfhydryl content

After Zinc depletion

- All functions within monocytes were impaired
- Cytotoxicity decreased in Natural Killer Cells
- Phagocytosis is reduced in neutrophils
- Normal function of T-cells are impaired
- B cells undergo apoptosis.

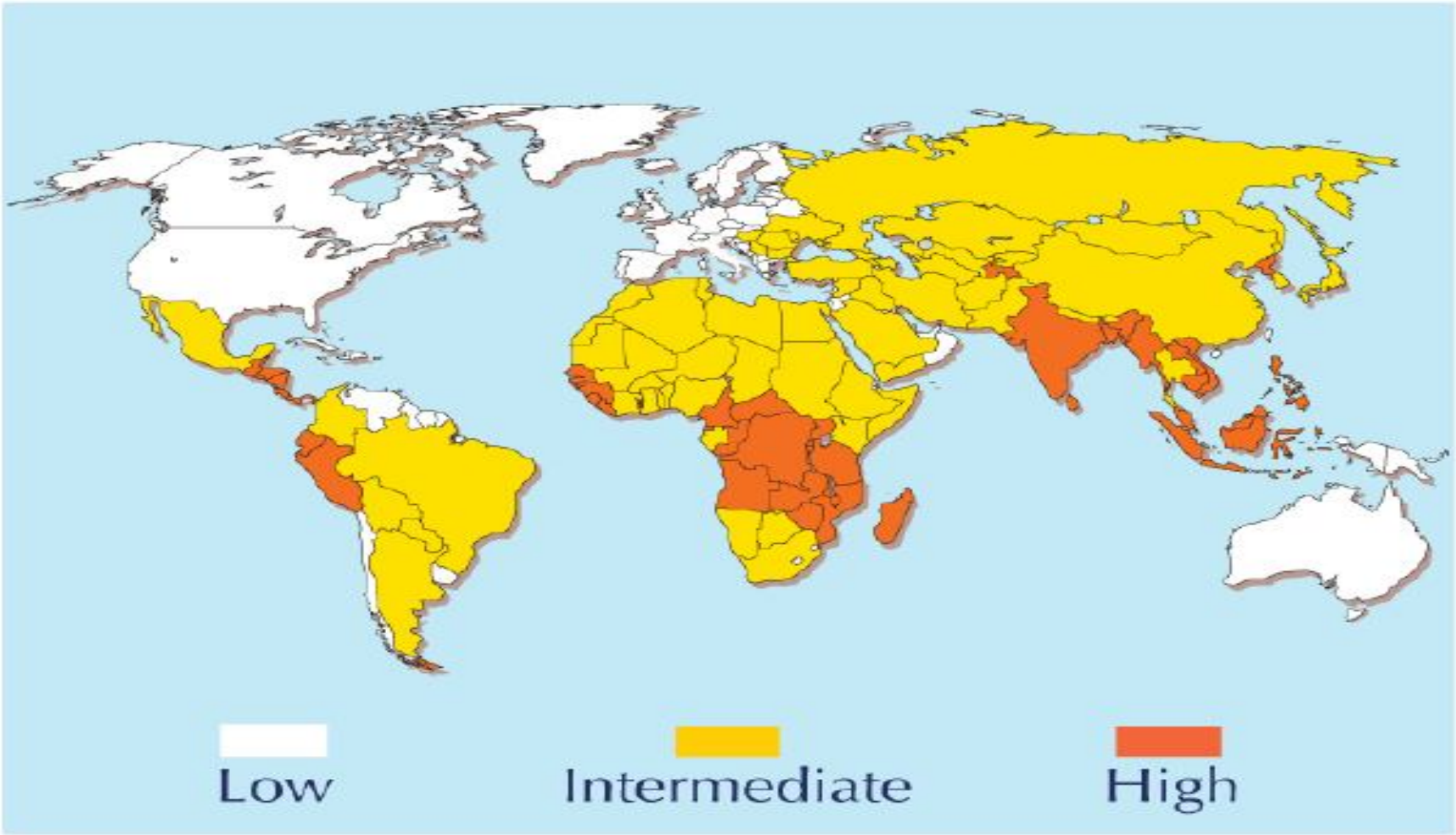
Zinc deficiency manifests as

- Growth retardation
- Delayed sexual maturation & impotence
- Impaired testicular development
- Hypogonadism & hypospermia
- Alopecia
- Acroorifical skin lesions
- Other, glossitis, alopecia & nail dystrophy
- Immune deficiencies
- Behavioral changes
- Night blindness
- Impaired taste (hypoguesia)
- Delayed healing of wounds, burns, decubitus ulcers
- Impaired appetite & food intake
- Eye lesions including photophobia & lack of dark adaptation

Zinc deficiency has varied expressions such as impaired immune function, skin disorders hypogonadism, stunting of growth, anorexia and cognitive dysfunction.(5,6) In countries like ours common cause of zinc deficiency of zinc is due to dietary deficiency. It may be due to inadequate zinc containing food intake or decreased absorption due to inhibitory effects of fibers & phytates, present in cereals, legumes & nuts. (7) It can also arise from mucosal abnormalities of mucosa and loss of integrity in the intestine seen in persistent diarrhoea.(8)

Studies suggest that there are greater risk of diarrhoea, pneumonia and growth failure in zinc-deficient population. (9-12).Effectiveness of zinc supplementation in early recovery and reduction of severity of pneumonia has been shown by number of studies.(13,14) In this study, serum zinc level in children with pneumonia and healthy controls compared.

PREVALENCE OF ZINC DEFICIENCY



ACRODERMATITIS ENTEROPATHICA

PROGRAMME OPTIONS TO PREVENT ZINC DEFICIENCY

Dietary intervention

Dietary modification programme to increase zinc, vitaminA, and iron by

1) Increase intake of food with high content and bioavailability of zinc

2) Increase intake of foods known to enhance zinc absorption

3) Use of soaking, germination and fermentation to induce Phytase

Plant breeding strategies to increase the zinc content of plant.

Micronutrient supplementation- Studies quote that it is practical and cost effective to add zinc to iron or multivitamin supplements.

Fortification is used in two blended products, corn soy blend and wheat soy blend. Three salts for fortification are zinc sulphate, zinc oxide and zinc gluconate.

SIDE EFFECTS OF ZINC

At the recommended doses of ten milligram in the early young infant & twenty milligram/day to the children more than six months old, there is no adverse reaction or side effects noted in zinc supplementation in any study whether it is given alone or in combination with oral rehydration solution or vitamins. The toxicity is said to occur due to its effect in copper absorption. It is not noted that the zinc supplementation given for two weeks in diarrhoea or in malnutrition this effect is never documented.

MECHANISM IN PNEUMONIA

Zinc having essential role in immunity, membrane functions, its anti oxidant functions all contribute to its importance in prevention of occurrence and prevention of progression of any infection including pneumonia. (9) Zinc deficiency increasing the inflammatory pathology in the respiratory tract with increasing damage to the cells is a proposed mechanism. Zinc also prevents the recruitment of white blood cells and release of cytokines from them and effectiveness of zinc said to increase with increase in the severity of pneumonia.

With this background this study is designed to know the serum zinc level in children admitted with severe pneumonia.

REVIEW OF LITERATURE

LITERATURE ABOUT ZINC ACTION

According to Shankar et al (5) zinc affects immune system at multiple levels starting from skin to gene regulations within cells such as lymphocytes. Zinc works at level of DNA replication, RNA transcription, division of immune cells and their activation. Zinc deficiency affects T lymphocytes, B lymphocytes and macrophages. Zinc has an antioxidant role. It stabilizes cell membrane. Zinc deficiency potentiates apoptosis.

This is the most cited study in all zinc related studies which was published in American journal of clinical nutrition. They brought out that zinc has effects on both innate immunity and specific immunity. Zinc deficiency presenting as acrodermatitis enteropathica shows that zinc is essential for epidermal cells which forms the first line in barrier to organisms. They listed the animal and human studies showing decreased lymphocytes in zinc deficiency. It was shown to be reduced up to fifty percent. In murine studies not only there is reduced lymphocyte counts but the functions also decreased with deficiency of zinc. In that T cell function was affected more than the B cells. They concluded that that zinc has an important role in the development and

effective function of immune system. Application of knowledge about zinc in immune system is essential for future planning and interventions such as supplementation or fortification of zinc as a preventive health care measure.

PROPHYLACTIC ZINC TO REDUCE PNEUMONIA

Following are the studies quoting the significance of zinc supplementation in reducing the incidence of pneumonia in children

1. Umeta et al. [21] looked for the effects on addition of zinc in children of age between six to twelve months for growth. It was done at Ethiopia. They selected hundred children with stunting and hundred children with normal height. They gave zinc and placebo to both the group in a blinded way. Results showed that there was increase in height,increase in weight, appetite improvement, decreased rate of cough development and significant decreased rate of diarrhoea. They showed increased frequency of vomiting in children received zinc. They concluded that zinc supplementation decreased the incidence of infectious diseases and the growth improvement found in the study may be due to this factor also.
2. Baqui et al (7) noticed decreased incidence of acute respiratory tract infection in children received zinc supplementation

compared to the group that not received supplementation. It is a randomised study involving a large sample of eight thousand and seventy children contributing eleven thousand and eight hundred and eighty one child years. This study was done at Bangladesh and got published in british medical journal. They started zinc supplementation for fourteen days after an episode of diarrhoea and looked for the occurrence of other morbidities. Observation made in this study that even shorter duration (fourteen days) supplementation of zinc decreasing incidence of acute respiratory tract infection highlightens the importance of zinc in infection and prevalence of zinc deficiency in developing countries.

3. Ninh et al. [23] showed that fortification of zinc in children decreased diarrhoea incidence by forty four percent and incidence of pneumonia by forty four percent. It was done at Vietnam.

4. Incidence of diarrhoea decreased by 8% and of pneumonia decreased by 44% and mortality decreased by 68% in children received zinc fortification according to sazawal et al . This study was done at india by giving ten milligram of zinc for more than six hundred children for six months.

5. Gardner et al [24], in Jamaica, indicated that administration of zinc in children reduced incidence of diarrhoea by eight percent and incidence of pneumonia by eighty-eight percent.

6. Rakesh agarwal et al (13) performed a meta analysis in effect of zinc supplementation in prevention of childhood diarrhoea and respiratory illness. There were previous studies analysing the effect of zinc given for two weeks. But for routine supplements they must be given for minimum few months so they included all randomized controlled trials with supplementation of zinc given for greater than or equal to three months in age group of children three months to five years. Occurrence of illness, their duration, severity, frequency were the outcome measures looked for. Data from 17 studies pooled in this analysis. Results revealed addition of zinc decreased frequency of diarrhoea (RR 0.86) and respiratory infections (RR 0.92) with few episodes of lower respiratory infections or pneumonia (RR 0.80). Rakesh et al in their analysis concluded that addition of zinc decreased the episodes and severity of diarrhoea and occurrence of respiratory illness. Though the analysis revealed that addition of zinc decreased the occurrence of both diarrhoea and pneumonia, the

decreased duration of illness and reduction in severity noted in diarrhoea was not seen with pneumonia. The analysis looked for only prophylactic benefits for zinc rather than therapeutic benefits. Authors recommend zinc supplementation in developing countries where prevalence of infections and malnutrition is high. In that places this intervention though providing small proportion in decreasing morbidity and mortality will be reflected in huge numbers. They also mentioned that the relatively limited reduction in morbitidy indicated the need for large, high quality studies to know subpopulations likely to benefit.

7. Zohra S lassi et al (14) in their Cochraine review(14) of MEDLINE(1966 to January2010) and other journals included all RCTs evaluating zinc supplementation on preventing pneumonia in children aged 2 to 59 months . They included six trials in pooled analysis. The strength of the study is it included the studies from developing countries.Most of the studies have excluded children with considerable comorbidities. Meta-analysis revealed zinc supplementation decreased the occurrence of pneumonia by thirteen percent (Rate Ratio 0.87)

and the overall prevalence of pneumonia by forty one percent (Rate Ratio 0.59.). Authors concluded that the analysis supported there is evidence to support to include zinc supplementation as a preventive strategy for practice. For research they advised further studies to implement intervention in large scales, methods to prevent zinc deficiency, health education and genetic engineering for production of zinc rich foods.

ZINC AS AN ADJUANT THERAPY IN PNEUMONIA

Brooks et al. (22), observed in Bangladesh, in addition to the antibiotic, administered twenty milligram of zinc in children less than two year old with severe pneumonia, and gave placebo to controls. Study population included about two seventy children. The outcome measured was disappearance of in drawing, absence of fast breathing, maintaining more than ninety five percent sao2 in the room air. From results they showed there was decreased duration of severe pneumonia by supplementation of zinc. They also noted that this effectiveness not holds good for wheezy infants. They concluded that increased zinc level augments immune response and hastens recovery

from inflammation. For large scale interventions they adviced further studies including follow up ones

POSSIBLE MECHANISM OF ZINC IN PNEUMONIA

Though large number of studies showing effectiveness of zinc in preventing and reducing pneumonia studies dealing with mechanism of zinc action how it does this is not clearly explained.

Pa tamba ngom et al (26) reviewed the literature and published in a immunology journal the possible mechanisms. They discussed that inadequate zinc is a common problem in asia and Africa as zinc rich foods are costlier and available in regional basis. They pointed out that diet is the only source for zinc in human being

In the review they highlighted that in vulnerable group like India up to twenty five percent of population is zinc deficient according to world health organisation

The mechanism of action was sought for proper recommendation because previous studies produced mixed results in case of decrease in severity and mortality. Only understanding the mechanism only can guide us recording who are the population benefit from addition of zinc, whether it will be useful or not and what are the risks? The authors quoted that both animal study and human

study showed thymic atropy in zinc deficiency and reversal of it with zinc supplementation. They proposed thymulin inactivity in zinc deficiency as one of the mechanism.

They also quoted that pneumococci destroys zinc dependent protease and there will be increased need of zinc during the infection. The antioxidant action of zinc and need of zinc dependent enzymes to reduce the reactive oxygen particles during infection makes the zinc deficiency overt and increase the severity of illness in deficient children

RESPONSE VARRIES WITH CAUSES

There are studies favouring the concept that zinc is not so effective in viral pneumonia as it is in bacterial pneumonia. As already quoted Brook et al showed that results of addition of zinc was not convincing when they included wheezy infants. As pneumonia with wheezing is common with viral pneumonia, question of effectiveness of zinc in viral pneumonia arises.

The finding of study done by Christian L Coles et al (27) was entirely different. This study was done at Christian Medical College, Tamilnadu, South India. They included around two hundred and ninety five children, divided them and gave zinc and placebo. They measured

CRP for all children and classified the children with pneumonia based on CRP in to those having bacterial pneumonia and non bacterial ones.

Results showed that in bacterial group those who received zinc had a longer stay than the group received placebo. The authors concluded that the response to zinc varies with individual pathogens and further studies are needed before routine recommendation of zinc supplementation.

VARIABLE OUTCOMES

Joseph Mathew from PGI, (28) Chandigarh reviewed by a systematic review about zinc in pneumonia. He looked for both therapeutic and prophylactic role of zinc in community acquired pneumonia. 15 randomised trials are reviewed 11 dealing with prophylactic effect of zinc and 4 with therapeutic effects of zinc. They concluded that there is no benefit of adding zinc to the standard treatment of pneumonia and supplementation doesn't prevent childhood pneumonia.

SERUM ZINC LEVEL IN PNEUMONIA

Though large number of studies about prophylactic zinc supplementation and zinc as an adjuvant to pneumonia treatment are available there are only few studies available about the serum zinc level in children having pneumonia. All studies recruited children with severe pneumonia for measuring the zinc level. Most of the following studies are done in developing countries.

Kumar et al (15) did a study on zinc levels. The study population was children admitted in the hospital with severe pneumonia. It was conducted in hospital in Lucknow, north India. This study was published in Indian pediatrics. Subject age group was children aged two months to five years. Blood zinc levels in fifty cases and fifty age, sex and nutritionally matched controls were compared. 74% were less than twelve months and remaining in the age group of greater than twelve months to five year. In the study group seventy percent were males and thirty percent females. Sixty six percent were of normal nutrition and thirty four were undernourished. They also did nasopharyngeal cultures for case. Results revealed that decreased blood zinc levels (OR 0.995; P value equal to 0.001) were significantly associated with Pneumonia.

Kumar et al concluded that children with severe pneumonia have significant lower blood zinc level than the children without pneumonia and advised further studies for recommendation of zinc in the treatment of pneumonia.

In a study done in turkey Secil Arica et al (16) compared the plasma zinc levels in children with pneumonia and controls. They enrolled 25 children of 0-24 months age with pneumonia as based on WHO diagnostic criteria and ten healthy controls with same age. Results showed that iron and zinc level in the controls were significantly more than children with pneumonia ($p<0.01$). They concluded that infections particularly pneumonia may occur more frequent in children having zinc deficiency.

In a Pakistan based study Pushpa et al (17) studied association of serum zinc level with severe pneumonia in children. Study done at Liaquat University, Jamshroo, Sindh-Pakistan. Fifty children with severe pneumonia in the age group of two-sixty months and fifty matched control were recruited. They used WHO definition for sever pneumonia definition and further classified nutritional status using weight for age. There were thirty five males and fifteen females equally among cases and controls. Fifteen children were of less than

one year old and thirty five children aged one to five years equally among cases and controls. It was done at 2008 and got published in Pakistan journal of nutrition at 2009. They did zinc analysis using atomic Spectrophotometer. Serum zinc level in children with pneumonia was significantly lower than controls. (p= 0.019). They concluded that children with severe pneumonia have lower level of zinc as compared to healthy controls.

AIM OF THE STUDY

- To compare serum zinc level in children with Severe pneumonia with age, sex and nutritional matched controls.

STUDY JUSTIFICATION

- Zinc deficiency as a predisposing factor for infection is well established by many studies (9,10, 19) as zinc has a role in immune response , antioxidant properties etc.
- In developing countries, it is the undernutrition which causes severe pneumonia, increased illness duration and increased mortality
- Of micronutrients zinc has important role in the formation and maintenance of individuals defense against the infections(5,9)
- Zinc supplementation in diarrhoea and severe acute malnutrition is routinely recommended by world health organisation(20)
- Zinc supplementation resulting decreased occurrence, early recovery and reduced severity of pneumonia has been shown by number of studies.(13,14,18)
- Recommendations for zinc as an adjuvant therapy for pneumonia in developing countries is given in standard paediatrics text books(3) .
- Though zinc supplementation is specifically recommended for developing countries, studies describing serum zinc level in pneumonia in our region are few.

- There is no study available demonstrating the serum zinc level in children with pneumonia.
- There is a need to demonstrate the zinc level in children with pneumonia in our setup for further recommendations.
- This study is well designed to compare the serum zinc level in children admitted with pneumonia to the matched controls

METHODOLOGY

- STUDY PLACE : Institute of child health and hospital for children. Madras medical college, Egmore, Chennai.
- STUDY DESIGN : Descriptional study.
- STUDY PERIOD : January 2012 to December 2012
- STUDY POPULATION : Children having clinical and radiological evidence of pneumonia in the age group of 3months to 5 years admitted in study period.
- CONFLICT OF INTEREST : Nil
- FINANCIAL SUPPORT : Nil
- ETHICAL COMMITTEE CLEARANCE: Obtained
- SAMPLE SIZE : 50 cases and 50 controls

INCLUSION CRITERIA

- All children with clinical and radiological evidence of pneumonia in the age group of 2 months to 5 years admitted in study period.
- Clinical evidence: severe pneumonia according to WHO classification.
- Radiological evidence: chest x ray reported as pneumonia in children with clinical evidence.

EXCLUSION CRITERIA

- Any child on zinc supplementation
- Aspiration pneumonia
- Chemical pneumonia
- Persistent pneumonia
- Neonates
- Severe acute malnutrition
- Co existing illness
- Chronic history/ Immunocompromised children

MANOEUVRE

This study is done at a tertiary care children's hospital in south India. This hospital receives local and referral cases from all over Tamilnadu and nearby states.. All children admitted with pneumonia are examined and those with chest indrawing are recruited inclusion and exclusion criteria.

Children are recruited to the study only after obtaining informed consent from the parents.Chest x-ray is taken as a part of routine evaluation for children with pneumonia at the time of admission itself as per the hospital routine.

Weight is measured using electronic weighing machine. Children were weighed with as little clothing as customs permitted. The child was not in contact with any other object.

For measuring length below the age of 2 years a horizontal measuring rod (or) infantometer was used. Length measurement needed two people. Shoes were removed & child was placed on a flat surface.

One person preferably the mother maintained the top of child's head against the fixed vertical head board with the child's eyes

directed upwards. The other persons firmly pressed the knees together and down so that they touched the horizontal surface and then moved the mobile foot board so that if touched the heels when the feet were at right angle. Accuracy was adjusted to the nearest0.5cm. Beyond the age of two years, a vertical measuring rod or stadiometer was used. The child was made to stand bare foot and the heels, buttocks, shoulders & occiput touching the wall and looking straight ahead. The chin was made to be straight (in Frankfurt planes). The observer read the measurement directly after lowering the cursor or placing a horizontally held book or wooden board in order to touch the top of head. The hair flattened and the accuracy measured to the nearest0.5cm.

Weight for length/ weight for height is calculated. According to world health organisation chart the nutritional status classified. Children having z score less than -3 are classified as severe acute malnutrition and excluded from study as per exclusion criteria. Children having z score between -3 to -2 are classified as moderate acute malnutrition and having z score more than -2 are classified as normal nutrition.

Controls with similar age (adjusted for 2 months), sex and nutritional status are recruited equal number for cases.

For both cases and control group, two millilitre of blood is drawn in a empty clean plastic tube. The blood is collected by venepuncture after properly preparing the site with povidone iodine and alcohol and allowing it to dry. The collected blood is allowed to clot. Serum separated after centrifuging the clotted sample. In the separated serum zinc level is obtained using photometry. All information are entered in data collection form.

STATISTICAL ANALYSIS

All data entered in data collection form are entered in excel spread sheet. For statistical analysis SPSS version 16 is used. The mean and standard deviation are calculated for continuous data. To compare the mean serum zinc between two groups Independent t test is used. For comparing more than two groups anova one way is used.

RESULTS

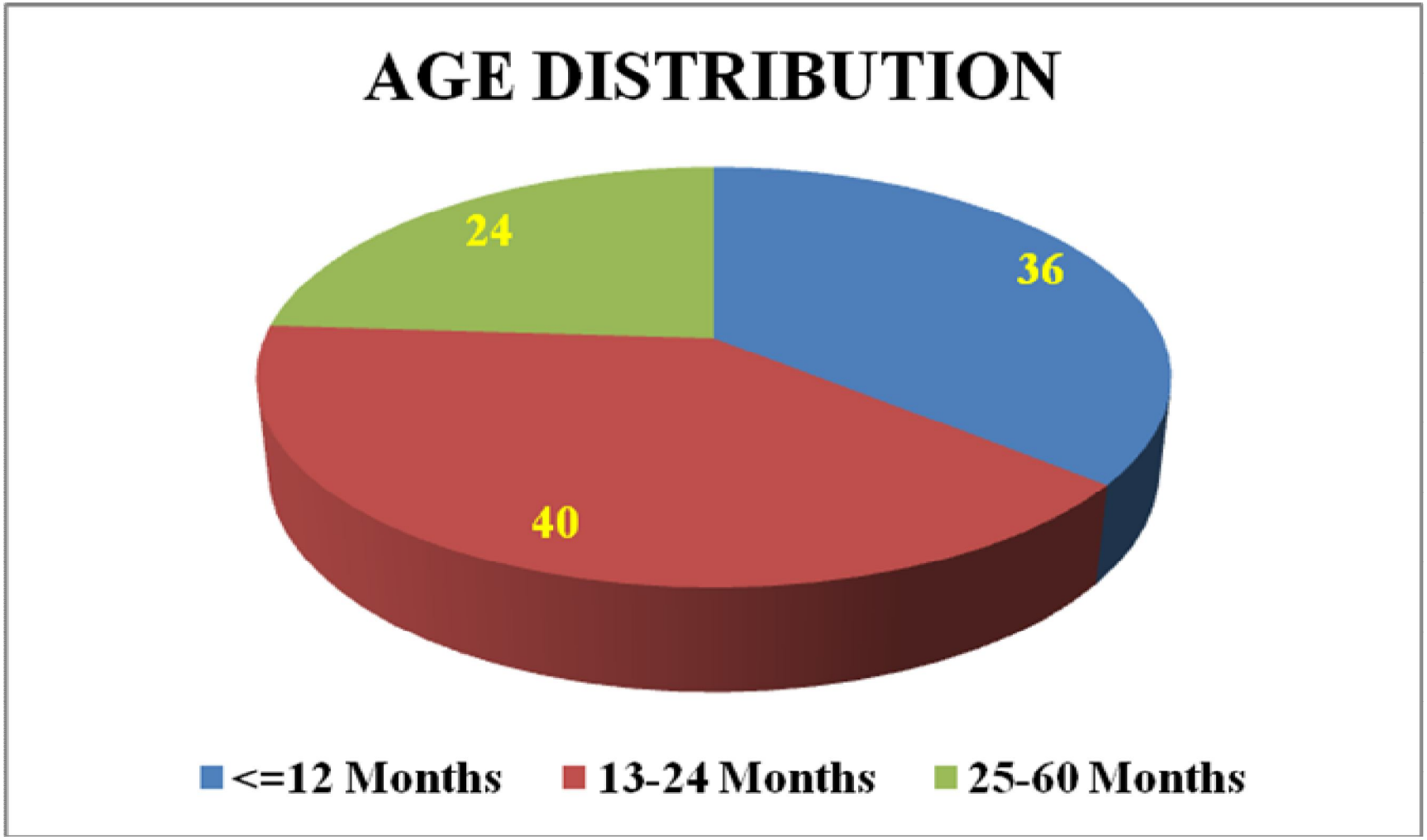
The study population consists of 100 children with 50 cases and 50 controls.

AGE DISTRIBUTION

The age distribution in cases are eighteen children less than or equal to twelve months of age. Twenty are between thirteen to twenty four months and twelve between twenty five to sixty months. Controls in the same age group nearest within two months are recruited

Age	Case	Control	Total Frequency	Percent	Valid Percent	Cumulative Percent
<=12 months	18	18	36	36	36.0	36.0
13-24 months	20	20	40	40.0	40.0	76
25-60 months	12	12	24	24.0	24.0	100.0
Total	50	50	100	100.0	100.0	

Table : 1 Age Distribution

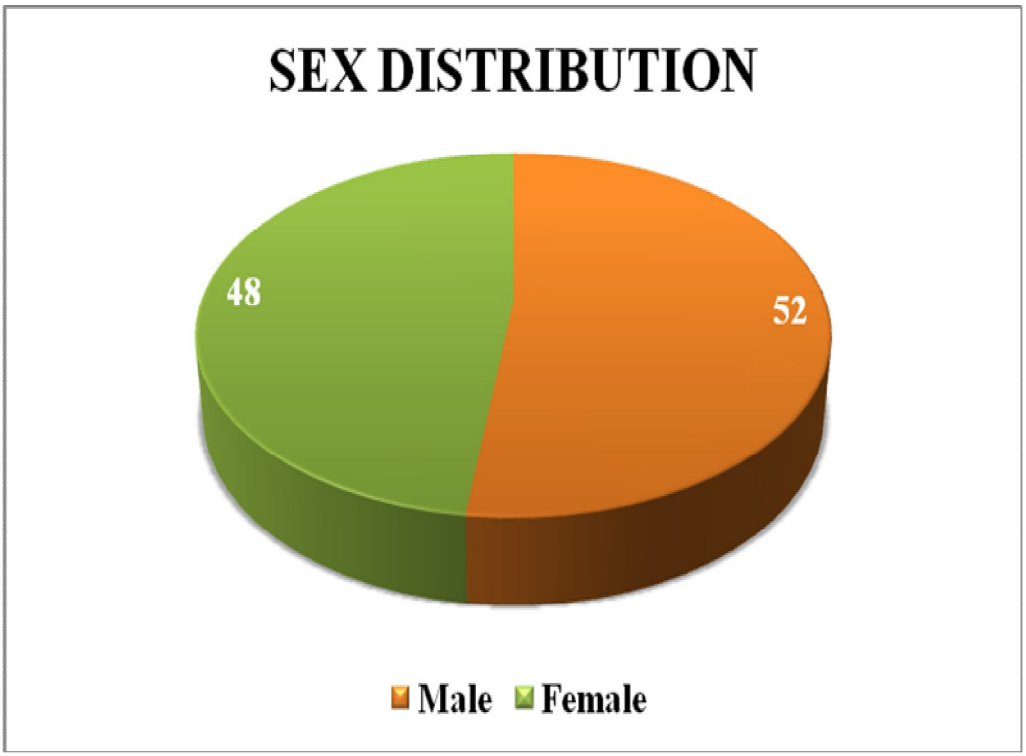

AGE DISTRIBUTION
24
36
40
<=12 Months
13-24 Months
25-60 Months

SEX DISTRIBUTION

Of the fifty children recruited with pneumonia, there are twenty six male children and twenty four female children. Equal number of controls are also recruited.

Sex	Case	Control	Frequency	Percent	Valid	Cumulative Percent
Male	26	26	52	52.0	52.0	52.0
Female	24	24	48	48.0	48.0	100.0
Total	50	50	100	100.0	100.0	

Table : 2 Sex Distribution



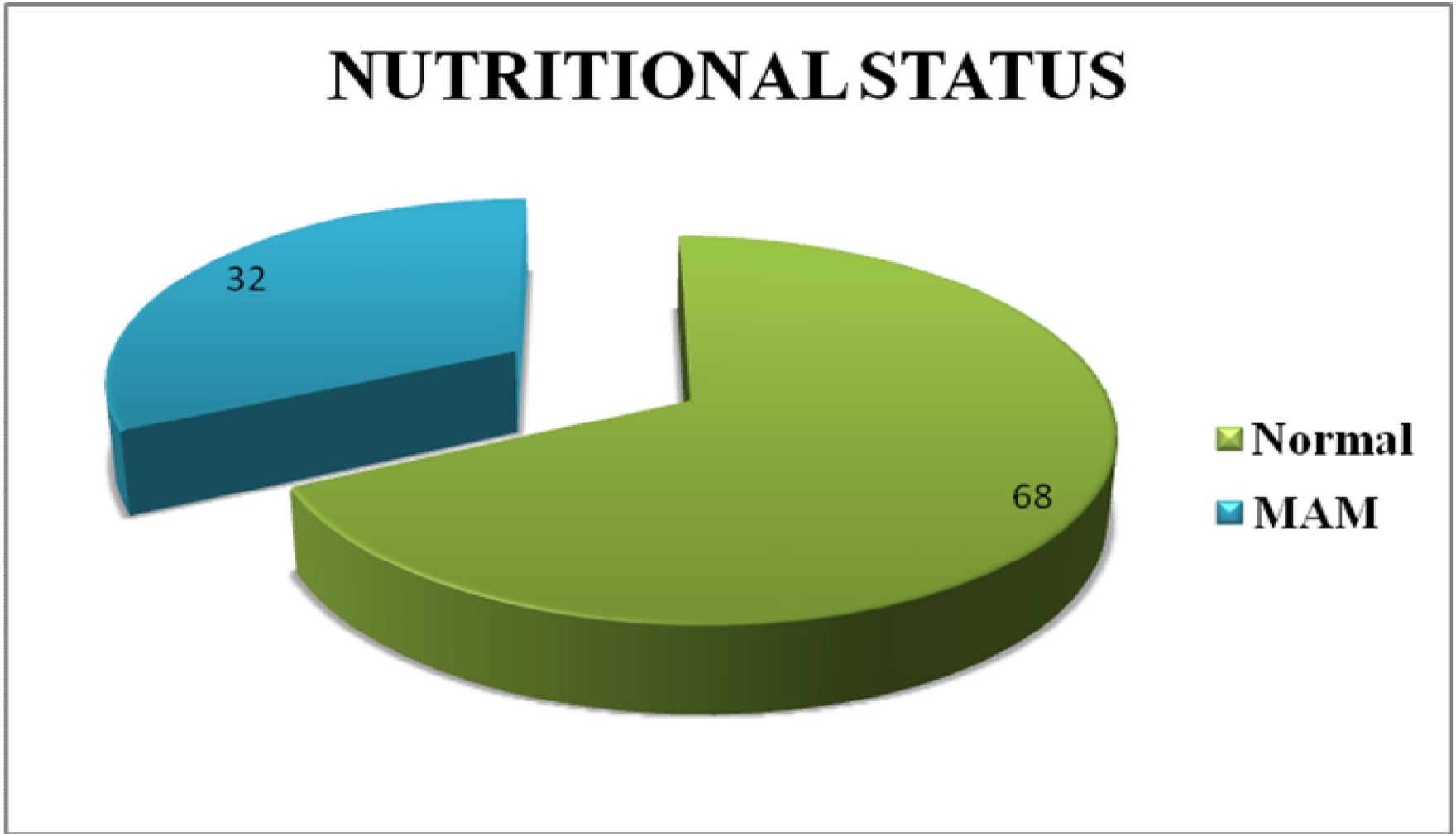
NUTRITIONAL STATUS

Nutritional status of children admitted with pneumonia are assessed at the time of admission. Weight for length / height calculated and nutritional status classified as described earlier. Thirty four children with normal nutrition and sixteen children with moderate acute malnutrition according to WHO classification are found. Children with severe acute malnutrition are excluded. Controls with appropriate nutritional status are included for each case Nutritional status in total study group is given in the Table.3

	Case	Control	Frequency	Percent	Valid Percent	Cumulative Percent
Normal	34	34	68	68.0	68.0	68.0
MAM*	16	16	32	32.0	32.0	100.0
Total	50	50	100	100.0	100.0	

Table : 3 Nutritional Status

*MAM-moderate acute malnutrition


NUTRITIONAL STATUS
32
68
Normal
MAM

SERUM ZINC LEVELS

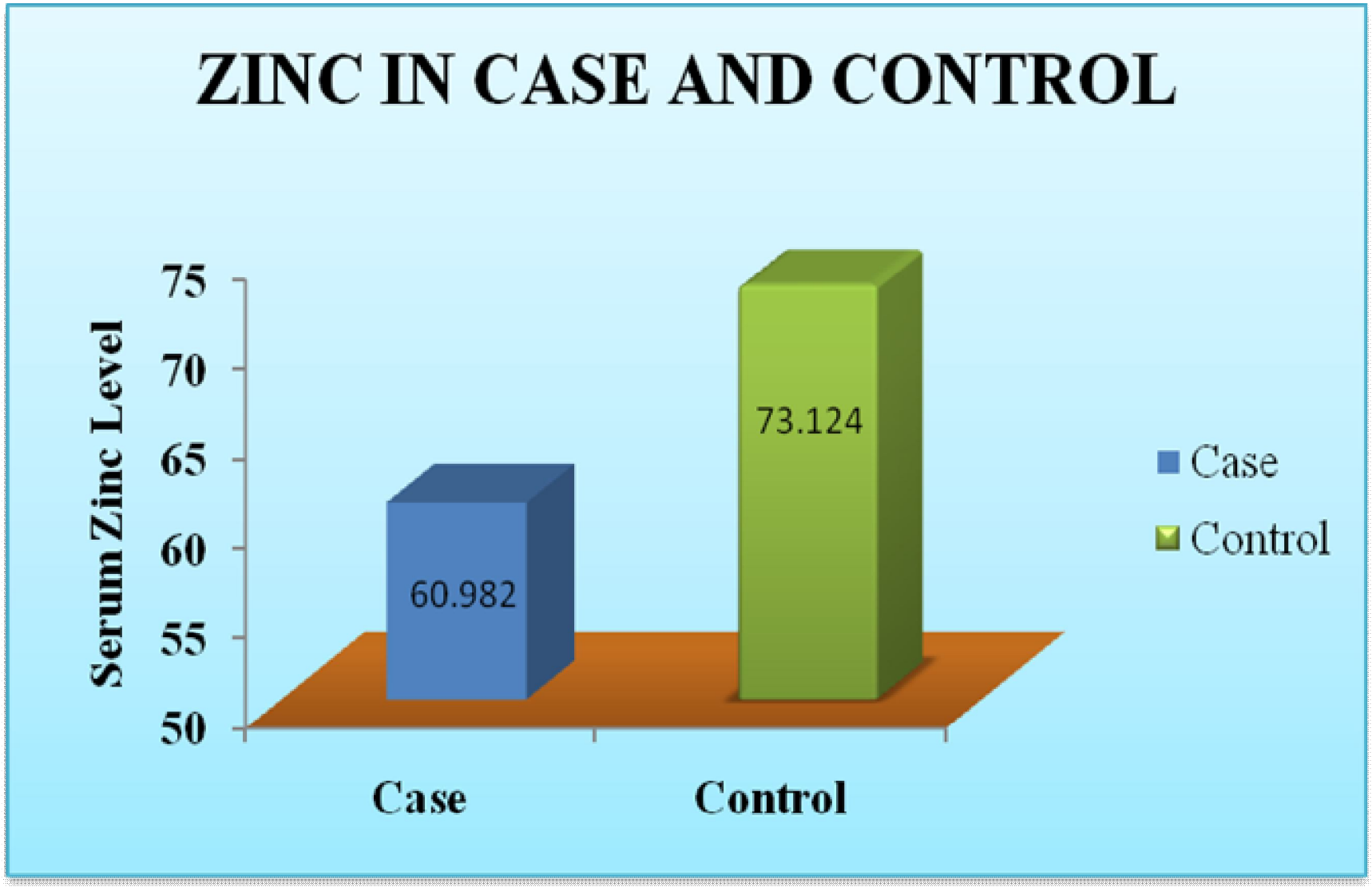
SERUM ZINC LEVEL IN PNEUMONIA

Mean serum zinc level in children with Pneumonia is compared with that of control group. There is a significant difference between children with pneumonia and controls in serum zinc levels. Mean serum zinc level in children with pneumonia is 60.982 microgram per decilitre. The mean serum zinc level in age, sex and nutrition matched controls is 73.124 microgram/decilitre .Mean serum zinc level is significantly lower in children with pneumonia than their matched controls (p=0.001)

Type	N	Mean Zinc Level*	Std. Deviation	P-value
Case	50	60.982	18.8926	0.001
Control	50	73.124	17.1420	

Table 4 : Zinc level in cases and control

*mean serum zinc level expressed in microgram/ decilitre


ZINC IN CASE AND CONTROL
Serum Zinc Level
75
70
65
60
55
50
60.982
73.124
Case
Control
Case
Control

AGE AND ZINC

The mean serum zinc level with in different age group of children with Pneumonia compared. There is no significant difference between the mean serum zinc between different age group of children admitted with pneumonia. (p=0.826)

Age	N	Mean*	Std. Deviation	P-value
<=12 months	18	57.728	15.6877	0.826
13-24 months	20	61.090	19.7358	
25-60 months	12	61.360	22.3598	

Table.5. Zinc level different age group in children admitted with pneumonia

* mean serum zinc level in microgram/ decilitre

The mean serum zinc level in each group showed significantly lower value compared with controls of each group

The mean serum zinc value in children less than or equal to twelve months of age with pneumonia is 57.72 microgram/decilitre. In the control group the mean serum zinc value is 70.80 microgram / decilitre.

Type	N	Mean*	Std. Deviation	P-Value
Case	18	57.728	15.6877	0.020
Control	18	70.800	16.3791	

Table : 6 Zinc in Children <=12 months old

* Mean zinc level mentioned in microgram / decilitre

The mean serum zinc level in children with pneumonia in the age group of 13-24 months is 61.090 microgram / decilitre and in the control group is 73.765 microgram / decilitre.

Type	N	Mean*	Std. Deviation	P-value
Case	20	61.090	19.7358	0.04
Control	20	73.765	18.1904	

Table : 7 Zinc in children 13-24 months old

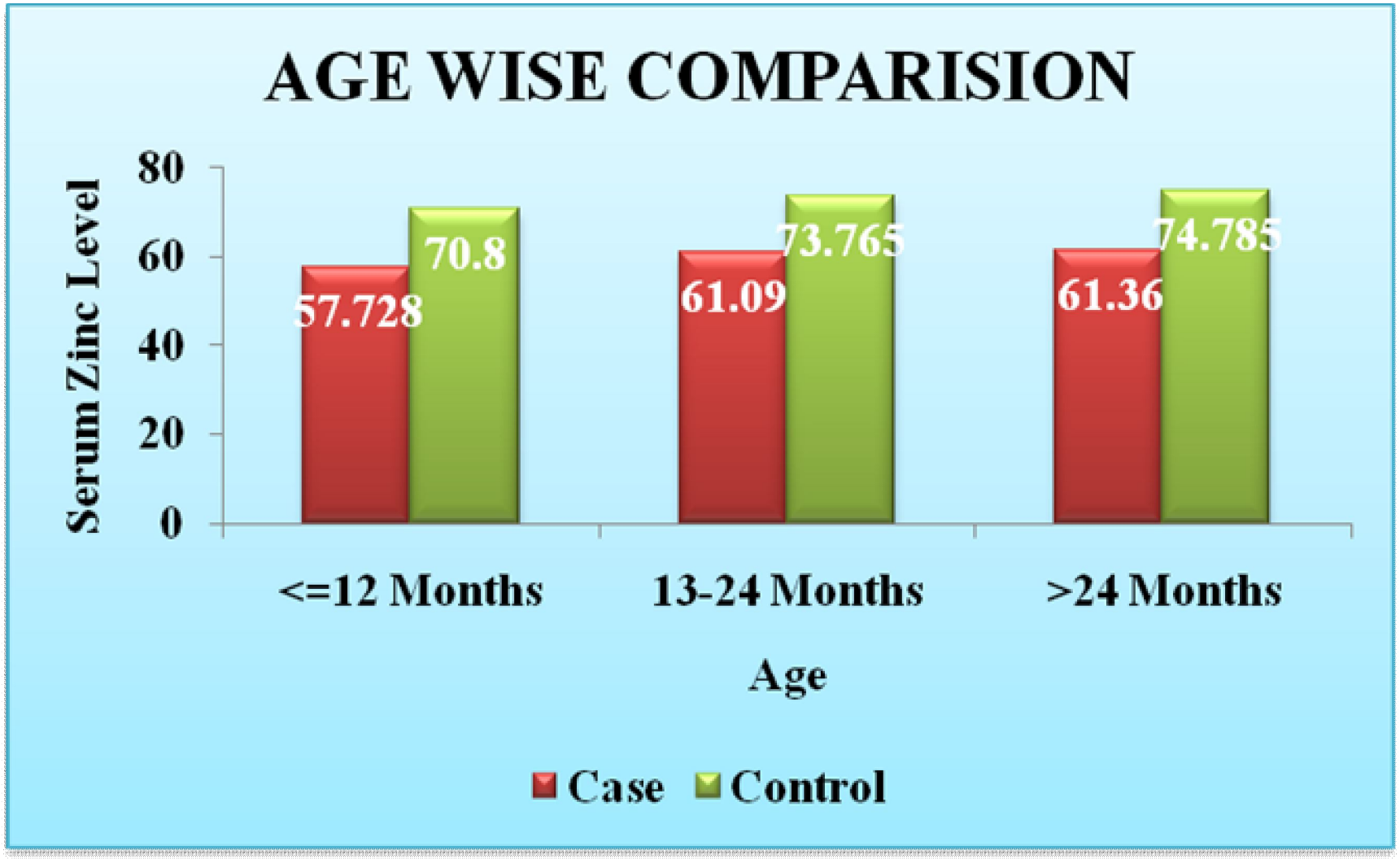
*mean zinc level in microgram/ decilitre

The mean serum zinc level in children with pneumonia in the age group of > 24 months is 61.360 microgram / decilitre and in control group is 74.785 microgram / decilitre.

Type	N	Mean*	P-value
Case	12	61.360	0.07
Control	12	74.785	

Table : 8 Zinc in children > 24 months

* mean serum zinc level in microgram/decilitre.


AGE WISE COMPARISION
Serum Zinc Level
80
60
40
20
0
57.728
70.8
61.09
73.765
61.36
74.785
<=12 Months
13-24 Months
>24 Months
Age
Case
Control

SEX AND ZINC

Mean serum zinc level in children admitted with pneumonia of both sexes compared. Mean serum zinc level in male children admitted with pneumonia is 61.98 microgram / decilitre. Zinc level in female children admitted with pneumonia is 59.90 microgram / decilitre. There is no significant difference between mean serum zinc level of both sexes in children admitted with pneumonia (p=0.700)

Sex	N	Mean Zinc level	Std Deviation	P-value
Male	26	61.985	18.1464	0.700
Female	24	59.896	20.0031	

Table : 9 Zinc in both Sex with Pneumonia

*mean serum zinc level in microgram/ decilitre

Serum zinc level of individual sex is compared in cases and controls. The mean serum zinc level in male children admitted with pneumonia is 61.985 microgram / decilitre. The mean serum zinc level in male children with controls is 73.800 microgram / decilitre. The mean serum zinc in male children admitted with pneumonia is significantly lower than male controls.(p= 0.017)

Type	N	Mean*	Std. Deviation	P-value
Case	26	61.985	18.1464	0.017
Control	26	73.800	16.2104	

Table : 10 Zinc in male children

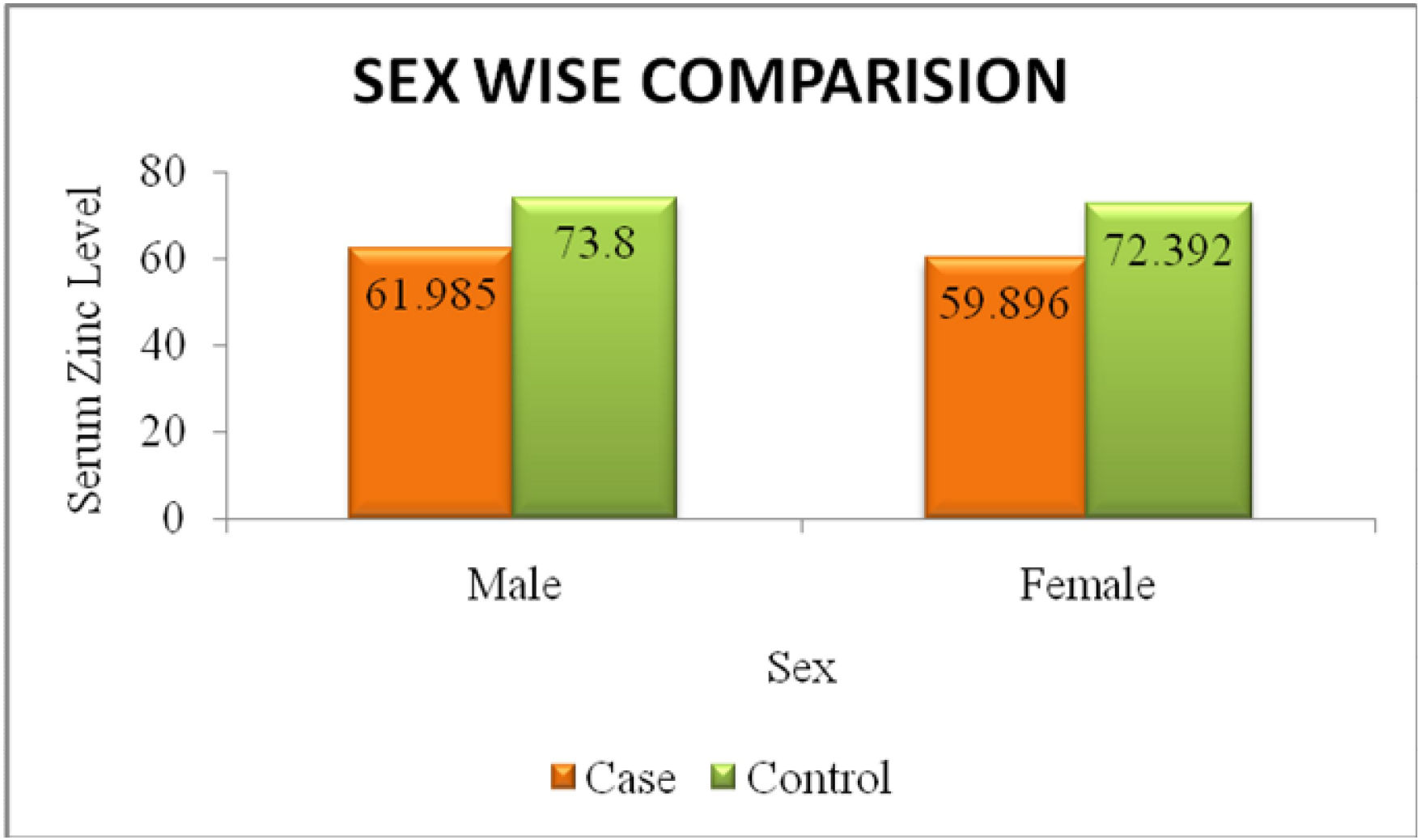
* mean zinc level in microgram / decilitre

The mean serum zinc level in female children admitted with pneumonia is 59.896 microgram / decilitre. Mean serum zinc level in female control is 72.392 microgram / decilitre. Zinc level is significantly lower in female children with pneumonia than female controls

Type	N	Mean*	Std. Deviation	P-value
Case	24	59.896	20.0031	0.029
Control	24	72.392	18.4205	

Table : 11 Zinc in female children

*** mean zinc level in microgram / decilitre**


SEX WISE COMPARISION
Serum Zinc Level
80
60
40
20
0
61.985
73.8
59.896
72.392
Male
Female
Sex
Case
Control

NUTRITIONAL STATUS AND ZINC

Nutritional status	N	Mean Zinc level	Std Deviation	P-value
Normal	34	63.744*	19.8348	0.02
MAM**	16	50.976*	15.3310	

Table : 12 Zinc in different nutritional status and pneumonia

*mean serum zinc level expressed in microgram/ decilitre

** MAM – moderate acute malnutrition

Mean serum zinc level compared between children admitted with pneumonia with normal nutrition and children admitted with pneumonia with moderate acute malnutrition. Mean serum zinc level (50.976 microgram/dl) in children admitted with pneumonia with moderate acute malnutrition is significantly lower than mean serum zinc level (63.7444 microgram/dl) of children admitted with pneumonia with normal nutrition (p=0.001)

Type	N	Mean*	Std. Deviation	P-value
Case	34	63.744	19.8348	0.006
Control	34	76.925	18.2868	

Table : 13 Zinc in normal nutrition in pneumonia

*mean serum zinc level in milligram / decilitre

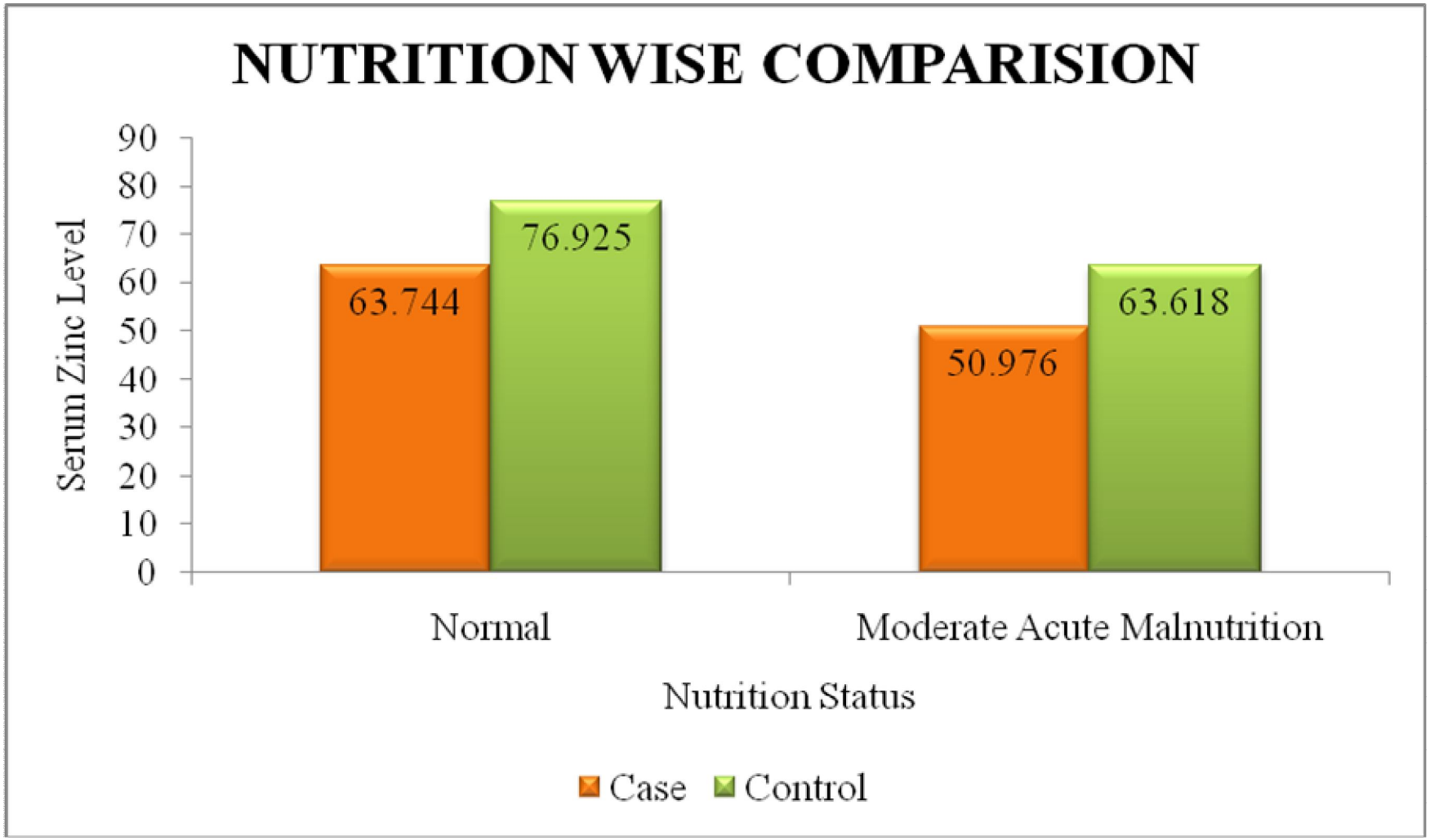
The mean serum zinc level in children admitted with pneumonia with normal nutrition is 63.744 microgram / decilitre. The mean serum zinc level in controls with normal nutrition is 76.925 microgram / decilitre. Zinc level in pneumonia group with normal nutrition is significantly low than control group with normal nutrition.(p=0.006).

Type	N	Mean*	Std. Deviation	P-value
Case	16	50.976	15.3310	0.02
Control	16	63.618	13.6636	

Table : 14 Zinc with MAM in Pneumonia

*mean serum zinc level in milligram / decilitre.

The mean serum zinc level in children admitted with pneumonia with Moderate acute malnutrition is 50.976 microgram / decilitre. The mean serum zinc level in controls with moderate acute malnutrition is 63.618 microgram / decilitre. Zinc level in pneumonia group with moderate acute malnutrition is significantly low than control group with moderate acute malnutrition.(p=0.02).


NUTRITION WISE COMPARISION
Serum Zinc Level
90
80
70
60
50
40
30
20
10
0
63.744
76.925
50.976
63.618
Normal
Moderate Acute Malnutrition
Nutrition Status
Case
Control

DISCUSSION

There is no significant difference between the mean serum zinc levels between different age group of children admitted with pneumonia. (p=0.826). This is similar to the findings of previous studies (15,17). The mean serum zinc level in all age group admitted with pneumonia have are low when compared to controls. It is statistically significant in all sub age group except in children greater than 25 months. In this age group though serum zinc level is low it is not statistically significant and it may be due to less number of children recruited in this age group. Studies done in serum zinc level in pneumonia ,diarrhoea showed similar results that age is not a confounding factor in serum zinc in pneumonia. It is observed in all studies irrespective of geographical area namely north India (15), turkey(16) except a study done at Pakistan (17) where puspha et al showed low serum zinc level in infant age.

Comparison of mean serum zinc level between male and female children recruited in this study doesn't showed any significant difference. There is no significant difference between mean serum zinc level of both sexes in children admitted with pneumonia (p=0.700). Both male and female children with pneumonia have

statistically low mean serum zinc level compared to controls. Most of the published data (15, 16, 17) had similar results. They all had similar finding that there was no statistical significant difference in serum zinc level between both sexes.

Of the total recruited children (including cases and control) sixty eight children are in normal nutritional status and thirty two children have moderate acute malnutrition. Analysis with in pneumonia group also shows that the mean serum zinc level in children with moderate acute malnutrition is significantly low than children with normal nutrition(p=0.02). Low mean serum zinc level in children in moderate acute malnutrition may be due to poor intake leading to zinc deficiency associated with other micronutrient deficiency. Similar finding found in study done by Kumar and associates (15). Further studies needed for recommending zinc supplementation in children with moderate acute malnutrition.

Mean serum zinc level is significantly lower in children with severe pneumonia than the matched controls (p=0.001).This is similar to the finding of the Kumar et el (15), Secil arica et al (16)and Puspha et al(17). Main proposed cause for having low mean serum zinc level is already existing zinc deficiency which increases the susceptibility of

child to get pneumonia by impairing child's immunity (18). Other explanation for low serum zinc level is shift of zinc from plasma to liver. This is said to caused by cytokines (interleukin-6) released in infection (5).

Deficiency of zinc, due to inadequate intake of food containing zinc or decreased absorption, is more commonly seen in developing countries.(19) It is one of the ten important factors leading to increased illness in children in developing countries(20).

Supplementation of zinc in children decreasing the morbidity and fatality in infections was shown by trials (9,13) Pneumonia being the leading killer infectious disease in children, effect of zinc supplementation has been extensively studied in pneumonia. Zinc supplementation though consistently shown to decrease the occurrence and preventive mortality due to pneumonia(13,14), effect as adjuvant treatment is variable(27).

The benefit of zinc supplement to prevent and decrease the severity of pneumonia is mainly due to correction of zinc deficiency. The finding of low mean serum zinc level in children with severe pneumonia favours this. There is need of further studies to recommend routine supplementation of zinc for children to prevent pneumonia and

for therapeutic use of zinc in severe pneumonia. Low serum zinc level found in children with pneumonia probably due to zinc deficiency highlights the importance of inclusion of food item containing good qualitative (absorbable) and quantitative amount of zinc in children's diet.

STUDY LIMITATIONS

- Cases are recruited as per clinical and radiological criteria. Etiological analysis is not done. This is not done because of low culture yield in cases of pneumonia. This drawback is partly overcome by including only children with clinical features of severe pneumonia and radiological evidence of consolidation. This occurs mostly with bacterial pneumonia. But individual organisms could not be identified.
- Follow up value after pneumonia resolution might have helped to differentiate low serum zinc level due to acute phase reaction.

SUMMARY

- Children admitted with severe pneumonia has significantly lower mean serum zinc level when compared to age, sex and nutritionally matched controls.
- Children with moderate acute malnutrition has significantly lower mean serum zinc level when compared to children with normal nutrition.
- There is no significant difference in serum zinc level in different age group studied.
- There is no significant difference in serum zinc level between both sexes in the study group.

CONCLUSION

Serum zinc levels are significantly low in children with severe pneumonia compared with age, sex and nutritionally matched controls.

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PROFORMA

Name	:
Age	:
Sex	:
IP NO	:
Weight	:
Height/length	:
Nutritional status	:
Address	:
Presenting complaints	:
Course of illness	:
History of other illness/ zinc intake	:
Examination findings	:
CXR findings	:
Serum zinc level	:
Treatment and Follow up	:

MASTER CHART

Sl. no	Type	age	sex	nutri_status	type_pneu	x-ray	synpneumonic effusion	zinc
1	1	2	2	2	1	1	1	32.4
2	1	2	2	2	1	1	2	57.5
3	1	1	1	2	1	1	2	51.3
4	1	3	1	2	1	1	2	85.9
5	1	2	1	2	1	1	2	57.8
6	1	3	1	1	1	1	2	54.4
7	1	1	2	2	1	1	2	78.4
8	1	1	1	1	1	1	2	36.2
9	1	3	1	1	1	1	2	48.1
10	1	3	1	2	1	1	2	52.2
11	1	3	2	2	1	1	2	58.1
12	1	3	1	2	1	1	2	84.6
13	1	1	2	2	1	1	2	38.1
14	1	1	1	2	1	1	2	70.4
15	1	2	2	1	1	1	2	40.4
16	1	2	1	2	1	1	1	54.6
17	1	3	2	1	1	1	2	92
18	1	1	2	1	1	1	2	72.8
19	1	2	2	2	1	1	2	72.6
20	1	3	1	2	1	1	2	64.8
21	1	3	2	2	1	1	2	39
22	1	2	2	2	1	1	2	40.4
23	1	1	2	1	1	1	2	34.4
24	1	1	1	1	1	1	2	71.4
25	1	2	2	1	1	1	2	96.4
26	1	2	1	1	1	1	2	52.3
27	1	3	2	2	1	1	2	73.2
28	1	1	2	2	1	1	2	32.8
29	1	2	1	2	1	1	2	78.2
30	1	1	1	2	1	1	1	56.4
31	1	2	1	1	1	1	2	54.8
32	1	2	2	2	1	1	2	38.2
33	1	1	2	2	1	1	2	42.8
34	1	1	1	1	1	1	2	72.3
35	1	2	1	2	1	1	2	54.2
36	1	2	1	2	1	1	2	73.2
37	1	1	2	1	1	1	2	74
38	1	1	1	2	1	1	2	70.4
39	1	1	2	2	1	1	2	54.1
40	1	2	1	2	1	1	2	36.4
41	1	2	2	2	1	1	1	52.4

42	1	2	1	1	1	1	2	91.8
43	1	1	2	2	1	1	2	74.6
44	1	1	2	1	1	1	2	55.7
45	1	3	1	2	1	1	2	34.5
46	1	2	1	2	1	1	1	71.8
47	1	1	1	2	1	1	2	36.2
48	1	2	2	2	1	1	2	54.2
49	1	3	2	1	1	1	2	76.4
50	1	2	1	2	1	1	2	78.4
51	2	1	1	1				68
52	2	1	1	1				62.8
53	2	1	1	1				60.3
54	2	1	1	2				80.4
55	2	1	1	2				61.3
56	2	1	1	2				90.4
57	2	1	1	2				90.6
58	2	1	1	2				62.8
59	2	1	2	1				80.7
60	2	1	2	1				50.2
61	2	1	2	1				64
62	2	1	2	1				66.5
63	2	1	2	2				82.6
64	2	1	2	2				46.7
65	2	1	2	2				64.9
66	2	1	2	2				72.8
67	2	1	2	2				70.6
68	2	1	2	2				78.8
69	2	2	1	1				73.2
70	2	2	1	1				59.3
71	2	2	1	1				66.8
72	2	2	1	2				74.8
73	2	2	1	2				64.6
74	2	2	1	2				90.2
75	2	2	1	2				58.2
76	2	2	1	2				73.2
77	2	2	1	2				104.8
78	2	2	1	2				116.6
79	2	2	1	2				79.3
80	2	2	2	1				62.8
81	2	2	2	1				70.4
82	2	2	2	2				62.7
83	2	2	2	2				73.5

84	2	2	2	2				58.4
85	2	2	2	2				92.6
86	2	2	2	2				36.4
87	2	2	2	2				84.2
88	2	2	2	2				64.3
89	2	3	1	1				68.6
90	2	3	1	1				84.2
91	2	3	1	2				98.5
92	2	3	1	2				54.2
93	2	3	1	2				108.4
94	2	3	1	2				64.3
95	2	3	1	2				60.2
96	2	3	2	1				72.6
97	2	3	2	1				78.6
98	2	3	2	2				64.7
99	2	3	2	2				63.8
100	2	3	2	2				88.4