

## Comparative Study of Oral Zinc In The Treatment Of acute Diarrhea.

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**Abstract: BACKGROUND:** Diarrhoea is a major public health problem in children under the age of 5 years. It may lead to deaths in children below 2 years of age, due to diarrhea occurring during the first 2 years of life. Zinc deficiency is more in children in developing countries. Supplemental zinc provides to treat both acute and persistent diarrhoea in children.

**OBJECTIVES:** To determine the effects of daily supplementation with 20 mg of elemental zinc on the duration and severity of acute and persistent diarrhoea.

**METHODS:** The present study carried out in Govt. Head Quarters hospital Tiruppur, from 20<sup>th</sup> December 2018 to 18<sup>th</sup> March 2019 over a period of 3 months. A detailed clinical study of 100 children between the age group of 6 months to 5 years with acute and persistent diarrhoea was done. Zinc was given to 50% of cases and wasn't given to the rest of 50%. Duration of hospital stay and duration of diarrhoeal episodes were compared in both the groups. **RESULTS:** Patients administered with Zinc had significantly less duration of hospital stay. 93.47% patients with zinc therapy were recovered within 6 days and 76.08% patients who didn't receive zinc were recovered within 6 days.

**CONCLUSION:** The diarrhoeal episodes were common in diseases like acute gastroenteritis, acute febrile illness and lower respiratory tract infections. Patients who were taken elemental zinc supplement had significantly less duration of hospital stay and less diarrhoeal episodes on follow up compared to the non-zinc group.

**Keywords:** Zinc supplement, Acute Diarrhoea, Persistent Diarrhoea, zinc deficiency

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### I. Introduction

The diarrhoeal disease is one of the leading causes of illness and death in young children in developing countries.<sup>1</sup> Mortality rate of the diarrhoea disease in children below 5 years of age has dropped from approximately 700,000 deaths in 2011 to nearly 594,000 deaths in 2012, diarrhoea still remains one of the leading causes of child deaths around the world.<sup>2</sup> The World Health Organization and UNICEF have estimated that 2.5 billion episodes of diarrhoea were found in each year with children less than 5 years in developing countries.<sup>3</sup>

Persistent diarrhoea defines that longer duration of diarrhoeal episodes, produce greatest effect on these outcomes. Treatment of acute diarrhoea starting with oral rehydration solution, resulting in decreased mortality from dehydrating diarrhoeas but there is no reduction in the duration of episodes or their consequences due to diarrhoea, such as malnutrition.<sup>4</sup>

According to WHO guidelines for the management of diarrhoea recommends that early oral rehydration therapy and zinc supplementation in children between 6 and 60 months of age. This therapy is based on the beneficial effect of zinc treatment to reduce the duration and severity of diarrhoeal episodes in children less than 5 years old.<sup>5</sup>

18% reduction in diarrhoeal incidence was observed by the administration of Zinc supplementation in children with diarrhoea, 41% reduction in pneumonia, the leading causes of morbidity, stunting, and death in young children in developing countries.<sup>6</sup> Daily supplementation with zinc in combination with other nutrients, is unaffordable and expensive for poor countries. The foods richest in zinc are from animal sources, but these are not often included in toddlers' diets.<sup>7</sup>

Zinc helps to reduce diarrhoea morbidity and mortality by taking along with low-osmolality ORS and continued feeding, and also have beneficial effects on pneumonia in 2-3 months of therapy.<sup>8</sup> Zinc is one of the

most important trace elements that serves over 300 biological functions for human health and provides effects on multiple systems, including the gastrointestinal tract<sup>9</sup>.

Zinc is not stored in the body, so its level can be determined by the balance of dietary intake, absorption, and losses. Children with acute diarrhoea shows zinc deficiency because of the intestinal loss, and chronic zinc deficiency may leads to occurrence of diarrhea<sup>10</sup>.

Zinc regulates intestinal fluid transport and mucosal integrity, zinc has a special role in immunity, and zinc can modify expression of genes encoding several zinc-dependent enzymes, such as metallo proteases, cytokines and uroguanylin, zinc can modulate oxidative stress, and zinc is able to minimize the loss in diarrhea<sup>11</sup>.

Zinc works against invading intestinal pathogens and several toxins, including *Ciguatera fish toxin*, *Clostridium difficile toxin*, *Cryptosporidium parvum toxin*, *Rotavirus enterotoxin*, *Helicobacter pylori vacuolating toxin*, and *Vibrio para haemolyticus enterotoxin* induce a direct secretory effect in the enterocyte modifying intracellular Ca<sup>2+</sup><sup>12</sup>.

### SCALE USED IN DIARRHOEA (Acute Gastro enteritis)

The standard diagnostic scale used to identify bacterial pathogens is to perform stool cultures. This is time-consuming with a low sensitivity for pathogens. There is a lack of rapid and accurate diagnostic tools to predict the identity of gut pathogens at an early stage of the diseases. The Vesikari Scoring System (VSS) is the severity scale that was originally developed to evaluate the effectiveness and efficacy of rotavirus vaccines on 20 points<sup>12</sup>.

Scale component	Score on the Vesikari Scale			
	0 Points	1 Point	2 Points	3 Points
Duration of diarrhea (hr)	0	1–96	97–120	≥121
Maximum no. of watery stools per 24 hr	0	1–3	4–5	≥6
Duration of vomiting (hr)	0	1–24	25–48	≥49
Maximum no. of vomiting episodes per 24 hr	0	1	2–4	≥5
Maximum recorded rectal temperature (°C) †	<37.0	37.1–38.4	38.5–38.9	≥39.0
Unscheduled health care visit	None	NA	Primary care	Emergency department
Treatment	None	Rehydration with intravenous fluids	Hospitalization	NA

In the modified vesikari scale score one variable in the original score was replaced with the variable of unscheduled health care visits to better measure the effect of acute gastroenteritis in outpatients, given that the ability to perform frequent in person assessments in an outpatient cohort of children can be challenging. Score range from 0 to 20, with higher score indicating more severe disease.<sup>12</sup>

### ROLE OF ZINC IN DIARRHEA

According WHO claims that nutritional therapy containing mineral and vitamin supplements (Figure 1). Vitamin A, other micronutrients, such as folic acid, iron and B12 vitamin, for the action on the intestinal mucosa and on the immune response, should be recommended to patients with persistent diarrhea<sup>13</sup>.

Zinc is essential trace elements which is important for good health, proper development and functioning of the body. It is the main constituent of large number of enzymes and important role in metabolic processes such nucleic acid transcription and translation, protein synthesis, cell division and growth<sup>14</sup>.

The mechanism of Zinc reducing diarrhoea is unknown but could result from stimulating Na absorption and/or inhibiting anion secretion. Zinc administration corrects an underlying micronutrient deficiency that had contributed to the child's diarrhea<sup>15</sup>.

While taking zinc it helps to boost the body's immune response through a defense cascade, mobilization and sequestration of zinc to metallothionein-rich tissue, rapid up regulation of immune defense-specific protein synthesis, it stimulates the immune defense activity such as macrophages, lymphocytes, and natural killer cells, and antibody-dependent cytotoxicity. Children with good zinc intake may have a more robust immune response than those with poor zinc status<sup>16</sup>

Zinc helps to boost up the production of antibodies and circulating lymphocyte against infectious agents. Zinc also helps to maintain gut mucosal barrier integrity. Oral zinc sulphate administration may causes side effects like stomach upset, heartburn and nausea. Oral zinc precipitates vomiting due to its metallic aftertaste<sup>17</sup>.

For preventing the diarrhoea by zinc supplementation of a soy protein diet is used. Its for the recovery stage from severe protein-energy malnutrition occurring during late stages. The infants who did not receive the zinc supplement for diarrhoea have a high sodium content.

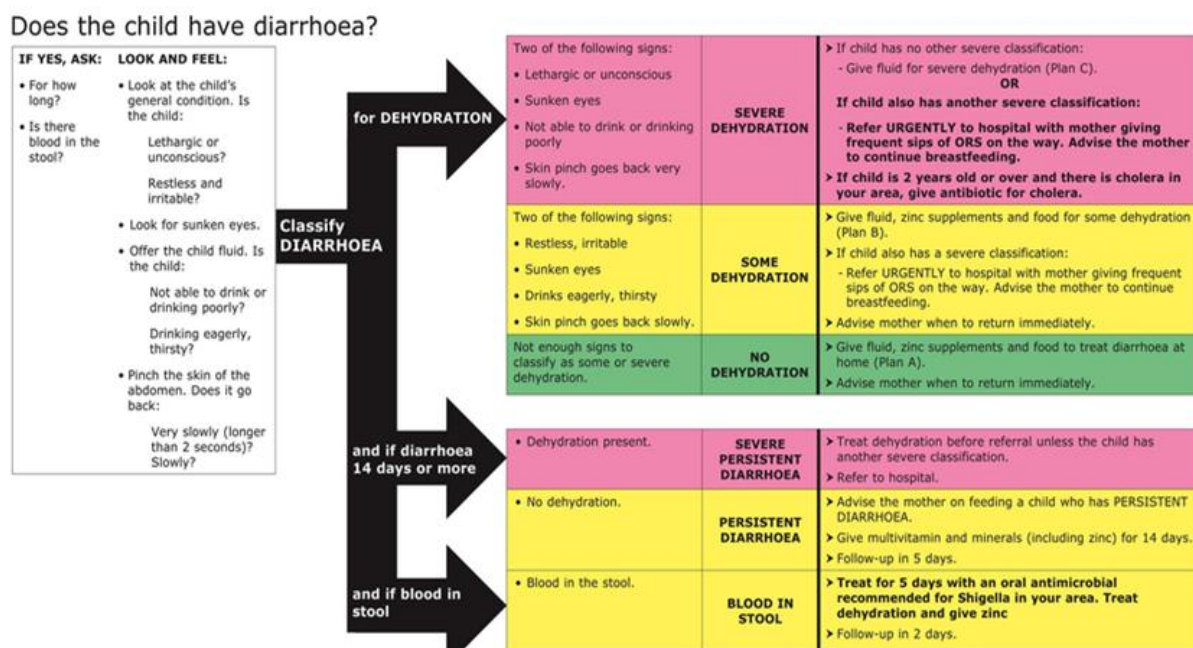


Figure 1: World Health organisation Treatment Chart<sup>18</sup>

Diarrhoea is a particularly deadly illness for young children, if acute diarrhoea left untreated its leads to death within a day or less. In this study we aimed to determine the effects of oral zinc in treatment of acute and persistent diarrhoea.

## II. Materials And Methods

The present study was carried out in Govt. Head Quarters hospital Tiruppur, from 20<sup>th</sup> December 2018 to 18<sup>th</sup> February 2019 over a period of 2 months. A detailed clinical study of 100 children between the age group of 6 months to 5 years with acute and persistent diarrhoea was done. Zinc was given to 50% of cases and was not given to the rest of 50%. Duration of hospital stay (in days) and duration of diarrhoeal episodes (in days) were compared in both the groups.

### INCLUSION CRITERIA

- > Patients having age in between 5 months to 6 years.
- > Patients with symptom of diarrhoea (Acute gastro enteritis , Acute febrile illness, and Lower respiratory tract infection etc)
- > Patients who were taken elemental Zinc for the treatment of diarrhoea.

### EXCLUSION CRITERIA

- > Immuno compromised patients
- > Outpatients came to the hospital
- > ICU patients.
- > Children with congenital lactose intolerance and those on lactose free diets.

Zinc sulphate was given to 50% of cases and was not given to the rest of 50%. The dose of zinc sulphate administered was 10mg OD for 14 days for children less than 1 year of age and 20mg BD for 14 days for children more than 1 year of age. Duration of hospital stay (in days) and duration of diarrheal episodes (in days) were compared in both the groups.

**STATISTICAL ANALYSIS**

The data obtained by performing questionnaires and Microsoft excel was used on normally distributed data .

**III. Results And Discussion**

**1. AGE DISTRIBUTION**

In Table 1. 45 patients (45%) were age group less than 1 years old, 32 patients (32%) were age in between 1-2 years old, 10 patients (10%) were age group in between 2-3 years old, 13 patients (13%) were age group between 3-5 years old. There is no significant association of age with diarrhoeal episodes.

Age in years	Number of patients	Percentage (%)
<1	40	40%
1-2	32	32%
2-3	18	18%
3-5	10	10%
Total	100	100%

**2. GENDER DISTRIBUTION.**

In Table 2: Out of 100 patients 54 patients (54%) were male and 46 patients(46%) were female. In both gender diarrhoea was developed, it seems like no association of gender with diarrhoea.

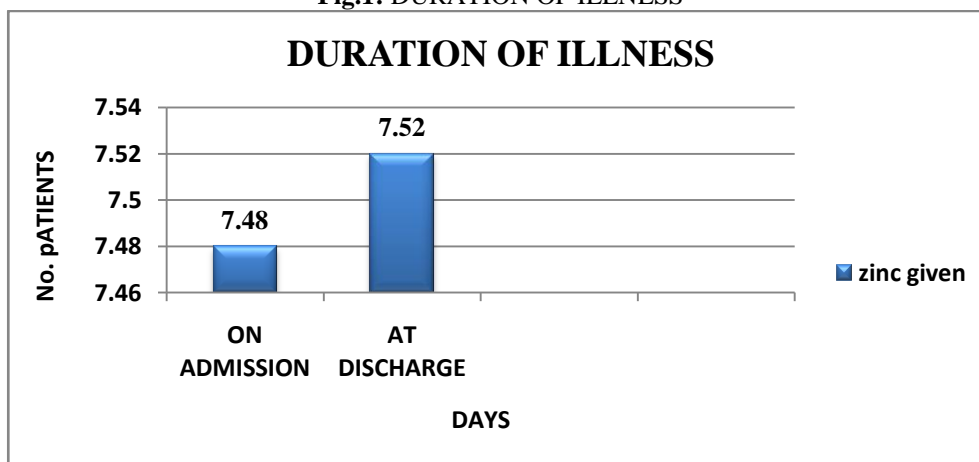
Gender	Number of patients	Percentage
Male	54	54%
Female	46	46%

**3.DURATION OF ILLNESS AT THE TIME OF PRESENTATION**

In Table 3. out of 100 patients 69 patients (69%) had illness for 1-2 days, 18 patients (18%) had illness for 3-4 days,10 patients (10%) had illness for 4-5 days and 3 patients (3%) had illness for more than 5 days.

Duration of illness ( days)	Number of patients	Percentage
1-2 days	69	69%
3-4 days	18	18%
4-5days	10	10%
>5 days	3	3%

**Fig.1: DURATION OF ILLNESS**

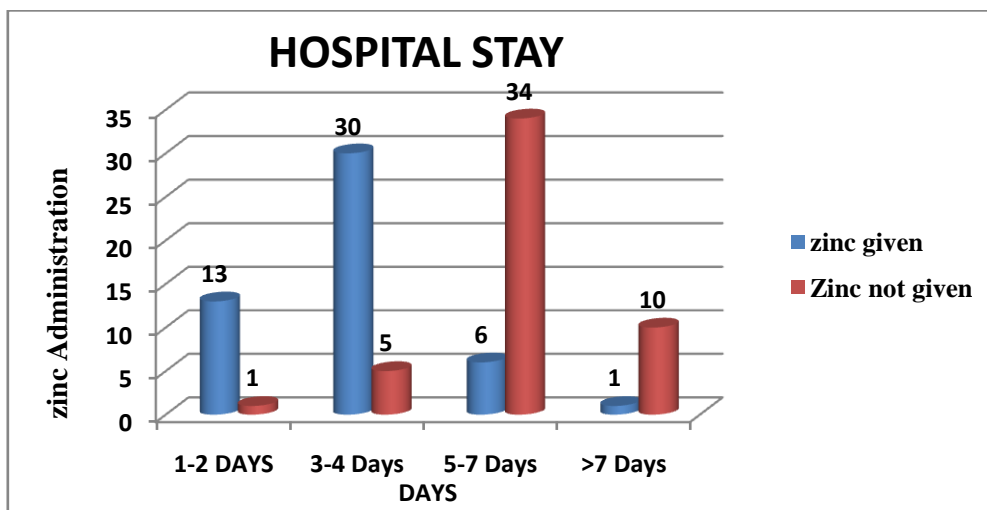


**4. EFFICACY OF ZINC ADMINISTRATION BASED ON DURATION OF HOSPITAL STAY IN DAYS.**

In Table 4: 13 patients who were taken zinc and 1 patient who didn't taken zinc was stayed on hospital for 1-2 days, 30 patients who were taken zinc and 5 patients who weren't taken zinc stayed on the hospital for 3-4days. 6 patients who were taken zinc and 34 patients who weren't taken zinc stayed on the hospital for 5-7days. Only 1 patient with zinc and about 10 patients without zinc therapy stayed on hospital more than 7days.

**Fig.2: Efficacy of zinc administration based on duration of hospital stay in days**

Hospital stay	Zinc Administration		Total
	Given	Not given	
1-2	13	1	14
3-4	30	5	35
5-7	6	34	40
>7	1	10	11
Total	50	50	100

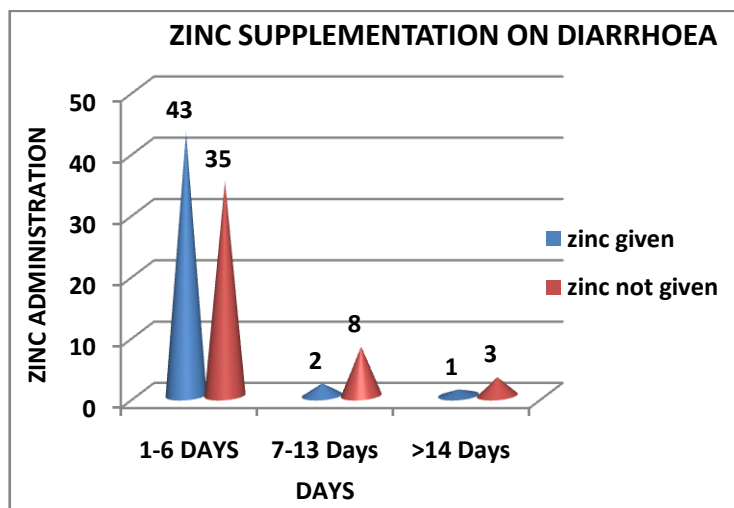


**5. IMPACT OF ZINC SUPPLEMENTATION ON DURATION OF DIARRHEAL EPISODES DURING FOLLOW UP.**

In Table 5: All cases were followed up till 14 days, out of which 8 cases were lost for follow up. The incidence of diarrhoea during follow up was lower in zinc supplemented as compared with those who did not receive zinc on follow up 93.47% of children in zinc group recovered within 6 days compared to 76.08% in the non-zinc group. In one case who received zinc supplementation, diarrheal episodes lasted till 14 days ,Three cases who did not receive zinc had diarrheal episodes up to 2 weeks.

**Fig.3** Impact of zinc supplementation on duration of diarrheal episodes during follow up.

Zinc	No. of Patients	Follow Up Days		
		1-6 days	7-13 days	>14 days
Given	46	43 (93.47)	2(4.34)	1(2.17)
Not Given	46	35(76.08)	8(17.39)	3(6.52)

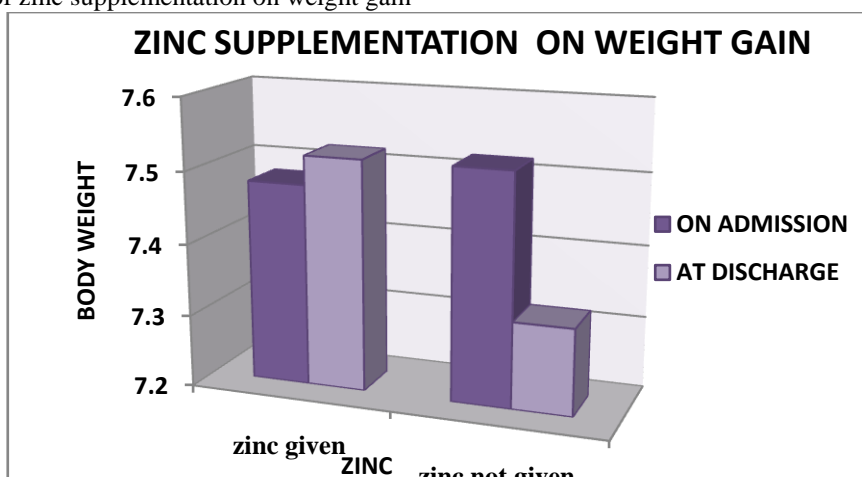


**6. IMPACT OF ZINC SUPPLEMENTATION ON WEIGHT GAIN**

In Table 6: on admission patients with zinc therapy had mean body weight of 7.48kg and at discharge mean body weight was 7.52kg. On admission patients without zinc therapy were shown mean body weight of 7.56kg and at discharge 7.32kg.

ZINC	Body Weight (kg)	
	On admission	At discharge
Given	7.48	7.52
Not given	7.56	7.32

Fig: 3 Impact of zinc supplementation on weight gain



In India diarrhoea kills approximately 650 children below the age of 5 years each day. According to Indian Academy of Paediatrics (IAP) combination of Oral rehydration solution (ORS) and oral zinc have been recommended for the treatment of acute and persistent diarrhoea in children.<sup>20</sup> Zinc is a nutritional supplement (mineral) as well as water-soluble compounds usually given as zincs sulphate, zinc acetate, or zinc gluconate. The relation between zinc and diarrhoea associated morbidity have been noted on different observational studies<sup>21</sup>. The incidence of diarrhoea cases in this study was 46%. Srivatsava JR et al, Hazra et al, Khanduja PC et al and Behera SK et al reported this to be 24.6%, 18.64%, 5.5% and 11.3%<sup>22,23,24</sup>.

Patients recommended with zinc had significantly less duration of hospital stay and only one patient stayed on hospital more than 7 days. But 10 patients who didn't take zinc were stayed on hospital for more than 7 days. A recently published epidemiological study from India by Sazawalet al showed a 7% reduction in the proportion of episodes lasting more than seven days if zinc supplementation was given within three days of the onset of diarrhoea<sup>25</sup>.

On follow up, 93.47% of children in zinc group recovered within 6 days compared to 76.08% in the non-zinc group. In Bhatnagar S et al study, proportion of diarrhoeal episodes lasting  $\geq 5$  days (odds ratio, 0.49; 95% CI – 0.25, 0.97) or  $\geq 7$  days less (odds ratio, 0.09; 95% CI: 0.01, 0.73) in the zinc group<sup>26</sup>. It is now recommended that all children under 5 years old should receive zinc supplement 20mg BD for 10-14 days for the clinical treatment of diarrhea<sup>27</sup>. During and after the diarrheal episodes zinc treatment given for 10-14 days is associated with reductions in severity and duration of illness, less mortality, and incidence of diarrheal cases in the months after zinc treatment<sup>28</sup>.

weight gain was observed at discharge in children with zinc supplementation (mean body weight 7.48 vs 7.52) but there was no weight gain in children without zinc supplement (mean body weight 7.56 vs 7.32) The same findings were observed in S.K Roy et al's studies and it reported to be weight gain at discharge was improved in children supplemented with zinc. The zinc supplemented group had gained in mean body weight (6.31 v 6.19 kg,  $p = 0.03$ ) but there was no gain in the placebo group (6.46 v 6.43 kg,  $p = 0.68$ )<sup>29</sup>. Zinc supplementation also promoted an increased weight gain velocity of 8.8g/kg/day among children recovering from severe malnutrition in Bangladesh<sup>30</sup>.

#### IV. Conclusion

Finally our study concludes that the incidence of Acute gastro enteritis was more in age group in between 1-2 years, Acute Febrile Illness was more in age group <1 years and Lower respiratory tract infection was more in age group 2-3 years. Patients in zinc group had significantly less duration of hospital stay and less proportion diarrhoeal episodes on follow up compared to the non-zinc group. On follow up 93.47% of children in zinc group recovered within 6 days compared to 76.08% in the non-zinc group. weight gain in children with zinc supplementation in acute diarrhoea, and significant benefit in reduction of the duration of diarrhoea.

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