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Letter to Editor

Paediatrics Section

# Does Zinc Really Improve the Outcome of Severe Pneumonia in Children?

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Dear Editor,

We read with great interest the article titled "Effect of Zinc Supplementation in Children with Severe Pneumonia: A Randomised Controlled Study" published in your esteemed journal in November 2018 [1]. The role of zinc in pneumonia is still debatable and authors did a commendable job for selecting such a difficult area for research. However, we want to share a few of our thoughts regarding this article.

In this study, authors had used WHO clinical case definition to include children with severe pneumonia. Although, it is an excellent tool at primary health care facility, however, at times it doesn't differentiate pneumonia from other close mimickers like acute bronchiolitis, first episode of wheeze [2]. Furthermore, viruses are the most common cause of pneumonia in children especially in younger children (2-12 months) and WHO case definition also doesn't differentiate viral from bacterial infection [3]. The aetiology of pneumonia may have an influence on role of zinc. Hence, it might have been good if authors should have also considered other criteria for the classification of pneumonia viz., radiological criteria [4].

Although, authors had mentioned chest X-ray, routine blood sample, CRP and throat swab in methods however they didn't provide any information regarding these investigations, which might be very informative.

In this study, there was no significant difference in mean serum zinc level at baseline as well as 3-months after the enrollment in both groups. In this context, it is very difficult to explain observed difference in time, for clinical resolution and hospital stay was due to only zinc supplementation. There may be other factors which can influence the outcome of pneumonia viz., breastfeeding, nutritional and vaccination status, exposure to smoke, crowding, family income, access to health care facilities etc., which should have been taken into account [5].

Authors had calculated sample size based on the time taken for the clinical resolution between two groups and they concluded that zinc supplementation significantly accelerates the clinical resolution compared to placebo (24.6% vs 32.5%, p=0.04) in less than three days. However, the data had been presented in proportion of patients in each group. This may affect the primary outcome as well as power of the study. If authors would have presented data in terms of mean duration hours or days of clinical improvement of severe pneumonia then the result may be more meaningful for clinical perspective.

The other outcome measure of this study was hospital stay which should ideally be mean duration of hospital stay, however, in this study, it has been classified as, up to five and more than five days. Furthermore, hospital stays up to five days was significantly more (54.3%) in zinc group. Thus, reaching the conclusion that zinc supplementation significantly reduced the duration of hospital stay in compared to placebo is not clearly supported by this study.

Lastly, authors had concluded that zinc supplementation can be considered in children with severe pneumonia, however, they didn't provide information about duration of supplementation as in this study even after two weeks of therapy it didn't change the serum level of zinc.

## REFERENCES

[1] Baruah A, Saikia H. Effect of zinc supplementation in children with severe pneumonia: a randomised controlled study. Journal of Clinical and Diagnostic Research. 2018;12(11):10-13.
[2] Bagri NK, Bagri N, Jana M, Gupta AK, Wadhwa N, Lodha R, et al. Efficacy of oral zinc supplementation in radiologically confirmed pneumonia: Secondary analysis of a randomized controlled trial. J Trop Pediatr. 2018;64(2):110-17.
[3] Howie S, Zaman SM, Omoruyi O, Adegbola R, Prentice A. Severe pneumonia research and problem of case definition: the example of zinc trials. Am J Clin Nutr. 2007;85:242-43.
[4] Cherian T, Mulholland EK, Carlin JB, Ostensen H, Amin R, de Campo M, et al. Standardized interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies. Bull World Health Organ. World Health Organization 2005;83(5):353-59.
[5] Tiewsoh K, Lodha R, Pandey RM, Broor S, Kalaivani M, Kabra SK. Factors determining the outcome of children hospitalized with severe pneumonia. BMC Pediatr. 2009;9(1):01-08.

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## AUTHOR'S REPLY

At the outset, we would like to thank the reader for an exhaustive review of our paper together with the question "Does zinc really improve the outcome of severe pneumonia in children?"

We agree with the reader that WHO ARI definition does not differentiate between viral and bacterial aetiology of LRTI. We had taken this WHO definition as it is difficult to confirm the aetiological diagnosis of LRTI in every hospital including tertiary care hospital. According to the reader, aetiology may have an influence on the role of zinc, but since the basic pathology is inflammation, action of zinc was seen irrespective of aetiology. To find out the effect of zinc on LRTI of different aetiology needs further studies. On the question of wheeze, we had excluded the cases which presented with wheeze as mentioned in our paper.

About the investigations, basic investigations like Chest X-ray, Blood RE, Throat swab C/S, CRP were done as routine investigations but was not mentioned in the paper as the results had no direct relationship with the objectives. However, for the reader's information we are providing the reports [Table/Fig-1].

| Variables | Zinc group | Placebo group | Total |
|---|---|---|---|
| **Hb (gm/dL±SD) n=532** | 9.4±1.6 | 9.3±1.3 | |
| **TLC** | n=265 | n=267 | n=532 |
| Increased | 56 (57.14%) | 42 (42.86%) | 98 (18.46%) |
| Normal | 209 (48.16%) | 225 (51.84%) | 434 (81.58%) |
| **ESR** | n=208 | n=188 | n=396 |
| Increased | 170 (51.05%) | 163 (48.95%) | 333 (83.88%) |
| Normal | 38 (60.31%) | 25 (39.68%) | 63 (15.87%) |
| **CRP** | n=220 | n=210 | n=430 |
| Increased | 175 (49.44%) | 179 (50.56%) | 354 (82.33%) |
| Normal | 45 (59.21%) | 31 (40.79%) | 76 (17.67%) |
| **Chest X-ray** | n=238 | n=220 | n=458 |
| Normal | 99 (50%) | 99 (50%) | 198 (43.23%) |
| Abnormal (alveolar infiltration, consolidation, pleural effusion) | 139 (53.46%) | 121 (46.54%) | 260 (56.79%) |
| **Throat swab culture** | n=216 | n=210 | n=426 |
| Bacteria | 131 (51.37%) | 124 (48.63%) | 255 (59.86%) |
| Sterile | 33 (58.93%) | 23 (41.07%) | 56 (13.15%) |
| Normal flora | 49 (47.12%) | 55 (52.88%) | 104 (24.41%) |
| Yeast | 3 (27.27%) | 8 (72.72%) | 11 (2.59%) |

**[Table/Fig-1]:** Laboratory parameters

About the difference between initial serum zinc level and at three months, we have already mentioned that zinc supplementation given for two weeks may not be sufficient to raise the serum zinc level up to three months and that may be the cause for no effect of zinc supplementation on recurrence of pneumonia. Yuan X et al., stated that serum zinc level increased in the zinc treatment group and returned to normal level on 12±2 days [1], but it was not clear about the duration and dose of zinc supplementation. Further studies are necessary to see the effect of oral zinc supplementation on serum zinc level by doing serial serum zinc estimation during supplementation and after supplementation. In our study, 98% children were from lower socioeconomic class (Revised Kuppuswamy's socioeconomic status scale) [2], 97% were exclusively breastfed, 96% children were completely immunised and most of them used firewood for cooking. About nutritional status, we had excluded the children with severe malnutrition. So, all these factors were comparable among all children.

About clinical resolution, 32.5% children of zinc group and 24.6% children of placebo group showed clinical resolution in less than three days; and 67.5% of zinc group and 75.4% children of placebo group showed clinical resolution in three or more days with p-value of 0.040.

About hospital days, 54.3% of children of zinc group and 45.4% of placebo group were discharged in five days or less. On the other hand, 45.7% of children of zinc group and 54.6% of placebo group were discharged in more than five days with a p-value of 0.035.

According to reader's suggestion, we are presenting the data in relation to average days for both clinical resolution and hospital days which also showed significant difference among the two groups [Table/Fig-2].

| | Zinc group | Placebo group | p-value |
|---|---|---|---|
| **Clinical resolution** | 3.49 days | 3.81 days | 0.0410 |
| **Hospital stay** | 5.86 days | 6.32 days | 0.0491 |

**[Table/Fig-2]:** Clinical resolution and hospital stay.

## REFERENCES

[1] Yuan X, Su-Yun Qian S Y, Li Z, Zhang ZZ. Effect of zinc supplementation on infants with severe pneumonia. World J Clin Pediatr. 2016;12(2):166-69.
[2] Singh T, Sharma S, Nagesh S. Socio-economic status scales updated for 2017. Int J Res Med Sci. 2017;5(7):3264-67.

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