

Original Research Article

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Effect of Vitamin A supplementation on preventing recurrent acute lower respiratory tract infections in children

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ABSTRACT

Background: Acute Lower Respiratory Tract Infections (ALRTI) remains the major cause of increased morbidity and mortality in under-five children. Vitamin A has a protective role against infections in children. Vitamin A supplementation is given to under-five children as part of the National Immunization Programme in India. The aim of this study was to find out the effectiveness of vitamin A supplementation in preventing the recurrent ALRTI (≥ 3 episodes per year) in under-five children.

Methods: A cross-sectional analytical study was conducted to find out the role of vitamin A supplementation in reducing recurrent ALRTI in under-five children who were enrolled in Anganwadi centers (AWC's) in Villupuram district, Tamil Nadu, India. Two hundred children of 1-5 years of age were selected by random systematic sampling. History was elicited and documents about vitamin A supplementation and previous episodes of ALRTI were verified. The association between recurrence of ALRTI and vitamin A supplementation was analyzed using chi-square test.

Results: The mean age of the children in this study is 24 ± 8 months. The median number of episodes of ALRTI per year is 2 (1-3). Among 200 children enrolled in the study, 127 (63.5%) children received vitamin A supplementation and 73 (36.5%) did not receive it. There is a significant decrease in the number of ALRTI episodes (less than 3 episodes per year) in the children who received vitamin A supplementation ($p < 0.001$).

Conclusions: Vitamin A supplementation along with the National Immunization Programme had shown reduced ALRTI episodes. Since, the number of ALRTI episodes are directly proportional to mortality due to pneumonia, reduction in number of episodes can decrease the Under-five mortality. Vitamin A supplementation is an important programme in this regard and needs to be scrupulously carried out.

Keywords: Acute lower respiratory tract infection, Children, National immunization programme, Prevention, Supplementation, Vitamin A

INTRODUCTION

Acute Lower Respiratory Tract Infection (ALRTI) is one of the major causes of morbidity and mortality in under five years age group.¹ Each year, around 4 million deaths

occur from 156 million episodes of ALRTI affecting the under 5 children. Viruses are the most common pathogens causing the illness in both developed and developing countries.² Two severe forms of ALRTI are bronchiolitis and pneumonia which contributes to the

majority of under 5 mortality.³ It is often difficult to distinguish between these two clinical conditions in under 5 children. Around 30 to 40% of the children who get hospitalized because of pneumonia are community-acquired in origin. About 20% of under five deaths are attributed to pneumonia, which is very significant in terms of mortality.⁴ Among them, viruses contribute to the hospitalization of 30 to 40% of cases with ALRTI. Respiratory Syncytial Virus (RSV) can be found in more than 20% of cases. Paramyxovirus and human metapneumovirus (hMPV) stand second in the list.⁵

Streptococcus pneumoniae is the most common bacterial cause of childhood pneumonia. Children with underlying diseases like malnutrition, measles, TB, HIV are at increased risk of *H. Influenza* type B, *Staphylococcus aureus*.

The risk factors like low birth weight, indoor air pollution, lack of exclusive breastfeeding, overcrowding, improper vaccination, malnutrition, vitamin A and D deficiency, passive smoking, sex, preterm delivery, zinc deficiency, and anemia may play a major role in morbidity and mortality of ALRTI.⁶ Some of the previous studies have proposed several characteristics, which can increase the susceptibility to ALRTI. Birth interval, birth order, previous ALRTI history, and vitamin A deficiency are among them.

ALRTI risk can be reduced by exclusive breastfeeding in infants. Breast milk provides leucocytes, lysozyme, lactoferrin, and secretory IgA which are the major immune factors that can reduce the risk of childhood pneumonia.⁷ Vitamin A supplementation has some beneficial effect in ALRTI similar to these immune factors. Vitamin A plays a major role in epithelial integrity of the respiratory system and plays a crucial role in immune function which in turn helps in reducing the recurrent ALRTI attacks in under 5 children.⁸ Vitamin A (retinol) also plays an important role in the production, growth, and differentiation of red cells, lymphocytes and antibodies, and epithelial integrity.⁹ A Cochrane Database Systemic review performed by D'souza RM et al, concluded that 2 lakh IU per day of vitamin A has associated with a decrease in pneumonia associated mortality in children with measles.¹⁰ The role of vitamin A supplementation in speedy recovery and reduction in the severity and prevention of subsequent episodes of ALRTI has been investigated on similar lines.¹¹⁻¹⁶

ALRTI usually presents with cough, tachypnea, fever, coryza, chest retraction, crackles, and wheeze. In pneumonia, blood investigations may show elevated white blood cell counts with left shift and may also show elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).¹⁷

As a part of the routine immunization schedule, vitamin A supplementation is given along with the National Immunization Programme (NIP) in India. Under this

programme, 1 Lakh International units (IU) vitamin A is given along with measles vaccine (recently changed to MR 1 vaccine) after completion of 9 months or 270 days. Thereafter, vitamin A is supplemented with 2 lakh IU biannually (once in every 6 months) up to 5 years of age to complete a total of 9 vitamin A doses.¹⁸ This schedule of vitamin A supplementation is being followed in all ICDS Anganwadi centers (AWC's). The Anganwadi workers in the AWC's are involved in the distribution and administration of vitamin A.

METHODS

Author's carried out a cross-sectional study to find out the role of vitamin A supplementation in reducing the recurrent attacks of ALRTI in under five children who were enrolled in Anganwadi center (AWC's) which is a part of Integrated Child Development Scheme (ICDS) of Villupuram district, Tamil Nadu, India. This study was conducted from January 2017 to December 2017.

For this study, three hundred and fifty nine Anganwadi centers (AWC) in Villupuram district, Tamil Nadu, India were selected within 15 kilometers (km) radius of SVMCH and RC, Ariyur, Pondicherry, India. Out of these 359 centers, 20 Anganwadi centers (AWC's) were selected on randomization by systematic sampling. Among 20 AWCs, 10 children (5 boys, 5 girls) were chosen for study from each AWC. Selection of children was done with randomization by systematic sampling.

Vitamin A supplementation is given to children by ICDS staff in the AWC's Once in every 6 months (Biannually). Anganwadi workers are involved in the distribution and administration of vitamin A.

The primary investigator had elicited the history from mother of each child about number of episodes of ALRTI in the previous one year and also verified the documents available regarding the status of vitamin A supplementation, the hospital visits and admissions and confirmed the number of episodes of ALRTI in the previous one year till the date of enrollment into this study.

Sample size was calculated to be 200 considering the prevalence of malnutrition in 9-59 months aged children which is 65% in rural Tamil Nadu, India, according to National Family Health Survey (NFHS 2015-16). They are the at-risk population for pneumonia mortality. With 95% Confidence Level or 5% level of significance ($\alpha=0.05$), $Z=1.96$. P =Prevalence) of vitamin A supplementation to 9-59 months age children=65% $q=(1-p)$ or percentage of failure which is $100-65 = 35\%$. d =Precision limit 10% confidence interval. Using formula= $Z^2P(1-q)/d^2$, 200 sample size obtained.

Ethical and scientific committee approval has been taken from the institute ethical and scientific committee respectively. Inclusion criteria include registered

beneficiary children aged 1-5 years from the selected AWCs who are supplemented with vitamin A along with the National Immunization Programme. Exclusion criteria include children with intrinsic problems like congenital abnormalities, congenital heart diseases, malabsorption, immuno-compromised children.

Definitions

Lower respiratory tract infection is defined as temperature $>38.5^{\circ}\text{C}$, refusal to feed, and respiratory rate $\geq 40/\text{minute}$ among children aged 1-5 years.¹⁹

Recurrent lower respiratory tract infection can be regarded as ≥ 3 annual episodes of documented bronchitis, bronchiolitis, or pneumonia.²⁰

Statistical analysis

Data were entered in Microsoft Excel data sheet and analyzed using SPSS version 19 software. Age of the

child and number of ALRTI episodes/day were expressed as Mean (SD) and median (IQR) respectively. Weight for age, height for age, Body Mass Index (BMI) were expressed as Mean (SD). Other variables were summarized as frequencies (Proportions). Association between recurrence of ALRTI and vitamin A supplementation was analysed using the chi-square test. A 'p' value of <0.05 was considered as statistically significant.

RESULTS

The mean age of the children in the study is 24 ± 8 months. The median number of episodes of ALRTI/year is 2 (1-3).

Among the 200 children enrolled in the study, 127 (63.5%) children received vitamin A supplementation and 73 (36.5%) did not receive any vitamin A supplementation. The baseline demographic characteristics are depicted in Table 1.

Table 1: Baseline demographic characteristics.

Variables	Results	
Gender, male: female, (n= 200)	100:100	
	Vitamin A-Received, (n=127)	Vitamin A-Not received, (n=73)
Age in months, Mean \pm SD	26 \pm 8.01	26 \pm 8.03
Socio economic class (class 3)	36%	37%
Socio economic class (class 4)	64%	63%
Weight for age (kg), Mean \pm SD	12.5 \pm 1.8	13 \pm 2.1
Height for age (cms), Mean \pm SD	88 \pm 7.4	90 \pm 6.9
Body mass index, Mean \pm SD	16.2 \pm 1.6	15.7 \pm 1.1
Proportion of children with pallor	19%	32%
Proportion of children with malnutrition	65%	68%

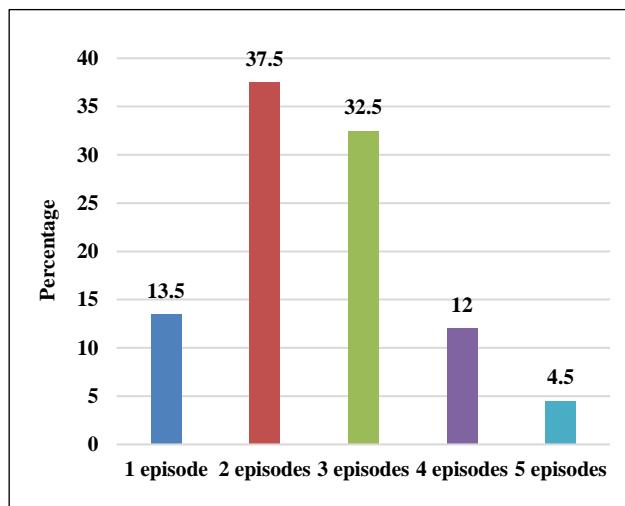


Figure 1: Frequency of acute lower respiratory tract infections (ALRTI) among the enrolled children.

On assessing the frequency of acute lower respiratory tract infections (ALRTI) among the enrolled children, there were 27, 75, 65, 24 and 9 children with one, two, three, four and five episodes of ALRTI per year respectively as depicted in Figure 1. There is a significant decrease in a number of ALRTI episodes (less than 3 episodes/year) in children who received vitamin A supplementation. Among the children who received vitamin A supplementation, there are 77 children (61%) in the non-recurrent ALRTI group. Majority of the children (66%) in the other group who did not receive vitamin A supplementation had recurrent ALRTI as depicted in Table 2 and Figure 2.

In Figure 2, vitamin A supplementation status (received or not) is represented on X-axis and percentage of children with ALRTI on Y-axis. In this figure, children with non-recurrent ALRTI (represented by blue bar) and recurrent ALRTI (represented by red bar) in two groups

(Vitamin A-received group and vitamin A-not received group) were depicted. Majority of the children (61%) in Vitamin A-received group had lesser number of ALRTI episodes (less than 3 episodes/year), whereas majority of the children (66%) in Vitamin A- not received group had recurrent ALRTI episodes (3 or more episodes/year).

Table 2: Frequency of ALRTI in relation to vitamin A supplementation.

Vitamin A supplementation	Number of children with ALRTI Episodes		P
	Non-recurrent	Recurrent	
Received	77 (61%)	50 (39%)	
Not received	25 (34%)	48 (66%)	0.001 ^a

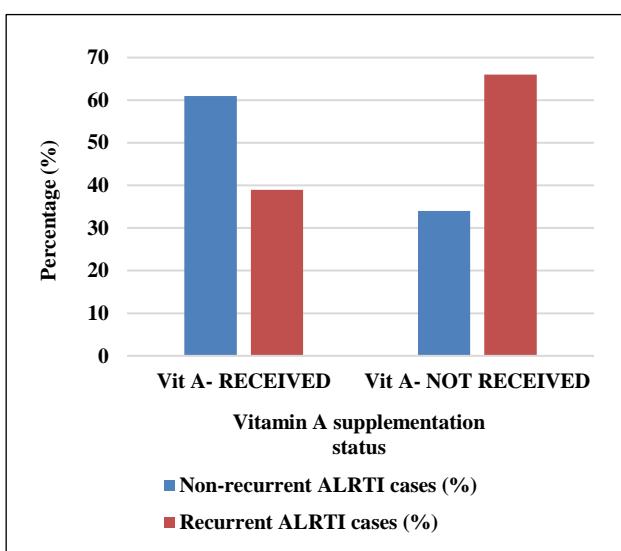


Figure 2: Frequency of ALRTI in relation to vitamin A supplementation.

DISCUSSION

Vitamin A deficiency leads to changes in respiratory epithelium along with suppression of humoral and cell-mediated immunity. This can make the child susceptible to infection.²¹

In this study, authors observed that there is a significant decrease in the incidence of recurrent ALRTI in children who received vitamin A supplementation compared to children who did not receive it ($p < 0.001$).

A study performed by Zhang X et al, showed that decreased level of serum Vitamin A is significantly associated with recurrent respiratory tract infections ($p < 0.05$).²²

There were no studies which mentioned the effect of vitamin A supplementation (given along with National immunization schedule) on the number of episodes ALRTI. However, few studies mentioned that vitamin A

supplementation in children with pneumonia had shortened recovery period and hospital stay.^{23,24} In a randomized double-blinded controlled trial performed by Si et al, moderately malnourished children with pneumonia who received vitamin A supplementation significantly had a shorter time of hospitalization after admission for pneumonia ($p=0.04$).²³

A randomized double-blinded controlled trial done by Long et al, in Mexico in which 736 children of 6-15 months age group received vitamin A supplementation.²⁵ In this study, there is 23% increase in respiratory infections in children who received vitamin A supplementation (RR:1.23; 95%CI: 1.02, 1.47, $P=0.02$). A similar increase in the incidence of respiratory infections after vitamin A supplementation was seen in the randomized controlled trial performed by Stanfield et al, with 11, 124 children of 6-83 months age group.²⁶ In this study, each child received 3 doses of vitamin A of 2 lakh International units (IU) four monthly once for three cycles.

Few other studies performed by Barreto et al, Bhandari N et al, Dibley et al, mentioned that there is no effect of vitamin A supplementation on morbidity on mortality due to ALRTI.²⁷⁻²⁹

A Cochrane Database systemic review done in 2008 by Chen H et al, concluded from their review that most of the studies did not show any effect of vitamin A on the incidence of ALRTI.³⁰ But, two studies included by them in the same review showed vitamin A supplementation has significantly reduced the incidence of ALRTI in children with poor nutritional status.²²

In this study, there is a significant reduction in recurrent ALRTI in children who received vitamin A supplementation along with National Immunization schedule ($p < 0.001$). Many studies as mentioned above did not suggest a positive relationship between vitamin A supplementation and number of ALRTI episodes. The findings of our study are different from the other studies probably due to sample size of the study participants, children of different ages (1-5 years), their nutritional status before and at the time of participation in the study. There are also differences in terms of dosage of Vitamin A (low and high dose), the number of doses received their monitoring period, the method of monitoring. Ours is a cross-sectional analytical study, whereas most of the studies mentioned above are randomized controlled trials. Documentation of the number of episodes and their defining criteria was also different in various studies. In this study, authors have clearly defined non-recurrent ALRTI (<3 episodes/year) and Recurrent ALRTI (≥ 3 episodes/ year) and found out their incidence in vitamin A supplementation group and the group which didn't receive it. Most of the studies mentioned about the incidence and number of episodes of ALRTI. But they were not defined as recurrent and non-recurrent ALRTI. More studies in this direction with a larger sample size

may strengthen the evidence for positive effects of vitamin A supplementation on recurrent ALRTI.

Smaller sample size. Children of different ages (1-5 year) in which the younger children may not have completed the full schedule of vitamin A supplementation. Serum vitamin A levels were not measured in this study.

CONCLUSION

Vitamin A supplementation along with the National Immunization Programme had shown reduced the number of episodes of ALRTI compared to children who did not receive it. Since, the number of ALRTI episodes are directly proportional to mortality due to pneumonia, less number of episodes can decrease the under-five mortality. Vitamin A supplementation is an important program in this regard and needs to be scrupulously carried out.

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