

# Effect of CMPA (Cow's Milk Protein Allergy) and Recurrent Respiratory Infections in Children with Down's Syndrome

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## ABSTRACT

**Introduction:** Down syndrome (DS) is the most prevalent genetic disorder with intellectual disability (ID) in India. It is associated with various disorders related to heart, respiratory and gastrointestinal tract. Cow milk protein allergy (CMPA) is commonly seen in down syndrome children. This CMPA seems to be responsible for increase in respiratory infection is found in children with Down syndrome compared to other children. In this study we have tried to investigate the correlation between incidences of respiratory infection after removing cow milk in children with Down syndrome. Study aimed to investigate the effect of cow milk protein allergy and its relation to the frequency of respiratory infections occurring in children with Down Syndrome.

**Material and Methods:** Children aged between 1 – 10 years with Down syndrome confirmed by karyotyping or genetic analysis were chosen for the study. Children should have cow cow milk in their routine diet in relation to respiratory symptoms and episodes were noticed before and after the consumption and removal of the cow milk in these children. Blood tests were performed to confirm the immunological profile.

**Results:** Fewer incidences of respiratory infections is seen in children with Down Syndrome, when the cow milk is removed from the regular diet. High incidence of IgA and IgE for cow's milk protein were seen in children with Down Syndrome. Infections were found to be significantly less in number during the course of cow milk free diet.

**Conclusion:** Children with high IgA and IgE levels are more susceptible to the cow milk protein allergen which might be the reason for recurrent infection which suggests that removal and modification of diet will help in the betterment of the children.

**Keywords:** Cow Milk Protein, IgE, Cow Milk Protein Allergen.

## INTRODUCTION

Down syndrome (DS) is a common chromosomal anomaly associated with multiple congenital malformations in live-born infants.<sup>1</sup> Currently, the incidence of Down syndrome in India is 1:800, which means approximately 32,000 babies with Down syndrome are born every year. The prevalence of Down syndrome in India is considered to be similar to global data.<sup>2</sup> When compared to other Intellectual and genetic disorders, Down syndrome is the most common chromosomal abnormality among live-born infants. Down syndrome is characterized by a variety of dysmorphic features and congenital malformations, including congenital heart disease (CHD) and gastrointestinal disease. Also, Down syndrome is associated with various immunological

impairments.<sup>3</sup> There is evidence that prevalence of thyroid disorders and diabetes mellitus is higher in children with Down syndrome.<sup>4</sup> Children with Down syndrome have an increased risk of respiratory tract infections. This might be associated with congenital heart disease, abnormal airway anatomy, and physiology, hypotonia, and aspiration.<sup>5</sup> There are several studies focused on the immune system of patients with Down syndrome to find the clinical problems.<sup>6</sup> Although multiple abnormalities are associated with the disease, respiratory infection is an important cause of morbidity and mortality which is frequently seen in these children in daily practice, but clinical evidence in the literature is sparse.<sup>7</sup> The prevalence of Down syndrome in India is considered to be similar to global data.<sup>8</sup> The exact prevalence is impossible to collect from the Indian subcontinent as there is a lack of registry for Down syndrome and other Intellectual and genetic disorders.<sup>9</sup> In Down syndrome patients, evidence suggests that multiple food allergies, gluten-gliadin sensitivity or intolerance are causing a coeliac disease-like picture with a malabsorption state for essential vitamins, minerals, and severe autoimmune disease. Food allergy is an increasingly reported health problem that particularly affects children. Cow's milk protein allergy mainly affects the young children.<sup>10</sup> Egg and milk are confirmed to be an allergen in asthmatic children although the incidence is low in the normal population<sup>11</sup>, data on children with Down Syndrome are not available particularly in Indian population. Milk contains protein such as casein,  $\alpha$ -lactoglobulin,  $\beta$ -lactoglobulin, bovine serum albumin and  $\gamma$ -globulin. Other factors that may affect the development of cow milk allergy are the timing of exposure, the magnitude, and frequency of exposure as well as the allergenicity of the protein itself.<sup>12</sup> This allergy is an immune mediated reaction or non-immune-mediated. The most common immune responses are immunoglobulin E (IgE) mediated, cell-mediated (non-IgE) or the combination of two.<sup>13</sup> As respiratory complications are the common cause of acute hospitalization among children with Down syndrome children, in this study, we hypothesized that these children with CMPA benefitable by early identification and suitable intervention. The study will also identify the effect of

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weaning cow's milk protein and follow up for the incidence of respiratory infection in these children.

Study aimed to study the incidence of respiratory infections and complications in Down syndrome children requiring medical intervention after Cow Milk Protein free diet.

## MATERIALS AND METHODS

This prospective observational study was conducted in children aged between 1 – 10 years with Down syndrome confirmed by karyotyping or genetic analysis. The diagnosis is confirmed by testing positive for CMP specific antibody (beta-lactoglobulin). The children should have cow milk as the part of their daily diet. These children should be free from any cardiac complications and malignancy. Children with cardiac complications, unable to present at the clinic during visits, unknown lab results will be excluded from the study. Sample collection was done during screening and at the end of the study. The period between the two visits is 12 months. The sample is analyzed for specific IgE, Total IgE, serum IgE, hemoglobin, hematocrit, total leukocyte count and differential count. The quality of life was evaluated using the questionnaire version 1.1 which has been approved by the Institutional Ethics Committee. The questionnaire was completed during the visits with the help of parents. The National Ethics committee at Chennai bearing the registration No: US-OHRP – IORG0006162 has approved the study.

## STATISTICAL ANALYSIS

Statistical analysis was performed using software SPSS v 17 (Chicago, IL, USA). The Chi-Square was used to analyze the significant difference between proportions. The variables

Age Group in Years	CMPA Positive	CMPA Negative	Total (%)
1 – 3	7 (21.2%)	26 (78.8%)	33
3.1 – 6	12 (33.3%)	24 (66.7%)	36
6.1 – 10	12 (38.7%)	19 (61.3%)	31
Total	31	69	100

**Table-1:** Age distribution in CMPI positive and negative group

Total IgE	Cow milk protein allergen		P value
	Positive	Negative	
Normal	12 (20.8%)	64 (84.2%)	<0.0001
Abnormal	19 (79.2%)	5 (15.8%)	

**Table-2:** Total IgE with Cow milk protein allergen (beta lactoglobulin)

were analyzed as categorical or continuous. Mc Nemar test was used to analyze the categorical data.

## RESULTS

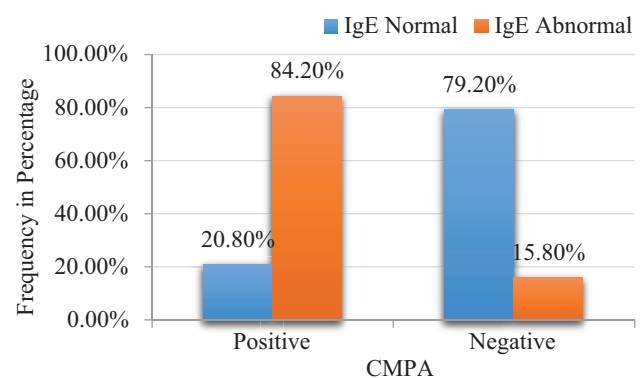
Incidence of CMPA incidence among various age groups were studied and it was noted that CMPA positive 31% and CMPA negative 69% (table-1).

Total IgE levels among DS children were studied and compared among the groups (CMPA positive and negative). There was statistical difference between the two groups, i.e. both the groups are associated ( $p < 0.05$ ) (table-2).

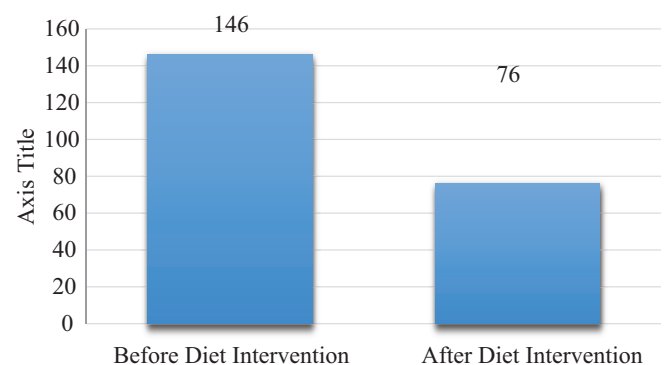
Another key indicator for classifying DS children based on the IgE status also showed statistically significant association (figure-1).

There is highly statistical significant difference ( $p < 0.05$ ) among positive cases than negative cases, using proportional analysis (table-3).

Incidence of cough was reported by the caretaker although cough is an indirect/vague indicator towards the study



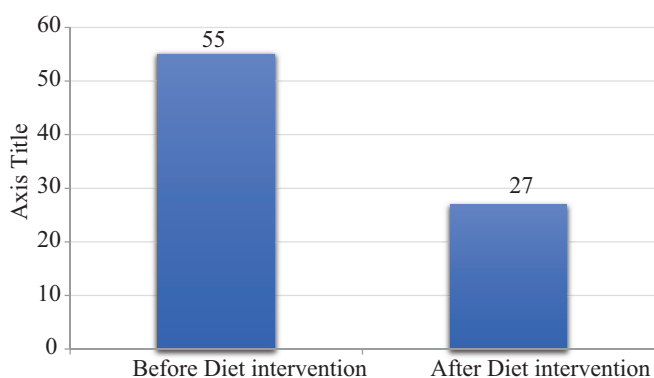
**Figure-1:** Total IgE levels in study population



**Figure-2:** Cough incidence and No of Hospitalization complications before and after advised diet

Pre and Post condition of cough among Cow Milk allergen (Positive / Negative) cases						
Cow Milk protein allergen			Cough after advised diet			Total
			No Cough	Dry	With Expectoration	
Positive	Cough before advised diet	Dry	1 (100%)	0	0	1
		With Expectoration	16 (53.3%)	13 (43.3%)	1 (3.4%)	30
	Total		17	13	1	31
Negative	Pre study condition	Dry	12 (19.4%)	50 (80.6%)	0	62
		With Expectoration	0	1 (14.3%)	6 (85.7%)	7
	Total		12	51	6	69

**Table-3:** Cough before and after advised diet



**Figure-3:** Number of hospitalization incidence

objective – consideration is necessary wherein micro-aspiration is high in these population. There is highly statistical significant difference ( $p < 0.05$ ) among positive cases than negative cases, using proportional analysis (figure-2).

Hospitalization was a critical analysis, hospitalization due to respiratory disorder is not presented. We can infer that diet intervention along with medical care would have higher impact in reducing the number of incidences of hospitalization (figure-3).

## DISCUSSION

This is the first study in India to describe the association of Cow's milk protein allergy and respiratory infections in children with Down syndrome. There are no studies suggest a role for an abnormal immune system in the pathophysiologic mechanism of increased susceptibility to respiratory infections in children with Down syndrome.<sup>14</sup> The abnormalities of the immune system associated with DS include: mild to moderate T and B cell lymphopenia, with a marked decrease of naive lymphocytes, impaired mitogen-induced T cell proliferation, reduced specific antibody responses to immunizations and defects of neutrophil chemotaxis.<sup>15</sup>

IgE mediated allergy usually manifests within minutes but no longer than two hours after ingestion of cow milk protein. Breastfed babies can also develop cow milk allergy as a result of protein in the maternal diet transferring through breast milk.<sup>16</sup> In the current study, the Total IgE with Cow Milk Protein allergen in Down syndrome children is significant when compared to the healthy children after the consumption of the cow milk protein free diet in all children.

Thus specialized children with Down syndrome with cow's milk allergy must strictly avoid cow's milk and cow's milk protein-based products. The children families must be instructed to read labels and identify milk-containing products. In these patients, the diagnosis primarily relies on a successful milk avoidance diet with clinical relapses after re-exposure to cow's milk proteins. Hospitalization is a critical indicator considered during the analysis, hospitalization due to respiratory disorder was not presented. We can infer that diet intervention along with medical care would have a higher impact in reducing the number of incidences of hospitalization. This was well proven in our study as the

hospitalization was decreased in patients where the cow milk is removed in their diet and thus the reduction in the respiratory infections is seen.

A well-balanced diet with adequate intake of calcium and other essential nutriment must be warranted.<sup>17</sup> The input of a pediatric dietician is most helpful in these patients. Mothers of breastfed infants with CMA should continue breastfeeding but avoid causal foods. There are no reliable tests for the investigation of non-IgE mediated CMA. The initial diagnosis was based on a suggestive history and absence of positive SPT or ImmunoCAP-RAST. The respiratory complications occurred in the patient after the advised diet is reduced as per the study findings. The incidence of cough was reported by the caretaker although a cough is an indirect/vague indicator towards the study objective – consideration is necessary wherein micro-aspiration is high in this population. Children with high IgE levels are more susceptible to the cow milk protein allergen which might be the reason which suggests the betterment of the children.

## CONCLUSION

To conclude in this study, it is advisable to remove cow's milk in children with Down Syndrome who experience recurrent infection, as this seems to be due to cow milk protein allergy. This correlation is very clearly evident in the study. A well balanced diet with adequate calcium and other nutrients will help in the betterment of children who are allergic to cow's milk. The decrease in incidence of recurrent respiratory infections helps in the overall growth and development of children with Down Syndrome.

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