

Serum immunoglobulin levels and lower respiratory tract infections in children with Down syndrome

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Abstract:

This study was conducted to evaluate the immunoglobulin levels in children with Down syndrome and correlate it with the occurrence of lower respiratory tract infection among them. This prospective cohort study included 30 children with Karyotypically ascertained DS and 30 age and sex matched healthy controls. Patients and controls with infections during the sample collection were excluded. Serum IgG, IgA and IgM concentrations were determined using automated nephelometer (Dade Behring, BN Prospec). Immunoglobulin levels were correlated with prevalence of infections among cases. The episodes of lower respiratory tract infections were more common among cases than controls. The mean serum immunoglobulin G (8.975 ± 1.51 to 18.02 ± 2.46 g/l) and A (0.93 ± 0.45 to 1.658 ± 0.46 g/l) levels tend to rise with increased episodes of lower respiratory tract infections. The mean serum immunoglobulin M levels (1.94 ± 0.75 to 0.74 ± 0.24 g/l) tend to be lower in patients with more episodes of lower respiratory tract infections. The prevalence of recurrent lower respiratory tract infections requiring hospitalization was common among children with Down syndrome compared to their age and sex matched control group. The combination of low levels of IgM with elevated levels of IgG and IgA was found in Down syndrome children with increased prevalence of infection. Therefore the higher incidence of respiratory tract infections could be the result of impaired immune system.

Key words: Down syndrome, Immunoglobulin levels, Lower respiratory tract infections, Hospitalization, Impaired immune system

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Introduction

Down syndrome (DS, Trisomy 21) occurs among one in 700 live births [1]. Children with Down syndrome are more prone to develop lower respiratory tract infections. It is the most common cause of hospitalization and admission to the pediatric intensive care unit among them [2]. This lower respiratory tract pathology is likely to be caused by abnormalities in immune response which may be primarily or secondarily related to the extra copy of chromosome 21 [3]. The present study was undertaken to assess the levels of immunoglobulins and correlate it with the prevalence of lower respiratory tract infections in children with Down syndrome.

Material and Methods

The study was carried out on thirty children with Down syndrome confirmed by karyotyping. (13 males and 17 females with mean age of 3.3 ± 2.21 years,

range 1.5 - 9). The study was approved by Institute Research and Ethics Committee. All children with DS and controls were free of infections at the time of sample collection. Detailed history regarding fever, nature of infection, number of hospital visits and hospitalization were taken for each case. One age and sex matched normal child was taken as control for each case. Serum IgG, IgA and IgM concentrations were determined using automated nephelometer (Dade Behring, BN Prospec). The data thus obtained was correlated with clinical data in cases. Statistical analysis was done by one way ANOVA using Graphpad Instat version 3.06. $P < 0.05$ was considered significant.

Results

The episodes of lower respiratory tract infections were more common in cases than controls. Out of 30 cases with DS, 17 children (56.6%) had 4-5 episodes of lower respiratory tract infections in the preceding.

Table 1: Immunoglobulin levels in cases and controls

Immunoglobulins	CASES Vs CONTROLS	P VALUE
IgG (n=30)	12.7±4.21 Vs 11.4±2.85	0.15
IgA (n=30)	1.23±0.51 Vs 1.00±0.55	0.09
IgM (n=30)	1.15±0.63 Vs 1.64±0.80	0.01

Table 2. Episodes of lower respiratory tract infections (LRTI) and hospitalization in cases and controls

No. of episodes of LRTI & hospitalization	No. of cases	%	No. of controls	%
LRTI				
0-3	6	20	3	10
4-5	17	56.6	0	0
>5	7	23.3	0	0
Hospitalisation				
<3	12	40	0	0
>3	18	60	0	0

Table 3. Correlation of lower respiratory tract infections (LRTI) with Ig levels among cases

No of episodes of LRTI during study period	IgG (MEAN ±S.D) (g/l)	IgA (MEAN ±S.D) (g/l)	IgM (MEAN ±S.D) (g/l)
0-3 (n=6)	8.975±1.511	0.9375±0.4512	1.94±0.75
4-5 (n=17)	11.83±3.288	1.163±0.4669	1.041±0.440
>5 (n=7)	18.028±2.464	1.658±0.4666	0.74±0.2447
P value	0.0001	0.0231	0.0003

one year, 7 children (23.3%) had more than 5 episodes and 6 children (20 %) had less than 3 episodes

Children with DS were hospitalized for lower respiratory tract infections whereas none of the controls were hospitalized for the same. Among cases 18 (60%) were hospitalized more than 3 times and 12 (40%) children were hospitalized less than 3 times.

The mean serum IgG level was found to be higher among cases (12.7±4.21 g/l) but was statistically insignificant when compared with controls (11.4±2.85 g/l). The mean serum IgA level was also found to be insignificantly higher among cases (1.23±0.51 g/l). However, significant decrease in the mean serum IgM level was observed in cases (1.15±0.63 g/l) when compared with controls (1.64±0.80 g/l).

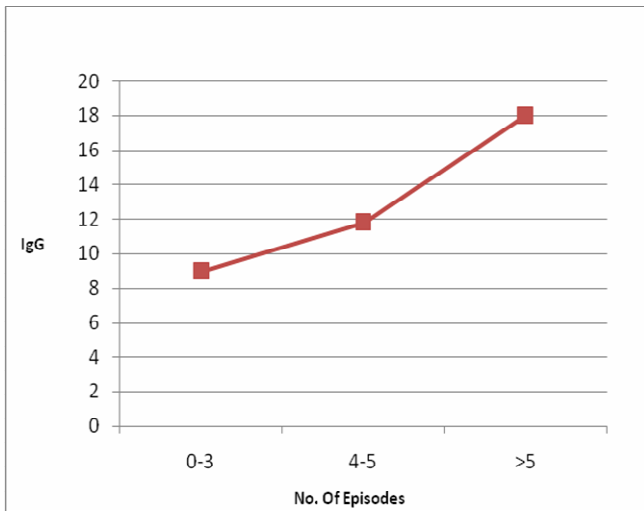


Figure 1. Correlation of episodes of LRTI with IgG

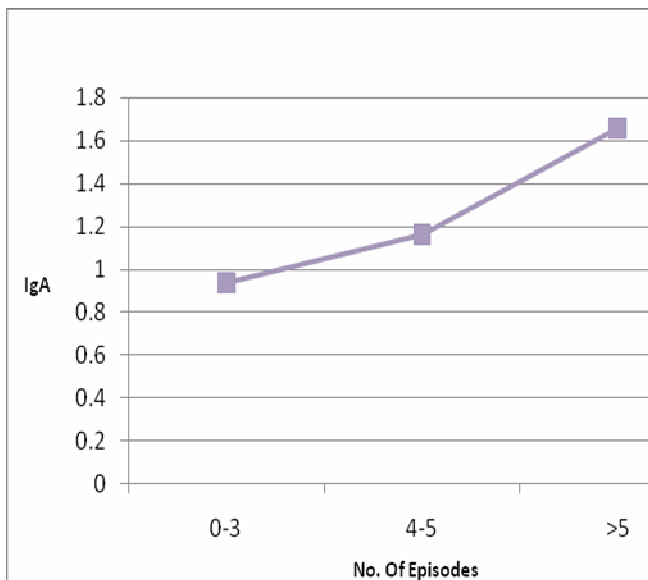


Figure 2. Correlation of episodes of LRTI with IgA

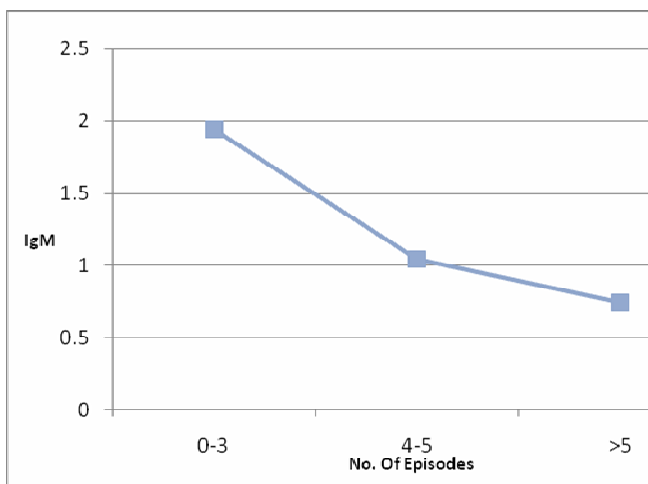


Figure 3. Correlation of episodes of LRTI with IgM

It was observed that the mean serum IgG levels tend to rise with the number of episodes of lower respiratory tract infections. The higher mean serum IgG level of 18 ± 2.464 was observed in children with Down syndrome who experienced more than 5 episodes of lower respiratory tract infections when compared with those who suffered less than 5 episodes. The mean serum IgA levels increased with the number of episodes of lower respiratory tract infections. Children who experienced more than 5 episodes of lower respiratory tract infections had higher mean serum IgA level of 1.658 ± 0.4666 when compared with children who had less than 5 episodes. In contrast, the mean serum IgM levels tend to be lower in patients with higher number of lower respiratory tract infections. Mean serum IgM concentration of 0.74 ± 0.2447 g/L was observed in children with Down syndrome who had suffered from more than 5 episodes of lower respiratory tract infections.

Discussion

In Down syndrome children, an impairment of specific and non specific immunity has been reported in previous studies. Decreased neutrophil chemotaxis, leucocyte opsonization, phagocytosis and bactericidal activity of leucocytes, abnormal serum immunoglobulin levels were described [4,5]. Alterations in the levels of serum immunoglobulin levels and the proneness to recurrent respiratory tract infections were evaluated in the present study.

The predisposition to recurrent lower respiratory tract infections associated with hospitalization was markedly increased in children with Down syndrome compared to their age and sex matched control group in the present study. When the levels of immunoglobulins were correlated with lower respiratory tract infections, significantly higher levels of IgG and IgA were associated with increasing episodes of lower respiratory tract infections. This is in accordance with the findings of Yuksel et al[6]. This is explained by slower elimination of infectious agents in Down syndrome which may cause over stimulation of the immune system and increased production of antibodies [3,7]

In contrast, significantly lower levels of IgM was associated with increasing episodes of lower respiratory tract infections. This corroborates with the findings of Kusters et al [3]. The lower IgM levels in spite of increased infections probably indicates lower anti-infective ability among children with Down syndrome.

The possible mechanism of altered production of immunoglobulins could be due to over expression of superoxide dismutase (SOD-1) gene coded on chromosome 21(21q22.1) that leads to impaired interaction between immature thymocytes and thymic stromal cells. This in turn causes partial reduction in the number and function of T lymphocytes owing to smaller thymus leading to decreased B – cell maturation which disturb the tolerogenic balance, generating a combination of immunodeficiency and immune dysregulation in Down syndrome individuals ultimately resulting in increased susceptibility to bacterial and viral infections [6]. Whereas in children with normal immune responses the presence of persistent or frequent microbial antigens in chronic or recurrent respiratory infection would be expected to produce a rise in serum immunoglobulin concentrations .

Abnormalities that affect the function of lymphocyte function associated antigen (LFA - 1) encoded on chromosome 21 compromises lymphocyte activation in mature lymphocyte which might disturb the subtle process of lymphocyte maturation. Based on the observation that LFA - 1 expression is increased on the lymphocytes from Down syndrome patients, it was postulated that over expression of LFA - 1 on lymphocytes due to gene over dosage and the subsequent lymphocyte over adhesiveness leading to abnormalities in lymphocyte development and function [9]. This could explain in part the immunological abnormalities of the humoral responses to foreign antigens demonstrated in Down syndrome.

To conclude, in the present study , combination of IgM deficiency and elevated IgG and IgA levels was associated with increased episodes of lower respiratory tract infections in Down syndrome individuals. Therefore the higher incidence of respiratory tract infections could be the result of impaired immune system.

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