Determining the Immunodeficiency in Patients with Down Syndrome at the University of Miami and Jackson Memorial Health Systems

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INTRODUCTION

Down Syndrome (DS) is known to be associated with immunodeficiency, leading to higher risks of cancers, infections, autoimmunity, and lymphoproliferation [1].

These patients can have lymphopenia, humoral deficiency, impaired neutrophil function, and immune dysregulation [2].

However, the prevalence of immune dysfunction in Down Syndrome is not well characterized.

METHODS

Retrospective study on Down Syndrome patients evaluated by immunologists at the University of Miami and Jackson Memorial Health Systems (2008-2023).

Approval from local Institutional Review Board (Study #20230956) obtained for review of electronic medical records.

Analysis involved demographics, immunological history, and pertinent laboratory data.

Lymphocyte subset values and immunoglobulin levels were evaluated against **age-specific normal ranges** [3,4].

RESULTS

Total: 17 charts available for review

Gender distribution:
- 7 females, 10 males

Racial & Ethnic breakdown:
- 13 identified as White, 4 as Black or African American
- 11 identified as Hispanic/Latino, 6 as Non-Hispanic/Latino

Age profile:
- Mean age at immunologic evaluation was 7.4 years (range 9 months to 20 years)
- Mean age at chart review was 10 years (range 14 months to 23 years)
- Total follow-up of 83 patient-years

Common infections: Otitis media (5/17), pharyngitis (2/17), frequent viral upper respiratory infections (4/17), bacterial lower respiratory infections (4/17), along with isolated cases of genitourinary infections, skin abscesses, and fungal infections.

LIMITATIONS

- Small sample size
- Single-center study
- Not sufficient power to perform further statistical analysis
- May not be representative of general Down Syndrome population
- Surgery or co-morbid conditions can affect results

Figure 1. Demographics

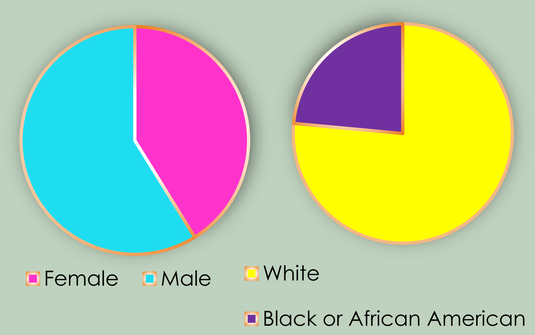


Figure 2. History of Infections

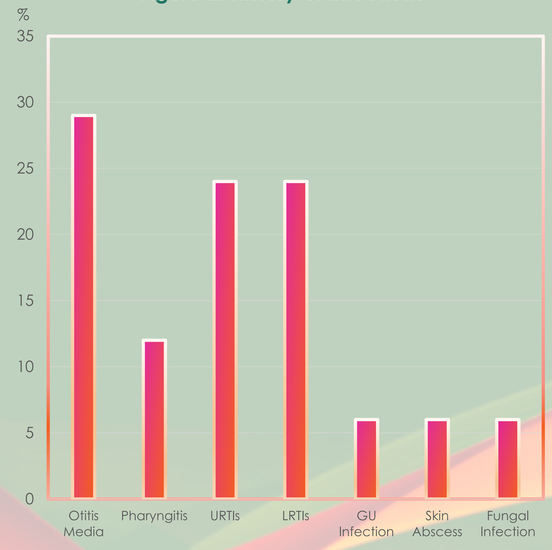
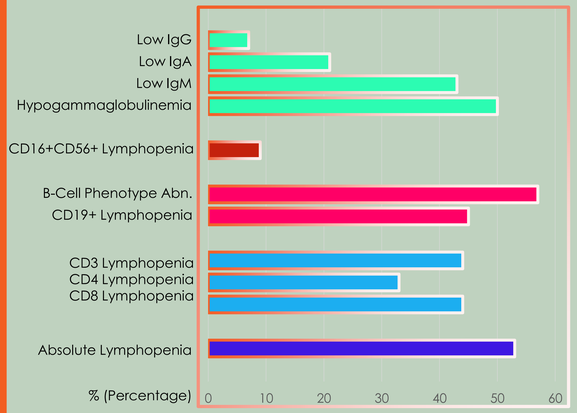


Figure 3. Immunological Laboratory Data



Immunoglobulin levels:
- 1/14 (7%) low IgG
- 3/14 (21%) low IgA
- 6/14 (43%) low IgM
- 7/14 (50%) hypogammaglobulinemia (any type)

Natural Killer Cells
- **CD16+CD56+ Lymphopenia:** 1/11 patients (9%)
- **NK function** was normal in 2/2 (100%) patients measured with chromium release assay, CD107a degranulation, and/or perforin/granzyme expression

B-cells
- **Phenotyping abnormalities:** observed in 4/7 (57%), including decreased absolute number of B cells, increased percentage of CD21-/CD38- naïve B cells; increased percentage of CD21-/IgM++ transitional B cells, and decreased percentage of isotype-switched (IgM-/IgD-) memory B cells
- **CD19+ lymphopenia**: 5/11 patients (45%)

T-cells
- CD3 lymphopenia in 4/9 patients (44%)
- CD4 lymphopenia in 3/9 (33%)
- CD8 lymphopenia in 4/9 (44%)

Absolute lymphopenia:
- 9/17 patients (53%), based on Absolute Lymphocyte Count
- 5/17 patients had cardiac surgery
  - Pre-op: 2/5 had normal ALC, 1/5 lymphopenia, 2/5 without results
  - Post-op: 4/5 patients had lymphopenia

Prophylaxis:
- 1 patient was recommended to start IVIG
- No patients required prophylactic antibiotics

Table 1. Pneumococcal Vaccine Titers*

Pneumococcal Vaccine Titers	#	%
Protective at baseline	2/12	17%
Non-protective at baseline	9/12	75%
No baseline titers available	1/12	8%
Patients receiving additional vaccine	8/12	67%
Protective titers post-additional vaccine	3/8	38%
Non-protective titers post-additional vaccine	4/8	50%
No titers available post- additional vaccine	1/8	13%

Non-protective pneumococcal titers

* Titers were considered protective if at least 50% of the titers checked were above 1.3 mcg/dL.
- Non-protective titers present in 9/12 patients (75%) at baseline
- Non-protective titers persisted in 4/8 patients (50%) even after an additional pneumococcal vaccine
- Vaccine given was Pneumococcal Polysaccharide Vaccine (PPSV23)
- Some patients had missing data for baseline titers, post-additional vaccine titers and/or did not receive the additional pneumococcal vaccine

Diphtheria, Tetanus and MMR Titers
- 9/9 (100%) of patients were tested for diphtheria and tetanus titers which showed protective levels
- 1/1 (100%) patient was tested for measles, mumps, and rubella titers which showed protective levels

DISCUSSION

- **Infections**: Our study agrees with literature: increased respiratory + ENT infections [5,6,7].
- **Absolute lymphopenia:** Our study shows 53%, compared to 80% in another [5].
- **T-cells:** Our study agrees with reduced T cell numbers reported [6] but differs to another showing normal T cell numbers but reduced naïve T cell % [5].
- **B-cells:** Previous research supported our findings, reporting low CD19+ B cell counts, reduced switched memory, and naïve B cells [5,7].
- **Immunoglobulins:** Our findings are consistent with research noting normal IgG and IgA levels but decreased IgM levels, contrasting with a report showing mostly normal levels [5,7].
- **Immune response:** Our findings, and those of other studies, reveal suboptimal immune responses in children with DS, with decreased class-switched memory B cells [5,6,7].
- **NK cells:** Dysregulation extends to NK cells, with a significant increase in NK cell percentage in both child and adult DS groups, aligning with findings of our study [6,7].

FUTURE DIRECTIONS

- Compile full results for manuscript publication
- Future studies should include larger sample sizes and multiple centers

SCAN FOR REFERENCES: