News and Views

Presentation on Molecular Genetic Approach in Diagnosing Childhood Primary Immunodeficiency Disease (PID) Attending Six Major Hospitals in Bangladesh

Dr. Sudipta Roy, ARM L Kabir and Dr. Kazi Selim Anwar

Background

PIDs are a heterogeneous group of adaptive and innate immune system inherited disorders. However, these disorders remain under-recognized and under-reported in several developing countries due to a lack of awareness among physicians and the non-availability of diagnostic facilities.

Abstract

On this ongoing study 42 cases were enrolled, PID screening positive-31, clinical exome sequencing was done in 13 cases yielded pathogenic mutations were found in 3 cases, likely pathogenic in 2 cases and significance in 7 cases. Genetically of three pathogenic genes one each of SCID Gene- IL2RG (-), X-Linked agammaglobulinemia GeneBTK (-) AND immunodeficiency-8 Gene-CORO1A (+) . Two of likely pathogenic are Severe congenital neutropenia-2 Gene-GFI1 (-) and Vici syndrome, Gene-EPG5 (-).

Objective:

To confirm the diagnosis of clinically suspected screening-positive PIDs in Bangladeshi children using molecular genetics.

Methodology

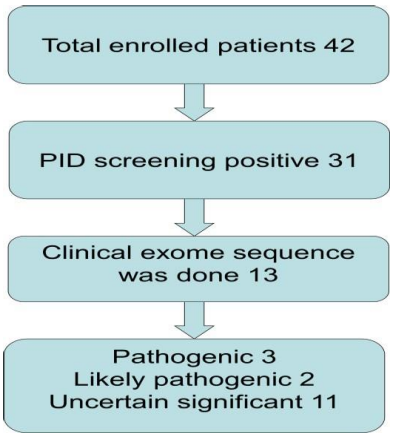
This is an ongoing longitudinal observational multicenter study in the pediatric department of 6 hospitals in Dhaka city funded by integrated health science research and development fund activity, Ministry of health and family welfare, Bangladesh over 2 years (September 2022 to August 2023). Study population -50. Children under 18 years with recurrent or persistent infections (3 or more) were enrolled. Exclusion criteria: chronic steroid ingestion, AIDS, PEM, NS, Leukemia etc.). PID screening tests (CBC, Serum antibody IgA, IgG, IgM, IgE and Lymphocyte Subset analysis), infection screening (CXR, MT, Gastric lavage etc.) were done. Clinical exome sequencing was performed in selected screening positive PID cases in Med Genome Labs Ltd., Bangalore, India for genetic analysis. Interim analysis was done after six months of study.

Result

Distribution of preliminary selected patients (42) fulfilling the inclusion criteria:

Conclusions

In the literature review, very few studies on PIDs have been published from Bangladesh and no molecular genetic analysis has been conducted yet. Our study shows 38% of clinically suspected patients have genetically confirmed PID. Large scale study is required to understand the molecular basis of PIDs in Bangladeshi children.



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Variable	Frequency
Age (Months)	31.29 ± 39.35
Sex	
Male	20 (71%)
Female	9 (29%)
M: F	2.2:1
Consanguinity	16 (51.6%)
H/O Sib death	5 (16.1%)
Affected Sib	4 (12.9%)
Mean age of onset (Months)	7.41 ± 9.25
Mean age of Diagnosis (Months)	30.56 ± 39.69

Table 1. Demographic profile of the study cases.

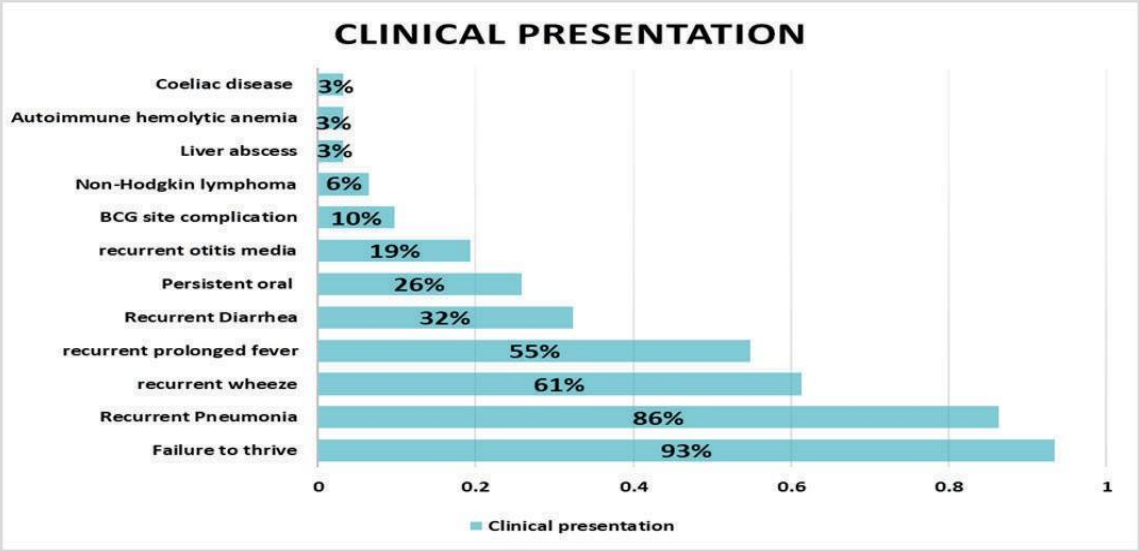

Chart 1 : The clinical presentation of PID patients

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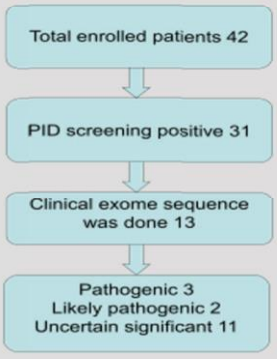

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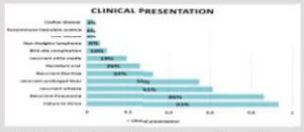

Chart 1. Bar Chart showing the clinical presentation of PID patients.

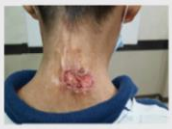

Figure 1. Chronic Nocardia infection in Hyper IgE syndrome.

Figure 2. BCG site abscess in SCID.

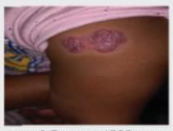

Figure 3. Exaggerated BCG response in NK cell deficiency.

Figure 4. Subcutaneous emphysema.

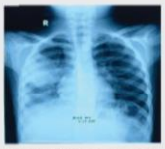

Figure 4. CXR showing consolidation (rt. Lung) in Hyper IgE syndrome.

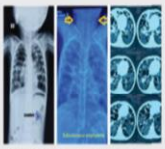

Figure 5. Bilateral cystic lesions & subcutaneous emphysema & Multiple cystic lesions in severe congenital neutropenia.

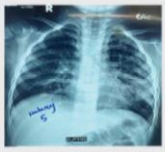

Figure 6. CXR showing bilateral consolidation in Bruton's agammaglobulinemia(X-linked).

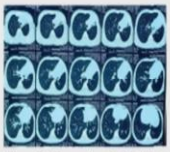

Figure 7. CT scan showing left-sided extensive bronchiectasis in Bruton's agammaglobulinemia (X- linked).

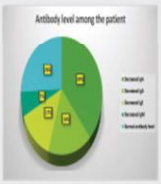

Chart 2. Pie chart showing antibody levels among the patient.

Chart 3. Pie chart showing the status of T cell, B cell, NK cell.

Findings of Clinical Exome Sequencing

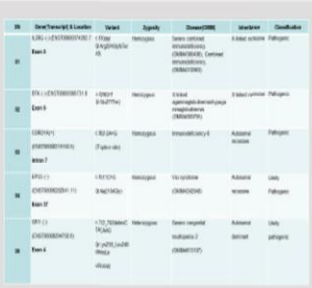

Table 2. Table showing Pathogenic or likely pathogenic mutation in 5 patients.

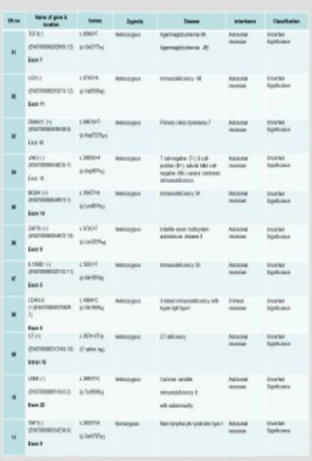

Table 3. Table showing mutation of uncertain significance in 11 patients.

CONCLUSIONS

In the literature review, very few studies on PIDs have been published from Bangladesh and no molecular genetic analysis has been conducted yet. Our study shows 38% of clinically suspected patients have genetically confirmed PID. Large scale study is required to understand the molecular basis of PIDs in Bangladeshi children.