Clinical profile of pediatric Primary Immune Deficiency (PID) disorders in a highly consanguineous population from south India

Reena Gulati, Vir S Negi, Haripraveen A

Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, India.

Introduction

Primary immune deficiency disorders (PIDs) are heterogeneous group of disorders of immunity, majority presenting early in life. PIDs, known to be genetic conditions are now called as Inborn errors of immunity (IEIs).

These are often subject to missed or delayed diagnosis as their symptoms overlap with common diseases of childhood, especially recurrent infections. or unusual or persistent infections and compromised growth and development. This may lead to compromised outcomes including failure to thrive, abnormally exaggerated response to live vaccines, persistent serious infections, and even early death.

Many PIDs are single gene disorders, have autosomal recessive (AR) inheritance and present in early childhood. Though phenotypically similar, the causative underlying gene mutations are known to significantly differ among different ethnicities. AR conditions occur with increased frequency among inbred populations.

We report the phenotypic and molecular profile of PIDs from a tertiary care centre in south India that caters to a population with a very high rate (~35%) of second and third degree consanguinity.

Objectives

Aim of the study:

To study the phenotypic and genotypic profile of (PID disorders) among children from a population with high rates of consanguinity.

Primary objective:

To determine the clinical and laboratory profile of Inborn errors of immunity or primary immune deficiency diseases in Tamil children from South India.

Contact

Dr. Reena Gulati

Professor, Department of Pediatrics and Clinical Immunology

JIPMER, Pondicherry, India

Email g97rina@gmail.com

Patients and methods

Patient data was collected in deidentified form from available records in the Hospital Information System of the institute.

Data was collected for a period of 3 years.

Study participants:

a. Inclusion criteria: Patients with clinical suspicion of PID/ inborn error of immunity, up to 18 years of age.

b. Exclusion criteria:

i) Patients with secondary immune deficiency e.g. HIV/AIDS,

ii) Patients on Immunosuppressive therapy

iii) Patients with recurrent infections secondary to diseases predisposing to recurrent infections e.g. congenital heart disease, genitourinary malformations etc.

Results

A total of 101 patients' data were analysed.

Males outnumbered females with a ratio of 54.2% to 45.8%.

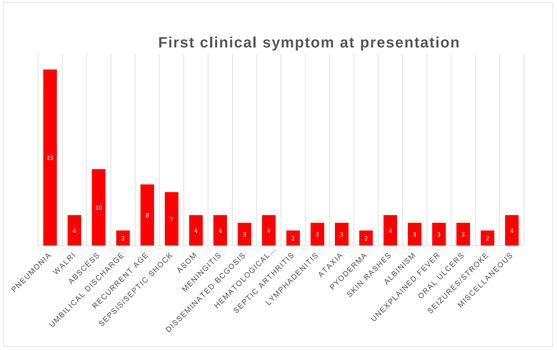

Fig 1. Frequency of the most frequently seen initial presentation

Table 1. Age group of patients at time of enrollment

Age group of the patient	(%)
Neonate	1.3
Infant	27.7
1-5 years	34.7
6-10 years	26.4
>10 years	9.7

Results

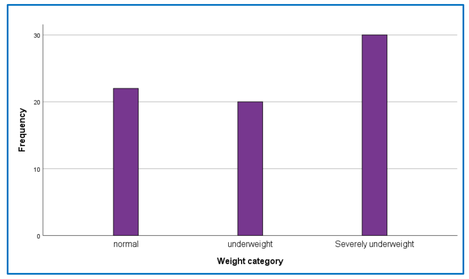

Fig 2. Categories of weight for age

Table 3. Parental consanguinity

Degree of consanguinity	(%)	Males (%)	Females (%)
Non consanguineous	47.2	67.6	32.3
Second degree	20.8	33.3	66.6
Third degree	31.9	47.8	52.2

Table 4. Infective organisms identified in specific PIDs

Infective organism identified	PID
CONS	Hyper IgM syndrome
CONS	SCID
Epstein Barr Virus	Severe congenital neutropenia
Salmonella typhi	SCID
Streptococcus pneumoniae	Selective IgA deficiency
Candida tropicalis, Stenotrophomonas maltophila	DiGeorge syndrome
Cytomegalovirus, Klebsiella pneumoniae, enterococcus	NOMID
Streptococcus oralis	CVID
Pseudomonas aeruginosa, Klebsiella pneumoniae	Atypical HUS
Staphylococcus hominis	Chronic granulomatous disease
Streptococcus pneumoniae, Acinetobacter baumanii	Hyper IgE syndrome
Enterobacter, Acinetobacter, Staphylococcus Cytomegalovirus	CVID
Streptococcus pneumoniae	X linked agammaglobulinemia
Streptococcus pneumoniae	Hyper IgM syndrome

Results

Table 4: Frequency of PIDs according to IUIS classification

Category	Frequency	PID
Predominantly antibody deficiency	26.3	Hyper IgM
		CVID
		Selective IgA deficiency
		XLA
		IgG subclass with IgA deficiency
Well defined syndromes	26.3	Hyper IgE
		Ataxia telangiectasia
		Wiskott Aldrich
		DiGeorge
		Dyskeratosis congenita
Congenital defects in phagocyte number or function	19.4	CGD
		LAD
		SCN
		GSD-1b
Combined immunodeficiencies	8.3	SCID
		Bare lymphocyte defect
Defects in intrinsic and innate immunity	7.2	MSMD
		Osteopetrosis
Immune dysregulation	8.3	ALPS
		Griscelli syndrome
		Hermansky-Pudlak syndrome
		Familial HLH
Complement deficiencies	2.7	Atypical HUS
		Hereditary angioedema

DISCUSSION

Children between 1-5 years constitutes the major group on our patients. Consanguinity was much higher (>50%) in patients compared to general population (35%). Only16.6% and had family history of PID while 26% had history of undiagnosed death in the family members. Majority were between 1-2 month of age at the time of onset of symptoms. There was one-fifth mortality of patients during the study period, much more in those requiring ICU care, indicating predominance and severity of recessively inherited single gene disorders of immunity. The median time between onset of symptoms and diagnosis was 15.5 months. Pneumonias, abscesses, recurrent diarrhea and septic shock were the most common initial presentations. Malnutrition was present in two-third of patients. More than one-third had delayed development. Unusual organisms and commensals were common pathogens. 'Well defined syndromes' and 'Predominant antibody defects' were the two most common classification IUIS groups. In the background of endemic tuberculosis infection, Mendelian susceptibility to mycobacterial disease is very common.

Reference

Bousfiha A, Jeddane L, Picard C, Al-Herz W, Ailal F, Chatila T, et al. Human Inborn Errors of Immunity: 2019 Update of the IUIS Phenotypical Classification. J Clin Immunol. 2020 Jan;40(1):66-81. doi: 10.1007/s10875-020-00758-x