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# **Original Research Article**

# Prevalence of hypersensitive pneumonitis specific IgG antibodies in the Indian population: A retrospective study

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#### ABSTRACT

Introduction: Identifying the underlying antigen responsible for Hypersensitivity Pneumonitis (HP) in patients poses a significant challenge within the confines of a typical clinical environment. Our primary objective in this study was to investigate the distribution and prevalence of Specific IgG antibodies among individuals diagnosed with HP, taking into account factors such as age, gender, and geographical location. Materials and Methods: A retrospective study spanning 5 years (from January 2018 to June 2023) was conducted, involving patients over the age of 18 who had undergone screening for HP. Data collected from 1087 patients was analysed, and the patients were categorized based on age, gender, location, and their specific IgG antibody status.

Results: Out of the total cohort of 1087 patients, 62.47% were female, while 37.53% were male. The overall positivity rate for HP panel testing was determined to be 49.22%. Among the patients subjected to testing, 174 individuals (16.01%) tested positive for at least one specific antibody. Notably, among patients aged 18 to 30 years, Penicillium emerged as the most prevalent specific IgG (48.28%), closely followed by fumigatus Fumigatus (44.83%). In contrast, for patients aged 31 to 45 years, Pigeon serum feathers exhibited the highest prevalence (39.69%). Moreover, the positivity rates varied across different regions in India

Conclusions: HP can be attributed to an array of agents commonly encountered in both workplace and home settings, encompassing microorganisms, animal and plant proteins, as well as organic and inorganic chemicals. Discerning the causative antigen not only holds immense value for physicians in optimizing patient treatment but also plays a pivotal role in pinpointing the source of exposure. Armed with this knowledge, physicians can provide patients with tailored advice to minimize their exposure risk, potentially leading to disease stabilization or even reversal. In summary, the successful identification of the etiologic antigen emerges as a formidable tool for enhancing the overall quality of patient care.

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# 1. Introduction

Hypersensitive pneumonitis (HP), also recognized as extrinsic allergic alveolitis, represents a lung condition arising from allergic reactions triggered by the inhalation of microorganisms, fungi/yeasts, plant or animal proteins, or chemical agents. This immune hypersensitivity response

can induce inflammation within the lung's alveoli and airways, potentially leading to the development of Interstitial Lung Disease (ILD).<sup>1,2</sup>

The incidence of HP varies significantly, influenced by factors such as geographical location, environmental shifts, and genetic predisposition. In the United States, HP accounts for less than 2% of ILD cases, with an annual occurrence of approximately 30 cases per 100,000

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individuals.<sup>3</sup> Notably, data from the *interstitial lung disease*-India registry indicates a substantial prevalence of 47.3% for HP within the spectrum of *interstitial lung diseases*.<sup>4</sup>

Historically, HP classification comprised acute, subacute, or chronic forms. However, recent guidelines endorsed by a clinical committee comprising the American Thoracic Society (ATS), the Japanese Respiratory Society, and the Asociacion Latinoamericana del Torax have categorized HP as either fibrotic or nonfibrotic. This classification stems from the primary diagnostic reliance on radiological or histopathological evidence of fibrosis. Fibrotic HP is associated with elevated mortality and morbidity rates, while nonfibrotic variants exhibit more favourable prognoses and treatment responses. Consequently, serum IgG testing has been advocated by the committee to identify potential antigens linked to both fibrotic and nonfibrotic forms of HP.<sup>5</sup>

Clinical presentations of both fibrotic and nonfibrotic HP commonly encompass symptoms like dyspnoea, cough, chest tightness, wheezing, and mid-inspiratory squeaks, with less frequent manifestations, including low-grade fever, weight loss, and malaise. These symptoms may manifest acutely, spanning weeks to months, or chronically, persisting over extended durations. Non-fibrotic HP may manifest acutely, with or without symptoms, whereas fibrotic HP typically unfolds insidiously and is often associated with specific exposure histories.<sup>5</sup>

Should an individual experience acute symptoms following exposure to an antigen, symptom onset typically occurs 8-9 hours post-exposure and may subside within 24-48 hours of cessation. Accurate diagnosis necessitates a meticulous inquiry into the individual's occupational history and potential exposure to antigens.<sup>2</sup>

However, HP is frequently underrecognized owing to its low incidence in the general population. It frequently masquerades as respiratory infections or idiopathic ILD, thereby contributing to potential underdiagnosis. Given its diverse clinical presentations, considering HP as a potential diagnosis across various clinical contexts is imperative.<sup>6</sup>

Diagnosing HP proves intricate as no definitive test exists. Diagnosis relies on a composite evaluation encompassing clinical, radiological, and histopathological examinations. Early identification offers the potential for reversibility, while untreated cases can progress to irreversible pulmonary fibrosis. Consequently, identifying the underlying antigen is pivotal for both prevention and prognosis prediction. Quantitative serologic testing of serum-specific immunoglobulins IgG (sIgG) serves as a crucial component in determining the causative antigen, aligned with ATS guidelines that endorse serum IgG testing to distinguish HP from other ILDs. This test boasts a sensitivity of 83% and specificity of 68%.<sup>7</sup> Elevated sIgG antibody levels can indicate exposure to specific antigens within a medical context, facilitating the identification of the triggering antigen responsible for HP's onset and diagnosis. Nonetheless, the absence of elevated sIgG levels does not unequivocally exclude the possibility of HP, primarily due to the limited availability and variability of commercially accessible antigens for routine testing. Despite these constraints, the determination of sIgG antibodies remains an indispensable facet of HP diagnosis and prognosis forecasting, with quantitative antigen sIgG analysis constituting a pivotal criterion within HP's diagnostic algorithms.<sup>8</sup>

At the Global Reference Lab, we conducted a retrospective study to assess the primary positive rate of Hypersensitive Pneumonitis antigens within the Indian population. This study encompassed an in-depth evaluation of prevalence, meticulously considering gender, age, and geographic factors.

#### 2. Materials and Methods

A comprehensive retrospective study was conducted at, Global Reference Laboratory, Mumbai, Maharashtra, spanning 5 years (from January 2018 to June 2023). Data collection and meticulous examination transpired in July 2023, with the requisite prior authorization secured for utilizing Laboratory Information Management System (LIMS) data from the independent ethics committee.

#### 2.1. Inclusion criteria

For this study, we meticulously scrutinized data derived from a total of 1087 patients, with no discrimination based on their clinical history. Serum samples were judiciously collected from a diverse population encompassing both male and female individuals aged 18 years and above. These serum samples were subjected to rigorous testing, focusing on *specific IgG* antibodies within the HP profile, utilizing the cutting-edge Thermo Fisher Scientific Phadia 250 analyzer, employing the fluorescent enzyme immunoassay technique.

Within this assay, diminutive vessels denoted as CAPs harboured corresponding antigens that elicited specific reactions with the IgG antibodies present in the patient's sera. Quantification of the human IgG antibodies bound to these antigens was meticulously conducted, facilitated by the utilization of *fluorescence* optics in conjunction with an enzyme-labelled anti-IgG, ensuring precision and reliability.

### 2.2. Exclusion criteria

Patients falling below the age of 18 years were excluded from the purview of this study, focusing our attention exclusively on the adult population to maintain research consistency and relevance.

Table 1: Hypersensitive pneumonitis profile interpretation

HP Antibody Panel	Method	Interpretation	Remarks
Penicillium chrysogenum (Specific IgG)	Fluorescent enzyme Immunoassay	<= 19.1 mgA/L	Woodworkers' lung
Cladosporium herbarum (Specific IgG)	Fluorescent enzyme Immunoassay	<= 36.0 mgA/L	Farmers lung disease
Aspergillus fumigatus (Specific IgG)	Fluorescent enzyme Immunoassay	<= 27.4 mgA/L	Mushroom workers lung
Mucor racemosus(Specific IgG)	Fluorescent enzyme Immunoassay	<= 10.0 mgA/L	Respiratory allergy
Alternaria alternata (Specific IgG)	Fluorescent enzyme Immunoassay	<= 13.1 mgA/L	Respiratory allergy
Pigeon serum proteins, feathers and droppings (Specific IgG)	Fluorescent enzyme Immunoassay	<= 30 mgA/L	Bird Fanciers lung

#### 2.3. Data analysis

Data recording was managed using MS Excel. To summarize discrete variables, frequencies and percentages were employed. To ascertain the association between HP antibodies and various factors, including Age group, Gender, and Region, the Chi-square test was deployed for statistical analysis. All statistical computations were performed using "R Studio version 1.4.1103". A two-tailed p-value of <0.05 was considered statistically significant.

# 3. Results

# 3.1. Overall demographic distribution of hypersensitive pneumonitis profile antibodies

A total of 1087 patients underwent testing for HP. Within this cohort, 679 individuals (62.47%) were female, whereas 408 (37.53%) were male. Among the females tested, the majority were found in the age groups of 46-60 years (68.27%), and 31-45 years (68.21%). In contrast, the highest number of males who underwent testing belonged to those above 60 years (43.66%). (Table 2)

#### 3.2. Region-wise Distribution of HP in India

Out of the 1087 patients included in the study, a majority of 603 individuals (55.47%) originated from the North region of India, while 350 patients (32.20%) were from the West region. (Table 3)

#### 3.3. Distribution of HP antibody positivity

Within the comprehensive HP panel encompassing the examination of six distinct antibodies, it was observed that *Specific IgG Penicillium Chrysogenum* exhibited the highest positivity rate among both females (36.38%) and males (31.86%). (Table 5)

# 3.4. Age-wise prevalence of HP antibodies

An analysis of age-specific prevalence within the cohort revealed intriguing trends. Among individuals aged 18 to 30 years, the highest occurrence of *Penicillium Chrysogenum* antibodies was observed, constituting 48.28% of this age group, with *Aspergillus fumigatus* closely trailing at 44.83%. For those falling in the 31 to 45-year age range, the predominant presence was associated with pigeon serum feathers (39.69%), closely followed by *Penicillium Chrysogenum* (39.07%). (Table 6)

#### 3.5. Regional Variation in HP antibody positivity

The North region of India has reported the highest overall test results, with a positivity rate of 30.68% for *Penicillium chrysogenum* and 20.52% for *Pigeon serum proteins*. It is noteworthy that the East region has exhibited the most significant positivity rates for specific antibodies. Despite having fewer participants, the East region has shown prevalence rates for *Aspergillus fumigatus* (38.71%), *Mucor racemosus* (28.57%), and *Penicillium chrysogenum* (45.16%). On the other hand, in the West region, different antibodies have shown the highest positivity rates. These include *Alternaria alternata* (24%), *Aspergillus fumigatus* (29.71%), *Penicillium chrysogenum* (42.0%), and *Pigeon serum proteins' feathers and droppings* (31.50%). (Detailed statistics are available in .Table 7)

# 3.6. The amount of HP antibodies that test positive in patients

Among the 1087 patients evaluated, 552 individuals (50.78%) exhibited no antibodies within the *Hypersensitive Pneumonitis* panel. In contrast, 174 patients (16.01%) yielded positive results for at least one antibody. 102 individuals (9.38%) displayed reactivity to two distinct antibodies, while a noteworthy cohort of 259 patients (23.83%) demonstrated reactivity to more than two antibodies. (Table 8 for a comprehensive breakdown).

Table 2: Distribution of hypersensitive pneumonitis profile antibodies age	e andgender-wise.
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		Gen				
Age Group	Fe	male	Ν	lale		
	n	%	n	%	Total	% of Total
18-30	18	62.07%	11	37.93%	29	2.67%
31-45	103	68.21%	48	31.79%	151	13.89%
46-60	269	68.27%	125	31.73%	394	36.25%
>60	289	56.34%	224	43.66%	513	47.19%
Total	679	62.47%	408	37.53%	1087	
n=Number of participa	ants, % =Percentage	2				
Table 3: Location-w	ise distribution of	f HP				
Region			n		%	)
East			31		2.85	5%
North			603		55.4	7%
South			103		9.48	
West			350		32.2	0%
n=Number of participa	ants. % =Percentage	<u>.</u>				
Table 4: Overall pos	sitivity of HP spec	cific IgG				
Table 4: Overall pos           HP Antibodies           Alternaria alternational		cific IgG	n		76	)
HP Antibodies		cific IgG	n 228		% 20.9	
HP Antibodies Alternaria alternat Abnormal Normal	a (Specific IgG)					8%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga	a (Specific IgG)		228 859		20.9 79.0	8% 2%
HP Antibodies Alternaria alternat Abnormal Normal	a (Specific IgG)		228 859 292		20.9	8% 2%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga	a (Specific IgG)		228 859		20.9 79.0	8% 2% 6%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal	a (Specific IgG) tus (Specific IgG)	)	228 859 292		20.9 79.0 26.8	8% 2% 6%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal Normal Cladosporium her Abnormal	a (Specific IgG) tus (Specific IgG)	)	228 859 292 795 181		20.9 79.0 26.8 73.1 16.6	8% 2% 6% 4% 5%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal Normal Cladosporium her Abnormal Normal	a (Specific IgG) tus (Specific IgG) barum (Specific I	)	228 859 292 795		20.9 79.0 26.8 73.1	8% 2% 6% 4% 5%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal Normal Cladosporium her Abnormal Normal Mucor racemosus	a (Specific IgG) tus (Specific IgG) barum (Specific I	)	228 859 292 795 181 906		20.9 79.0 26.8 73.1 16.6 83.3	8% 2% 6% 4% 5%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal Normal Cladosporium her Abnormal Normal	a (Specific IgG) tus (Specific IgG) barum (Specific I	)	228 859 292 795 181		20.9 79.0 26.8 73.1 16.6 83.3 19.4	8% 2% 6% 4% 5% 5%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal Normal Cladosporium her Abnormal Normal Mucor racemosus	a (Specific IgG) tus (Specific IgG) barum (Specific I	)	228 859 292 795 181 906		20.9 79.0 26.8 73.1 16.6 83.3	8% 2% 6% 4% 5% 5%
HP Antibodies Alternaria alternat Abnormal Normal Aspergillus fumiga Abnormal Normal Normal Normal Mucor racemosus Abnormal	a (Specific IgG) tus (Specific IgG) barum (Specific I (Specific IgG)	) [gG)	228 859 292 795 181 906 174		20.9 79.0 26.8 73.1 16.6 83.3 19.4	8% 2% 6% 4% 5% 5%
HP Antibodies Alternaria alternat Abnormal Normal Abnormal Normal Cladosporium her Abnormal Normal Mucor racemosus Abnormal Normal Normal	a (Specific IgG) tus (Specific IgG) barum (Specific I (Specific IgG)	) [gG)	228 859 292 795 181 906 174		20.9 79.0 26.8 73.1 16.6 83.3 19.4	8% 2% 6% 4% 5% 0% 0%
HP Antibodies Alternaria alternat Abnormal Normal Abnormal Normal Cladosporium her Abnormal Normal Mucor racemosus Abnormal Normal Normal Penicillium chryste	a (Specific IgG) tus (Specific IgG) barum (Specific I (Specific IgG)	) [gG)	228 859 292 795 181 906 174 723		20.9 79.0 26.8 73.1 16.6 83.3 19.4 80.6	8% 2% 6% 4% 5% 5% 0% 8%
HP Antibodies Alternaria alternati Abnormal Normal Aspergillus fumiga Abnormal Normal Mucor racemosus Abnormal Normal Normal Penicillium chryso Abnormal Normal Normal	a (Specific IgG) tus (Specific IgG) barum (Specific I (Specific IgG) ogenum (Specific I	) [gG)	228 859 292 795 181 906 174 723 377 710		20.9 79.0 26.8 73.1 16.6 83.3 19.4 80.6 34.6	8% 2% 6% 4% 5% 5% 0% 8%
HP Antibodies Alternaria alternati Abnormal Normal Aspergillus fumiga Abnormal Normal Mucor racemosus Abnormal Normal Normal Penicillium chryso Abnormal Normal Normal	a (Specific IgG) tus (Specific IgG) barum (Specific I (Specific IgG) ogenum (Specific I	) 'gG) IgG)	228 859 292 795 181 906 174 723 377 710		20.9 79.0 26.8 73.1 16.6 83.3 19.4 80.6 34.6	8% 2% 6% 4% 5% 0% 0% 8% 2%

n=Number of participants, % =Percentage

#### 4. Discussion

*Hypersensitive Pneumonitis* presents a diagnostic challenge due to the often-unknown triggering substance. Currently, no definitive method exists for HP diagnosis. However, testing with a range of common antigens may offer valuable insights, particularly in cases lacking an exposure history. Despite being a prevalent form of ILD, limited research has focused on HP epidemiology. Discrepancies in ILD and its subtypes, including HP, have arisen from differences in study methodologies, definitions, and actual environmental or cultural factors impacting occurrence and frequency.<sup>4</sup>

In our retrospective study at the Global Reference Laboratory, we observed a higher proportion of women (62.47%) undergoing HP testing compared to men (37.53%). A study conducted in North India, as reported in the European Respiratory Journal, found a similar trend with 73.3% of participants being female.<sup>9</sup> Another study by Evans et al. in the United States also identified a higher prevalence of HP among women than men. Additionally, their study revealed an increase in cases with age, particularly among adults aged 65 years and older.<sup>10</sup> Conversely, a study conducted in Turkey by Adem et al. showed a different pattern, with 52.6% of cases being male.<sup>11</sup>

In our research, slightly over half of the participants (50.78%) did not exhibit any antibodies in the HP panel, while the remaining 49.22% tested positive for HP panel

		Se	X			
HP Antibodies	Fe	male	Ν	P-value		
	n	%	n	%	P-value	
Alternaria alternata (	Specific IgG)					
Abnormal	140	20.62%	88	21.57%	0.7096	
Normal	539	79.38%	320	78.43%	0.7096	
Aspergillus fumigatus	(Specific IgG) grou	ıp				
Abnormal	194	28.57%	98	24.02%	0.1013	
Normal	485	71.43%	310	75.98%		
Cladosporium herba	rum (Specific IgG)					
Abnormal	121	17.82%	60	14.71%	0 1922	
Normal	558	82.18%	348	85.29%	0.1822	
Mucor racemosus (Sp	pecific IgG)					
Abnormal	116	20.14%	58	18.07%	0 4525	
Normal	460	79.86%	263	81.93%	0.4525	
Penicillium chrysoge	num (Specific IgG)					
Abnormal 247		36.38%	130	31.86%	0 1202	
Normal	432	63.62%	278	68.14%	0.1302	
Pigeon serum protein.	s feathers and dropp	pings (Specific IgG)				
Abnormal	180	29.08%	53	14.21%	< 0.0001	
Normal	439	70.92%	320	85.79%	< 0.0001	

#### Table 5: Gender-inclusive positivity of HP specific IgG

n=Number of participants, % =Percentage, p<0.05 is considered statistically significant

# Table 6: Age-wise prevalence of HP antibodies

				Age	Group				
HP Antibodies	1	18-30		31-45		46-60		>60	
Antibodies	n	%	n	%	n	%	n	%	p-value
Alternaria alter	rnata (Spe	ecific IgG)							
Abnormal	9	31.03%	47	31.13%	79	20.05%	93	18.13%	0.0031
Normal	20	68.97%	104	68.87%	315	79.95%	420	81.87%	0.0031
Aspergillus fun	nigatus (Sp	pecific $IgG$ )							
Abnormal	13	44.83%	50	33.11%	94	23.86%	135	26.32%	0.0217
Normal	16	55.17%	101	66.89%	300	76.14%	378	73.68%	0.0217
Cladosporium .	herbarum	(Specific IgG)							
Abnormal	10	34.48%	36	23.84%	58	14.72%	77	15.01%	0.0025
Normal	19	65.52%	115	76.16%	336	85.28%	436	84.99%	0.0023
Mucor racemos	sus (Speci	fic IgG)							
Abnormal	6	26.09%	36	28.35%	64	19.10%	68	16.50%	0.0246
Normal	17	73.91%	91	71.65%	271	80.90%	344	83.50%	0.0240
Penicillium chr	ysogenum	(Specific IgG)							
Abnormal	14	48.28%	59	39.07%	125	31.73%	179	34.89%	0.1590
Normal	15	51.72%	92	60.93%	269	68.27%	334	65.11%	0.1390
Pigeon serum p	proteins fe	athers and drop	pings (Spec	cific IgG)					
Abnormal	6	25.00%	52	39.69%	103	28.22%	72	15.25%	< 0.0001
Normal	18	75.00%	79	60.31%	262	71.78%	400	84.75%	

n=Number of participants, % =Percentage, p<0.05 is considered statistically significant

				Re	egion				
HP	East		North		South		West		-
Antibodies	n	%	n	%	n	%	n	%	p-value
Alternaria alter	rnata (Spe	cific IgG)							
Abnormal	6	19.35%	124	20.56%	14	13.59%	84	24.00%	0.1.420
Normal	25	80.65%	479	79.44%	89	86.41%	266	76.00%	0.1429
			Asperg	gillus fumigatus	(Specific Ig	G) group			
Abnormal	12	38.71%	154	25.54%	22	21.36%	104	29.71%	0 1000
Normal	19	61.29%	449	74.46%	81	78.64%	246	70.29%	0.1223
Cladosporium	herbarum	(Specific IgG)							
Abnormal	5	16.13%	96	15.92%	16	15.53%	64	18.29%	0.0000
Normal	26	83.87%	507	84.08%	87	84.47%	286	81.71%	0.8002
Mucor racemos	sus (Specij	fic IgG)							
Abnormal	6	28.57%	89	16.76%	17	18.09%	62	24.70%	0.0420
Normal	15	71.43%	442	83.24%	77	81.91%	189	75.30%	0.0438
Penicillium chr	ysogenum	(Specific IgG)							
Abnormal	14	45.16%	185	30.68%	31	30.10%	147	42.00%	0.0018
Normal	17	54.84%	418	69.32%	72	69.90%	203	58.00%	
Pigeon serum p	proteins fea	athers and drop	opings (Spec	cific IgG)					
Abnormal	6	21.43%	111	20.52%	13	13.54%	103	31.50%	0.0002
Normal	22	78.57%	430	79.48%	83	86.46%	224	68.50%	0.0002

#### **Table 7:** HP distribution in India

n=Number of participants, % =Percentage, p<0.05 is considered statistically significant

Table 8: Number of positive antibody tests.

Positivity	n	Percentage (%)
0	552	50.78%
1	174	16.01%
2	102	9.38%
3	90	8.28%
4	63	5.80%
5	51	4.69%
6	55	5.06%
Total	1087	100%

n=Number of participants, % =Percentage

antibodies. This aligns with a study by the National Data Coordinating Centre in India, which found a prevalence rate of 47.3% for HP in India. However, international studies have reported varying incidence rates, such as 6.4% in Saudi Arabia, 4% in Turkey, 2.6% in Greece, and 13.2% in Germany. These variations result from differences in antigens used in HP panels, as well as geographic, environmental, and cultural factors. Notably, the presence of *Specific IgG* implies exposure to the causative antigen but is not diagnostic of HP, and the absence of IgG to specific antigens does not exclude HP.<sup>4</sup>

In our study, 16.01% tested positive for at least one antibody, and 33.21% were positive for two or more antibodies. A study conducted in Thailand reported that 64.7% of participants had only one antibody, while 19.9% had multiple antibodies. Importantly, the number of antigens did not impact survival, histopathologic results, or radiographic findings. The type of antigen also did not affect survival. However, those exposed to *Mold* were more

likely to experience fibrotic HP compared to those exposed to avian antibodies.<sup>12</sup>

The highest antibody positivity in our study was for *Specific IgGPenicillium chrysogenum* among both females (36.38%) and males (31.86%). *Pigeon serum proteins and droppings* followed at 29.08% for females. *Specific IgGAspergillus fumigatus* showed positivity rates of 28.57% in females and 24.02% in males. Positivity for *Specific IgG Penicillium chrysogenum* was highest in the 18 to 30 years age group (48.28%), followed by Aspergillosis Fumigatus at 44.83%. Among the 31 to 45 years age group, the highest prevalence was of *Pigeon serum proteins* (39.69%).Prospective data from the ILD-India study by Collins et al. suggest that cooler pads may serve as a breeding ground for *mold*, reported by approximately 48% of individuals exposed to air coolers, potentially acting as the inciting antigen for HP.<sup>4</sup>

The occurrence of *Mold*-induced HP (Aspergillus, Cladosporium, Penicillium, and Mucor species) has been

on the rise due to factors such as humidifiers, heating, and ventilation systems. Nevertheless, *molds* can also be present in unexpected places in homes, such as fruits and vegetables, resulting in different types of HP.<sup>13</sup>

However, another North Indian study reported that 31.7% of patients were exposed to pigeon droppings.<sup>9</sup> Similarly, a German study by Sennekamp et al. found that most antibodies were against *avian antigens* (28%) and *Aspergillus fumigatus* (25%). Bird fancier's lung could be the cause of 40% of HP cases in Germany and the United States.<sup>14</sup>

Many studies have also reported bird-related HP as the most common antibody in Europe and North America, while Japan has reported domestic antigen exposure (*Mold*) as the most common cause of HP, followed by avian and other occupational exposures.<sup>1</sup> Nogueira et al. have substantiated that Bird Fancier's Lung (BFL) is the most common type of Hypersensitivity Pneumonitis (HP) found worldwide, accounting for 66-68% of all HP cases. BFL is caused by inhaling bird droppings and secretions.<sup>13</sup>

Our study findings indicate that the North region had the highest number of HP tests conducted (55.47%) and exhibited a positivity rate of 30.68% for Penicillium chrysogenum. On the other hand, the East region had high positivity rates for Aspergillus fumigatus (38.71%), Mucor racemosus (28.57%), and Penicillium chrysogenum (45.16%). In the West region, Penicillium Chrysogenum (42.0%) showed the highest positivity followed by Pigeon serum protein feathers and droppings (31.50%) and Aspergillus fumigatus (29.71%). Penicillium chrysogenum was found to have a high positivity rate in both the North (30.68%) and South (30.10%) regions. According to an Indian study, 45.8% of patients residing in urban areas across 11 cities were diagnosed with HP, with the highest number of cases (55%) coming from the North region, followed by East (43.4%), South (40.9%), and Western India (38.5%). It is possible that the decline in lung function in Indian urban cities compared to other countries could be linked to higher levels of ambient air pollution. The particulate matter in the air can reach the alveoli, contributing to this issue.<sup>15</sup>

#### 5. Limitations

The study was done using the Laboratory data of patient results and basic demographic details, however, it lacked the details of clinical condition and treatment history. This could have given more insights pertaining to the disease pattern and its outcome.

### 6. Conclusion

HP, a type of *interstitial lung disease*, results from repeated exposure to environmental and occupational antigens. Identifying specific antibodies and the source of exposure in suspected HP patients can be challenging. Our study,

which included 1087 patients, revealed that nearly half of them tested positive for HP. We found that the most common antibody in the Indian population is *Specific IgG Penicillium chrysogenum*, followed by *Aspergillus fumigatus* and pigeon serum feathers. The onset of symptoms in suspected HP patients may be linked to certain environments and workplaces. Avoiding exposure to the triggering antigen is crucial for improving HP prognosis and outcomes. HP is a complex syndrome that urgently requires more stringent and selective diagnostic criteria and validation, including broader panels of IgG and collaboration with occupational physicians as part of multidisciplinary expertise.

#### 7. Conflicts of Interests

None declared.

#### 8. Source of Funding

None.

#### 9. Acknowledgements

None.

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