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CHANGING ETIOLOGICAL PARADIGM OF ATYPICAL PNEUMONIA

Microbiology

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ABSTRACT

Atypical pneumonia is an acute infection of lung interstitium , difficult to detect by conventional gram staining and cultures. Etiological diagnosis have changed from bacterial to viral over the time by the help of advanced diagnostic tools, such as nucleic acid amplification tests . Method:Conventional culture methods, ELISA and multiplex PCR were used to detect atypical bacteria and respiratory viruses on 164 adults. Results: Microbiological diagnoses was ascertained in 76 (46.34%) out of 164. Dominant role of viral pathogens (34.61%), particularly H1N1(7.69%) and Influenza-A (5.76 %) with lesser roles of bacterial (5.6%) and fungal (3.84%) agents. PCR methodology was significantly more sensitive and specific for the detection of atypical pathogens ($p < 0.0001$). Conclusion : Our understanding of atypical pneumonia has shifted from primarily bacterial etiology to viral etiology .This change is due to advancements in diagnostic techniques.

KEYWORDS

Atypical pneumonia, Shift from bacterial to viral etiology , Multiplex PCR

INTRODUCTION

Atypical pneumonia is an acute infection of the lung interstitium. [1]

1st described in the early 20th century as these pathogens couldn't be detected by conventional gram staining and cultures.[2,3] Symptoms found usually are low-grade fever, dry cough, breathlessness, headache, vomiting, abdominal pain, diarrhea ,sore throat ,myalgias etc. [4] Bacterial etiology of atypical pneumonia includes *Mycoplasma pneumoniae* (1944) [5,6] , *Legionella pneumophila* after an outbreak in Philadelphia (1977) [7,8] and *Chlamydophila pneumoniae* (1984) .[9-12]

Although viral etiology of pneumonia is known since the discovery of Influenza virus (1933)[13] ,their significance was often overlooked. Advanced diagnostic tools, such as nucleic acid amplification tests have revealed that viral pathogens are not only common causes of atypical pneumonia but are actually more prevalent than bacteria.

Studies show that viruses account for about 44% of atypical pneumonia[14] . Common viral causes include influenza virus, parainfluenza virus, respiratory syncytial virus (RSV), adenovirus etc .[15] Rapid molecular testing like PCR especially multiplex PCR has greatly improved our ability to detect these respiratory viruses in clinical samples.[16,17]

The emergence of new viruses such as avian influenza A (H5N1), influenza A (H1N1) responsible for the 2009 pandemic and highly transmissible coronaviruses recently lead to various outbreaks and pandemics.[18,19]

Objective of our study was to find out etiological agents causing atypical pneumonia in our community.

MATERIAL AND METHODS

This descriptive observational study was conducted in the Department of Microbiology, in association with Department of Medicine, Respiratory Medicine and Paediatrics at Gajra Raja Medical College & J.A. Group of Hospitals, Gwalior, a tertiary care hospital for 1 year (2022 -2023).

This study was conducted after the Institutional Human Ethical Committee approval (19/IEC-GRMC/2022) before the commencement of the study.

Patient who were suspected or had primarily atypical pneumonia pulmonary features like fever, non-productive cough, chest pain, chest discomfort, breathlessness ,sore throat and extra pulmonary symptoms like generalised body pain, joint pain, myalgia ,rash, headache, confusion, altered sensorium, unconsciousness, abnormal body movements, weakness, nausea, vomiting, abdominal pain, diarrhoea and difficulty in urination considering their negative conventional cultures for typical pneumonia causing organisms were enrolled for the study.

Total of 164 samples were processed that included 87 sputum, 36 blood , 27 nasopharyngeal and oropharyngeal swabs, 9 bronchoalveolar lavages , 3 tracheal aspirates and 2 gastric aspirates.

Specific agars like PPLO (Pleuropneumonia like organism), BCYE (buffered charcoal yeast extract agar) and SDA (Sabouraud dextrose agar) *by* Himedia Laboratories Pvt. Ltd. were used to isolate *Mycoplasma pneumoniae* , *Legionella spp*. and fungal elements respectively.

IgM ELISA was used for identification of *Leptospira spp. and Herpes Simplex virus* by Novatec Heathcare Co.,Ltd and XEMA Co. Ltd . respectively.

Multiplex PCR were used to detect *Mycoplasma pneumoniae, Chlamydia pneumoniae* and respiratory viral pathogens- Influenza A (HINI,H3N2), Influenza B, Respiratory synchytial virus SARS-CoV-2, Adenovirus, Epstein Barr virus and Human herpes 6 & 7 virus by using Biorad CFX96 real time pcr system by various kits by Himedia Laboratories Pvt. Ltd . and altona diagnostics .

The statistical analysis was performed using IBM SP SS Statistics version 26 (IBM Corp., Armonk, NY, USA) and MedCalc version 15.6 (MedCalc Software Ltd, Ostend, Belgium).

RESULTS

1. Distribution Of Pathogenic And Non Pathogenic Organisms Isolated From The Specimens Obtained From The Study Participants (n=156)

S. No.	Organisms	Frequency (n)	Percentage (%)
1.	HHV-7	8	5.6
2.	H1N1 virus	12	7.69

3.	SARS-CoV-2	6	3.84
4.	Adenovirus	9	5.76
5.	Herpes Simplex virus	6	3.84
6.	Influenza- A virus	9	5.76
7.	Leptospira Spp.	8	5.6
8.	Epstein Barr virus	1	0.64
9.	Influenza- B virus	3	1.93
10.	Candida albicans	3	1.93
11.	Non albicans candida	1	0.64
12.	Aspergillus fumigatus	1	0.64
13.	Aspergillus flavus	1	0.64
14.	Non-pathogenic organism	88	56.41
Total		156	100

2. Distribution Of Mixed Pathogenic Organisms Detected By PCR From The Specimens Obtained From The Study Participants (n = 8)

S.No.	Mixed Organisms	Frequency(n)	Percentage (%)
11.	H1N1 And Influenza-A virus	3	37.5
22.	Adenovirus and HHV-7	3	37.5
33.	Human Herpes Virus -6 & 7	2	25
Total		8	100

3. Pathogens Identified Using Various Types Of Tests (n = 164)

S.No.	Type of test performed	Positive	Negative	Positivity Rate (%)	Chi Square	p value
1.	Culture	6	158	3.65	67.351	p < 0.0001
2.	IgM ELISA	14	150	8.54		
3.	PCR	56	108	34.12		

DISCUSSION

Our study confirms the dominant role of viral pathogens (34.61%), particularly H1N1(7.69%) and Influenza-A (5.76 %), in atypical pneumonia, while highlighting the lesser roles of bacterial (5.6%) and fungal (3.84%) agents.

This finding is in line with Jain et al. (2015), which also reported a higher prevalence of respiratory viruses compared to bacteria. The prominence of H1N1 and Influenza-A viruses, consistent with previous studies by Sachdeva et al. (2018)[20] highlights the ongoing relevance of these viruses in atypical pneumonia.

The presence of mixed infections and the detection of less common pathogens like Human Herpes Virus-7 and Leptospira spp. suggest that atypical pneumonia is a multifactorial condition requiring diverse diagnostic and treatment strategies.

The rarity of fungi as causative agents, with Candida albicans and Aspergillus spp. being detected in only a small percentage of cases, reflects the generally lower incidence of fungal infections compared to viral causes.

The higher proportion of males (62.8%) observed in our study, consistent with other studies, could indicate a gender-related predisposition or reporting bias.

The predominance of middle-aged adults (50 - 60 years) in our study, with a mean age of 49 years, suggests that age-related factors might influence susceptibility .

CONCLUSION

Our understanding of atypical pneumonia has shifted from primarily bacterial etiology to viral etiology .This change is due to advancements in diagnostic techniques.

No etiological agent could be ascertained in 88 (53.65%) patients in our study as there are many more viruses causing atypical pneumonia which we could not cover in our study, some may require more elaborative study to detect them and another reason can be their too low concentration which can be detectable.

We could not isolate *Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila*, H3N2 and Respiratory Syncytial Virus inspite of using culture and PCR may be to herd immunity, cyclical nature of the organism, seasonality, geographical distribution and interrupted transmission through the use of masks as all are spread by respiratory route.

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