Clinical Value of Two Detection Methods for *Mycoplasma Pneumoniae* Antibody in the Diagnosis of *Mycoplasma Pneumoniae* Infection in North China

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Research

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Abstract

Background: To analyze the detection of *Mycoplasma pneumoniae* in adults and children in North China using two antibody detection methods, and to guide prevention and treatment.

Methods: A retrospective study was conducted from September 2017 to May 2021. *Mycoplasma pneumoniae* total antibody was detected using particle agglutination (PA). Anti-*Mycoplasma pneumoniae* IgM in patients with respiratory tract infection was detected by indirect immunofluorescence. All patients were divided into 9 groups according to age: ≤1, 2-3, 4-6, 7-14, 15-18, 19-39, 40-59, 60-79, ≥80,

Results: The positive rate of *Mycoplasma pneumoniae* total antibody in 5,666 patients with community-acquired pneumonia was 40.13%. In adults and children, the positive rates were 19.92% and 77.3% (p<0.05), respectively. The positive rates in males and females was 37.89% and 42.40% (p<0.05), respectively. The positive rate for anti-*Mycoplasma pneumoniae* IgM in 5,746 patients with respiratory tract infection was 28.56%, and 10.37% and 36.82% in adults and children (p<0.05), respectively. In males and females, the positive rate for anti-*Mycoplasma pneumoniae* IgM was 24.56% and 33.38% (p<0.05). The highest positive rates for total antibody and anti-*Mycoplasma pneumoniae* IgM were recorded in autumn. Of the 1,975 patients tested for *Mycoplasma pneumoniae* antibody using both methods simultaneously, 26.71% were negative for total antibody and 8.63% had titers ranging between 1:40 and 1:80 when positive for IgM antibody. When negative for anti-*Mycoplasma pneumoniae* IgM, total antibody titer was ≥1:160 in 34.94% of the patients.

Conclusion: *Mycoplasma pneumoniae* is the main cause of respiratory tract infection and its incidence is highest in autumn. Because *Mycoplasma pneumoniae* was more commonly detected in women and children, screening should be strengthened in these groups.

Background

Mycoplasma pneumonia (*M. pneumoniae*) is one of the main causes of respiratory tract infection and the main cause of CAP (community-acquired pneumonia) in children and adults[1,2]. *M. pneumoniae* incidence has increased in recent years, with an epidemic peak every few years and infection rates of up to 30%[3–5]. Because it can adhere to the surface of respiratory epithelial cells, *M. pneumoniae* triggers direct cytotoxicity. By triggering airway inflammation, it can also cause cell swelling and necrosis, leading to pharyngitis, bronchitis, or atypical pneumonia[6–8]. Its clinical manifestations are easily confused with those of other respiratory pathogens. Because it lacks cytoderm, *M. pneumoniae* is resistant to antimicrobial agents targeting the cytoderm, such as β-lactams), and is only sensitive to fluoroquinolones, macrolides, and tetracyclines[9]. *M. pneumoniae* resistance to an increasing number of macrolides has been reported in recent years[10,11]. Thus, rapid, and accurate diagnosis of *M. pneumoniae* infection is key to effective treatment.

M. pneumoniae is mainly detected through etiological and serological methods. Etiological detection includes culture, double antibody sandwich test[12], and molecular biology methods. Serological detection includes ELISA, GICT (immune colloidal gold technique), CLIA (chemiluminescent immunoassay), IFA (indirect immunofluorescence assay), CFA (complement ratification assay), CAT (cold agglutination test), and PA (particle agglutination). In culture, isolated *M. pneumoniae* grows slowly, slowing its clinical diagnosis[13], and although PCR is effective, it is complex, and difficult to deploy widely. Serological detection of *M. pneumoniae* is fast and more easily executed at clinics. Due to high high sensitivity and specificity, *M. pneumoniae* antibody detection is often used for diagnosis[14,15].

To determine the rates of *M. pneumoniae* infection in patients with respiratory tract infection in North China, we carried out a retrospective study on the detection of *M. pneumoniae* IgM antibody and total antibody. The aim of this study was to understand the trend and prevalence of *M. pneumoniae* infection in different populations of North China, and to guide the choice of *M. pneumoniae* detection strategies and treatment.

Patients And Methods

Study population

This study retrospectively analyzed cases with symptoms, signs, and chest radiographs consistent with CAP that were examined at Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine between September 2017 and May 2021. Pneumonia was defined by the presence of fever, acute respiratory symptoms like cough, tachypnoea, difficult breathing, and presence of new infiltrate on chest radiography or consolidation not attributable to some etiologies. The study included 5,666 patients, who were tested for total *M. pneumoniae* antibodies by particle agglutination (PA), 5,746 patients who were tested for *M. pneumoniae* IgM antibodies by IFA, and 1,975 patients whose sera were tested for total *M. pneumoniae* antibodies and *M. pneumoniae* IgM antibodies using the methods above. The study was approved by the ethics committee of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine. Written informed consents were obtained from all the children's parents or guardian.

PA and IFA methods

Total *M. pneumoniae* antibody was evaluated by PA for the presence of IgG and IgM. Blood sa*mp*les (2mL) from patients were obtained. After centrifugation, serum were detected using the passive agglutination test (Serodia-Myco II kit, Fujirebio, Tokyo, Japan). Titers of 1:40 or more were reported as positive for the *M. pneumoniae* total antibody.

M. pneumoniae IgM antibodies were tested by IFA. Blood samples (2mL) from patients were obtained.After centrifugation, serum were detected using the Pneumo slide IgM test (Vircell, Granada, Spain). Serum samples were then diluted at 1:2 PBS and treated with anti-human IgG sorbent. They were then added to every well containing the Pneumoslide IgM slide and incubated for 90 minutes at 37°C. The slide was then washed twice with PBS and dried. The fluorescent secondary antibody was added and incubated for 30 minutes at 37°C. The slide was then washed twice with PBS and observed by fluorescence microscopy. Apple green fluorescence signal in the periphery of the cell indicated that samples were positive for *M. pneumoniae*.

Statistical Analysis

Data were analyzed using SPSS 22.0. The Chi-square test was used to compare positive rates between different groups. $P < 0.05$ indicated statistical significance.

Results

Positive rate of total M. pneumoniae antibodies in adults and children with CAP

The positive rate of total *M. pneumoniae* antibodies in the 5,666 patients with CAP was 40.13% (2274/5666, Table 1). The positive rates in adults (19.92%, 731/3670) was significantly lower than in children (77.30%, 1543/1996) (χ^2 = 1772.042, p = 0.000). The positive rate was significantly lower in males (37.89%, 1080/2850) than females (42.40%, 1194/2816) (χ^2 = 11.969, p = 0.001). In the adult group, the positive rate was significantly lower in males vs females (16.75%, 306/1827 vs 23.06%, 425/1843, χ^2 = 22.993, p = 0.000). In children, the positive rate in males vs females did not differ significantly (75.66%, 774/1023 vs 79.03%, 769/973, χ^2 = 3.236, p = 0.072). The positive rate of total *M. pneumoniae* antibodies among children and adults was statistically significant. The positive rate of total *M. pneumoniae* antibodies among children was statistically significant ($\chi 2$ = 87.350, P = 0.000), and the highest positive rate was 86.46% in children aged 7–14 years (group 4). The positive rate of total *M. pneumoniae* antibodies in adults was statistically significant (χ^2 = 268.818, p = 0.000), and the highest positive rate was 42.16% in adults aged 19–39 (group 1). The positive rate in male vs female children in group 1 and 3, and adults in group 1 and 3 was statistically significant, (p = < 0.05).

Table 1

The positive rate of *M. pneumoniae* total antibody and Anti-*Mycoplasma pneumoniae* IgM in adults and children with CAP

Characteristic			M. *pneumoniae total* antibody			Anti- *M. pneumoniae* IgM		
			positive rate (positive /total)	positive rate (positive / total)		positive rate (positive /total)	positive rate (positive / total)	
				male	female		male	female
			40.13% (2274/5666)	37.89% (1080/2850)	42.40% (1194/2816)*	28.56% (1641/5746)	24.56% (772/3143)	33.38% (869/2603)*
Adults			19.92% (731/3670)	16.75% (306/1827)	23.06% (425/1843)*	10.37% (186/1794)	9.57% (99/1035)	11.46% (87/759)
Children			77.30% (1543/1996)	75.66% (774/1023)	79.03% (769/973)	36.82% (1455/3952)	31.93% (673/2108)	42.41% (782/1844)*
χ2			1772.042**	1741.505**	175.944**	423.057**	187.318**	273.663**
		Age						
Children	Group 1	≤1	58.82% (10/17)	80.00% (8/10)	28.57% (2/7)*	30.63% (49/160)	27.38% (23/84)	34.21% (26/76)
	Group 2	2-3	63.49% (193/304)	63.19% (91/144)	63.75% (102/160)	40.29% (498/1236)	35.61% (235/660)	45.66% (263/576)*
	Group 3	4-6	72.87% (529/726)	69.71% (267/383)	76.38% (262/343)*	37.89% (532/1404)	32.98% (250/758)	43.65% (282/646)*
	Group 4	7-14	86.46% (760/879)	85.40% (386/452)	87.59% (374/427)	33.17% (338/1019)	27.98% (148/529)	38.78% (190/490)*
	Group 5	15-18	72.86% (51/70)	64.71% (22/34)	80.56% (29/36)	29.57% (38/133)	22.08% (17/77)	37.50% (21/56)
Adults	Group 1	19-39	42.16% (234/555)	36.21% (84/232)	46.44% (150/323)*	29.79% (84/282)	26.38% (43/163)	34.45% (41/119)
	Group 2	40-59	26.79% (165/616)	23.14% (59/255)	29.36% (106/361)	6.64% (16/241)	6.72% (9/134)	6.54% (7/107)
	Group 3	60-79	15.15% (245/1617)	13.61% (126/926)	17.22% (119/691)*	7.18% (58/808)	7.4% (37/500)	6.82% (21/308)
	Group 4	≥80	9.89% (87/880)	8.94% (37/414)	10.73% (50/466)	6.05% (28/463)	4.20% (10/238)	8.00% (18/225)
χ2			2013.119**	1058.719**	968.942**	507.277**	232.436**	274.175**

* note：Male versus female, *P＜0.05, **P<0.05

The positive rate of M. pneumoniae **IgM antibodies in adults and children with CAP**

The positive rate of *M. pneumoniae* IgM antibody in the 5,746 patients with respiratory tract infection was 28.56% (Table 1). The positive rate in adults (10.37%, 186/1794) was significantly lower than in children (36.82%, 1455/3952) (χ^2 = 423.057, p = 0.000). The positive rate in males (24.56%, 772/3143) was significantly lower than in females (33.38%, 869/2603) (χ^2 = 54.313, p = 0.000). In adults, the positive rate in males vs females (9.57%, 99/1035 vs 11.46%, 87/759) did not differ significantly (χ^2 = 1.696, p = 0.193). In children, the positive rate was significantly lower in males vs females (31.93%, 673/2108 vs 42.41%, 782/1844) (χ^2 = 46.456, p = 0.000). The positive rate of *M. pneumoniae* IgM antibody among children and adults was statistically significant. The positive rate of IgM antibody in children group was statistically significant (χ^2 =

19.462, $p = 0.001$), and the highest positive rate was 40.29% in children aged 2–3 years (group 2). The positive rate of IgM antibody in the adult group was statistically significant ($\chi 2 = 268.818$, $P = 0.000$), and the highest positive rate was 29.79% in adults aged 19–39 years (group 1). The positive rate in male and female children in group 2, 3, and 4 was statistically significant ($p = < 0.05$).

M. pneumoniae **infection trends in North China**

The positive rates of total *M. pneumoniae* antibody and IgM antibody in each year and season between September 2017 and May 2021 are shown in Table 2–3 and Fig. 1. 2019 had the highest positive rate. In each year, the highest positive rate of total *M. pneumoniae* antibodies were recorded in autumn, with the highest and lowest positive rates recorded in the autumn of 2019 (66.67%), and spring of 2020 (19.18%), respectively. The positive rate of *M. pneumoniae* IgM antibody was highest in autumn except for 2018, when it was highest in winter. The highest and lowest positive rates were recorded in autumn 2019 (44.29%) and spring 2020 (6.72%), respectively.

Table 2
The positive rate of *M. pneumoniae* antibody in each year between 2017 and 2021

Year	M. *pneumoniae total* antibody			Anti- *M. pneumoniae* IgM		
	Total	Positive	positive rate	Total	Positive	positive rate
2017	663	232	34.99%	933	279	29.90%
2018	1811	670	37.00%	1710	470	27.49%
2019	1855	923	49.76%	1782	692	38.83%
2020	843	301	35.71%	818	109	13.33%
2021	494	148	29.96%	503	91	18.09%

Table 3
The positive rate of MP antibody in each season between 2017 and 2021

	Season	M. *pneumoniae total* antibody			Anti- *M. pneumoniae* IgM		
		Total	Positive	positive rate	Total	Positive	positive rate
2017	Autumn	454	176	38.77%	737	214	29.04%
	Winter	548	125	22.81%	549	157	28.60%
2018	Spring	380	120	31.58%	419	101	24.11%
	Summer	410	152	37.07%	294	82	27.89%
	Autumn	523	276	52.77%	430	124	28.84%
	Winter	433	133	30.72%	528	200	37.88%
2019	Spring	404	161	39.85%	448	158	35.27%
	Summer	364	167	45.88%	354	132	37.29%
	Autumn	534	356	66.67%	439	212	48.29%
	Winter	489	267	54.60%	426	95	22.30%
2020	Spring	146	28	19.18%	119	8	6.72%
	Summer	205	61	29.76%	212	21	9.91%
	Autumn	180	69	38.33%	177	29	16.38%
	Winter	262	74	28.24%	268	38	14.18%
2021	Spring	334	109	32.63%	346	70	20.23%

Analysis of the consistency between M. pneumoniae **total antibody** M. pneumoniae **IgM antibody in adult and children with CAP**

In the 1,975 cases positive for *M. pneumoniae* IgM antibody, 26.71% were negative for total antibody, and 8.63% had a titer range of 1:40 − 1:80. Of the cases that were negative for anti-*M. pneumoniae* IgM antibody, 34.94% had a total antibody titer ≥ 1:160 (Table 4).

Table 4
The corresponding IgM antibody at different titers of total MP antibody between 2017 and 2021

M. *pneumoniae total* antibody													
Anti- *M. pneumoniae* IgM (+)	Titers	1: 40 – 1□80		1: 160		1: 320		1: 640		1: 1280		□□	
	Characteristic	n	%	n	%	n	%	n	%	n	%	n	%
		43	8.63	32	6.43	25	5.02	35	7.03	230	46.18	133	26.71
	Adults	9	11.11	4	4.94	3	3.70	0	0	5	6.17	60	74.07
	Children	34	8.15	28	6.71	22	5.28	35	8.39	225	45.18	73	17.51
M. *pneumoniae total* antibody													
Anti- *M. pneumoniae* IgM (-)	Titers	1: 40 – 1□80		1: 160		1: 320		1: 640		1: 1280		□□	
	Characteristic	n	%	n	%	n	%	n	%	n	%	n	%
		129	8.73	85	5.75	61	4.13	60	4.06	310	20.99	832	56.33
	Adults	75	9.35	31	3.87	15	18.70	3	0.37	14	1.75	664	82.79
	Children	54	8.00	54	8.00	46	6.81	57	8.44	296	43.85	168	24.89

Discussion

M. pneumoniae is a common pathogen that mainly causes human respiratory tract infections. This study retrospectively analyzed data on 5,666 respiratory tract infection cases where total *M. pneumoniae* antibody was detected using the PA method and 5,746 cases where *M. pneumoniae* IgM antibody was detected using IFA. The results showed that the positive rate of total *M. pneumoniae* antibody in the 5,666 respiratory patients was 40.13%, which was higher than the 27.20% reported by Huang Haiying[16] in Guangzhou. The positive detection rate in children was much higher than in adults, and also higher than that reported in relevant literature. When children are admitted at our hospital with suspected *M. pneumoniae* infection, blood is first collected using the finger prick method due to difficulty collecting venous blood, and GICT(immune colloidal gold technique), used for primary screening. Children cases in which antibody titer is detected using PA were initially positive or weakly positive based on GICT, thus the positive rate was higher than that of adults and other areas. Of the 41,230 children tested for *M. pneumoniae* antibody using GICT, 8,825 (21.40%) were positive, which is consistent with previous reports.

The positive rate of *M. pneumoniae* antibody in females (42.40%) was higher in males (37.89%), which is consistent with previous reports[4].The positive rate of total *M. pneumoniae* antibody in children increased with age, with the highest positive rate detected in 7–14 year-olds. In adults the highest positive rates were detected in 19–39 year-olds. It is reported that people with low and defective immune function and infants with low ability to produce antibodies may fail to produce antibodies or produce them at low titers[17]. This may be due to the immature immune system of infants, insufficient antibody generation after initial infection with *M. pneumoniae*, limited movement by infants, and less chance of *M. pneumoniae* infection, which affects the detection of total anti-*M. pneumoniae* antibody. Children aged 7–14 years gradually develop immunity and increase their range of activity in places like schools, and adults aged 19–39 have complete immune systems and spend longer in schools and workplaces. Thus, they have a higher increased chance of cross-infection with *M. pneumoniae*. After repeated infection with *M. pneumoniae*, the antibody titer increased gradually, which increased the positive rate of total antibody. The positivity rate for *M. pneumoniae* falls with increasing age, probably due to gradual weakening of the immune system with advancing age and fewer opportunities for elderly people to go out. Thus, screening for *M. pneumoniae* total antibody in preschool and school-age children should be strengthened.

The positive detection rate of *M. pneumoniae* IgM antibody in 5,746 respiratory patients was 28.56%, which is slightly lower than reported in Ningbo city[18]. The positive rate was 10.37% in adults and 36.8% in children. The positive rate was highest in 2–3 year-olds, and highest in 19–39 year-olds. IgM levels generally start rising a week after infection, peaking in 2–3 weeks, before starting to fall in 4 weeks and reaching minimum levels 2–3 months after infection[19]. IgA antibody levels rose rapidly in the early stage of *M. pneumoniae* infection, peaked at 7–14 days, and fell back earlier. IgG rises 14 days after infection and generally peaks 5 weeks after infection, and is persistent[20]. The positive rate of *M. pneumoniae* IgM antibody in each group was lower than the total antibody positive rate. IgM antibody is a diagnostic index for early *M. pneumoniae* infection and its detection can allow early diagnosis. Thus, clinicians should consider *M. pneumoniae* as the main respiratory tract infection in children and adolescents, especially in early childhood and pre-school age.

Analysis of annual and seasonal *M. pneumoniae* total antibody and IgM levels revealed that they were highest in 2019.The *M. pneumoniae* antibody positive rate was highest in autumn each year, which is the same as the peak of incidence in Hebei Province(China)[21]. The fall of 2019 was the highest, and the spring of 2020 was the lowest, which was related to the COVID-19 outbreak. From then on, people in China wearing masks and going out less. Infected people are the main source of *M. pneumoniae* infection. It is suggested that reducing cross infection and good protection can reduce *M. pneumoniae* infection rates.

In the 1,975 CAP patients tested for *M. pneumoniae* antibody using particle agglutination and indirect immunofluorescence when the *M. pneumoniae* IgM antibody was negative, 34.94% of the patients had a total antibody titer ≥ 1:160. This suggests that testing for *M. pneumoniae* IgM antibody alone misses some *M. pneumoniae* infections. A negative serum IgM antibody result does not rule out acute infection. In cases that were positive for *M. pneumoniae* IgM antibody, 26.71% were negative for *M. pneumoniae* total antibody. Probably because in the early phases of infection, IgM is quickly generated but not IgG, which fails to meet the reagent methodological judgment standards. It may also be related to methodological sensitivity. IFA uses a two-step method, and its sensitivity is better amplified by reaction with a fluorescent binder, whereas PA is slightly less sensitive than IFA. The total antibody titer in 8.63% of the patients was between 1:40 and 1:80. “Expert consensus on laboratory diagnostics and clinical practice of Mycoplasma pneumoniae infection in children in China (2019)[22] and other research recommends that PA antibody titers ≥ 1:160 indicate a recent or present infection[20,23]. It is suggested that we should simultaneously detect IgM antibody and dynamically monitor changes in total antibody titer for this population. This may enhance sensitivity and specificity in *M. pneumoniae* diagnosis and minimize missed diagnoses.

Conclusions

M. *pneumoniae* is the main cause of respiratory tract infection and its positive rate is higher in women and children of Tianjin. Thus, detection of respiratory tract infections in these groups should be strengthened. Autumn is the season of high incidence of *M. pneumoniae* in North China. Strengthening protection and reducing cross infection may reduce *M. pneumoniae* infection. Simultaneous detection of IgM antibody and dynamically monitoring total antibody titers can improve *M. pneumoniae* detection and minimize missed diagnoses.

Declarations

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Author Contributions

Conceived and designed the experiments: Li Ren and Xuehong Wen.

Performed the experiments: Jupeng Wang, Lina Zhu, Mingkun Ma, Guangye Wu and Shaohong Li.

Drafted and wrote the final version of the manuscrip: Jupeng Wang and Lina Zhu.

Guidelines for clinical diagnosis: Hui Chen, Suxiang Guo.

All authors read and approved the final manuscript.

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Availability of data and materials

The access to datasets generated and/or analyzed during the current study is not publicly available due to the hospital's research policy to guarantee the privacy of the participants, whose research data are confidential. Aggregate analyses are however available on reasonable request to the corresponding author.

Ethics approval and consent to participate

An informed, written consent was obtained from all parents/guardians prior to including the patients in the study.

Consent for publication

Not applicable.

Competing Interest

The authors have declared no conflict of interest.

References

1. Liu YF, Gao Y, Chen MF, et al. Etiological analysis and predictive diagnostic model building of community-acquired pneumonia in adult outpatients in Beijing, China. (1471–2334 (Electronic)).
2. McCulloh RJ, Patel K. Recent Developments in Pediatric Community-Acquired Pneumonia. Curr Infect Dis Rep. 2016;18(5):14.
3. Chaudhry R, Ghosh A, Chandolia A. Pathogenesis of Mycoplasma pneumoniae: An update. Indian J Med Microbiol. 2016;34(1):7–16.
4. Yan C, Sun H, Zhao H. Latest Surveillance Data on Mycoplasma pneumoniae Infections in Children, Suggesting a New Epidemic Occurring in Beijing. J Clin Microbiol. 2016;54(5):1400–1.
5. Dumke R, Schnee C, Pletz MW, et al. Mycoplasma pneumoniae and Chlamydia spp. infection in community-acquired pneumonia, Germany, 2011–2012. Emerg Infect Dis. 2015;21(3):426–34.
6. Valade S, Biard L, Lemiale V, et al. Severe atypical pneumonia in critically ill patients: a retrospective multicenter study. Ann Intensive Care. 2018;8(1):81.
7. Wang X, Zhong LJ, Chen ZM, et al. Necrotizing pneumonia caused by refractory Mycoplasma pneumonia pneumonia in children. World J Pediatr. 2018;14(4):344–49.
8. Canavan TN, Mathes EF, Frieden I, et al. Mycoplasma pneumoniae-induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: a systematic review. J Am Acad Dermatol. 2015;72(2):239–45.
9. Dumke R, Benitez AJ, Chalker V, et al. Multi-center evaluation of one commercial and 12 in-house real-time PCR assays for detection of Mycoplasma pneumoniae. Diagn Microbiol Infect Dis. 2017;88(2):111–14.

10. Zhou Z, Li X, Chen X, et al. Macrolide-resistant Mycoplasma pneumoniae in adults in Zhejiang, China. Antimicrob Agents Chemother. 2015;59(2):1048–51.
11. Zhang Y, Zhou Y, Li S, Yang D, et al. The Clinical Characteristics and Predictors of Refractory Mycoplasma pneumoniae Pneumonia in Children. PLoS One. 2016;11(5):e0156465.
12. Li W, Liu Y, Zhao Y, et al. Shang S. Rapid diagnosis of Mycoplasma pneumoniae in children with pneumonia by an immuno-chromatographic antigen assay. Sci Rep. 2015;5:15539.
13. Waites KB, Talkington DF. Mycoplasma pneumoniae and its role as a human pathogen. Clin Microbiol Rev. 2004;17(4):697–728. table of contents.
14. She RC, Thurber A, Hymas WC, et al. Limited utility of culture for Mycoplasma pneumoniae and Chlamydophila pneumoniae for diagnosis of respiratory tract infections. J Clin Microbiol. 2010;48(9):3380–82.
15. Chen K, Xu W, Yang C. Comparison of Indirect Immunofluorescence and Passive Particle Agglutination for the Detection of Mycoplasma Pneumoniae Antibodies. Clin Lab. 2019;65(3).
16. Huang HY, Zhou Q, Jia HY, et al. Epidemiological survey of Mycoplasma pneumoniae infection in different populations in Guangzhou area. Chin J Nosocomiol. 2015;25(2):300–2.
17. Zhao F, Liu L, Tao X, et al. Zhang J. Culture-Independent Detection and Genotyping of Mycoplasma pneumoniae in Clinical Specimens from Beijing, China. PLoS One. 2015;10(10):e0141702.
18. Chen M, Fan ML, Zhu SP. Epidemiological characteristics of Mycoplasma pneumoniae infections, in Yinzhou area of Ningbo during 2009–2011. 23. 2013;17:4219–31.
19. Lee SC, Youn YS, Rhim JW, et al. Early Serologic Diagnosis of Mycoplasma pneumoniae Pneumonia: An Observational Study on Changes in Titers of Specific-IgM Antibodies and Cold Agglutinins. Med (Baltim). 2016;95(19):e3605.
20. Lee WJ, Huang EY, Tsai CM, et al. Role of Serum Mycoplasma pneumoniae IgA, IgM, and IgG in the Diagnosis of Mycoplasma pneumoniae-Related Pneumonia in School-Age Children and Adolescents. Clin Vaccine Immunol. 2017;24(1).
21. Wang L, Feng Z, Zhao M, et al. A comparison study between GeXP-based multiplex-PCR and serology assay for Mycoplasma pneumoniae detection in children with community acquired pneumonia. BMC Infect Dis. 2017;17(1):518.
22. [Expert consensus on laboratory diagnostics and clinical practice. of Mycoplasma pneumoniae infection in children in China (2019)]. Zhonghua Er Ke Za Zhi. 2020;58(5):366–73.
23. Matas L, Dominguez J, De Ory F, et al. Evaluation of Meridian ImmunoCard Mycoplasma test for the detection of Mycoplasma pneumoniae-specific IgM in paediatric patients. Scand J Infect Dis. 1998;30(3):289–93.

Figures

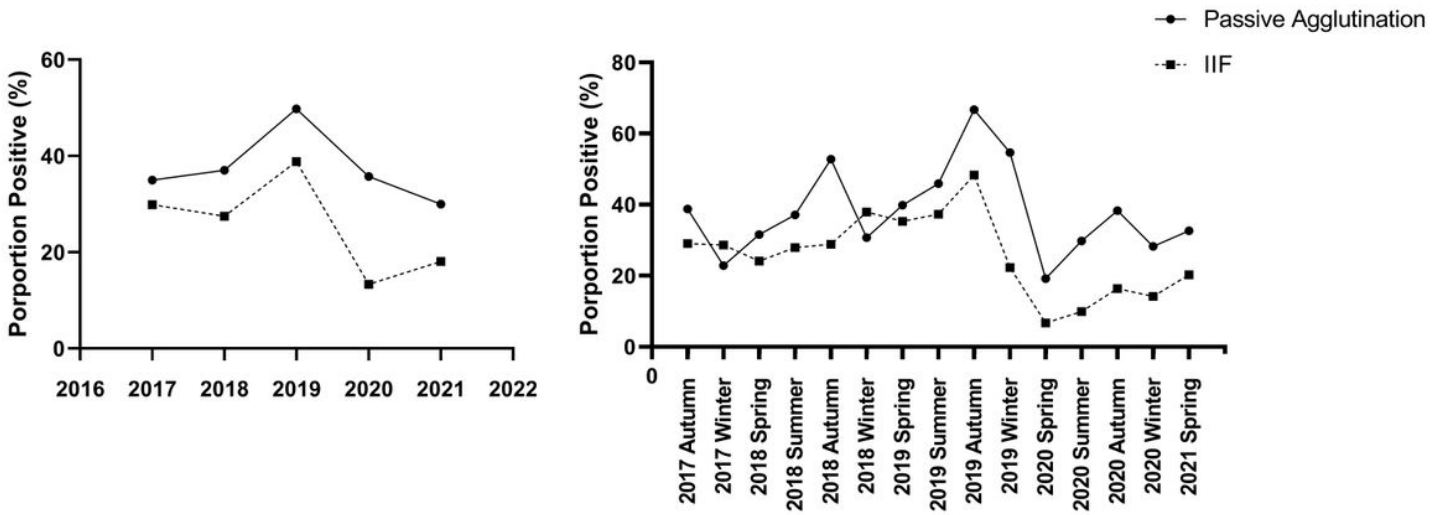

Figure 1

The positive rates of M. pneumoniae total antibody and anti-M. pneumoniae IgM in each year and season betweenr 2017 and 2021