ORIGINAL ARTICLE

Analysis on the Chinese Medicine Syndromes and Demographic Characteristics of Patients with Influenza-Like Illness in Clinics of China*

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ABSTRACT **Objective**: To investigate Chinese medicine (CM) patterns and epidemiological characters of patients with influenza-like illness (ILI) syndromes in clinics in China. **Methods**: A prospective multi-center observational epidemiology survey on the clinical CM patterns of ILI and its prevalence was conducted from September 2009 to April 2010. A unified survey questionnaire was developed for data collection of ILI symptoms and CM patterns. Totally 45 hospitals from 22 provinces, municipality cities and autonomous regions of China participated this study. The collected data were input by EPI-data v3.1 and analyzed by SPSS 18.0, which included descriptive analysis and Chi-square test for group comparison. **Results**: A total of 5,967 ILI patients were included in the study. The proportion of the 18–34 aged group (56.2%) was the largest; students (41.0%) were more than other occupations. Majority of the patients had the wind-heat invading Lung (Fei) syndrome (76%), while in Southwest China mainly wind-heat invading Lung syndrome and wind-cold tightening the exterior syndrome occurred. The typical symptoms of ILI were ranked as fatigue (80.9%), cough (72.2%), sore throat (67.2%), muscular soreness (67.1%), headache (65.4%), aversion to cold (60.1%), thirst (55.1%) and nasal obstruction (48.1%). **Conclusions**: The ILI patients in clinics were mainly teenagers and young adults. In regard to CM syndrome, wind-heat invading Lung syndrome prevailed in all regions except the Southwest China. The characteristics of CM syndrome of ILI patients may be relevant to age and region distribution.
KEYWORDS   clinic, influenza-like cases, Chinese medicine syndrome, epidemiology, multi-center survey

The pandemic influenza A (H1N1) spread globally since its first outbreak in Mexico in March 2009. On April 30, 2009, World Health Organization (WHO) announced that the pandemic alert level of influenza was raised to grade 5. On the same day, the Ministry of Health of China announced that the H1N1 was included into the category B infectious disease based on "Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases", and prevention and control measures of it should be conducted according to category A infectious diseases. Although Chinese medicine (CM) is effective in treating influenza, it has special diagnostic and curative procedures: differentiation, and then treatment. There are some reports about CM differentiation patterns of H1N1 and its epidemiological characters.[1] But there are only a few studies on large samples about its syndromes reported. In order to know more about its CM syndrome, based on a H1N1 clinical study project supported by State Administration of Traditional Chinese Medicine (SATCM), the relative information of influenza-like illness (ILI) patients were collected from 45 hospitals around the country in order to analyze the prevalent characteristics of ILI and provide references for prevention and treatment of the disease with clinical integrative medicine.

METHODS

Data Sources

The ILI data (including H1N1, suspected mild cases and confirmed cases) came from fever clinics, emergency clinics and in-patient departments of 45 hospitals in 22 provinces, municipality cities and autonomous regions all over China from December

2009 to April 2010. These hospitals participated a clinical research project designed by Guangdong Provincial Hospital of Chinese Medicine (GHCM). All the investigators were trained together before the study, and a unified case report form (CRF) was adopted. Specialized investigators organized by GHCM were responsible for the quality control. In total, 5,967 eligible case report forms were collected.

Diagnosis Criteria

The main references is WHO information for laboratory diagnosis of pandemic virus (H1N1) in humans (revised 2009)[2] or "The Influenza A H1N1 Clinic Program" (the 3rd edition, 2009) revised by the Ministry of Health, China.[2] The CM syndrome differentiation refers to the Criteria by SATCM.[3] ILI is classified to 3 syndromes: wind-heat invading Lung (Fei), toxic-heat invading Lung, wind-cold tightening the exterior.

Inclusion Criteria

The inclusion criteria included the following: (1) have flu-like symptoms (e.g., fever, runny nose, stuffy nose, sore throat, cough, headache, muscular soreness, fatigue, vomiting, diarrhea, etc.);[4] (2) positive in type-A influenza-like viral nucleic acid test of throat swab; (3) aged ⩽ 65 years.

Exclusion Criteria

(1) Severe flu-like symptoms cases, critical illness and multiple organ failure; (2) persons with mental illness.

Data Management and Statistical Analysis

The original data were input with EPI-data v3.1 simultaneously by two partners to build a database and then checked for its consistency. The processed data were then analyzed with SPSS 18.0 software. The quantitative data were shown as standard deviation, maximum, minimum and median (M). The counting data were displayed by percentage and data were compared between groups by chi-square test. A P value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics Analysis of Population Sociology

Among all the patients investigated, the largest prevalence was in 18–34 aged group (56.2%), followed by that of school children and teenagers (17.2%, aged 7–17). Younger or older groups had lower prevalence. The age compositions were compared between male and female, and the difference was statistically significant (χ^2=37.70, P=0.001, Table 1). As for occupation distribution, students were the most likely reported in clinics (41.0%), and the 2nd one was that of office workers (25.1%). The differences of occupation compositions and gender distribution of ILI patients in clinics were statistically significant (χ^2=222.80, P=0.001, Table 2).

Table 1. Comparison of Age Composition between Sexes among ILI Patients in Clinics from December 2009 to April 2010 [Case (%)]

Age (Year)	Male	Female	Total
<7	202 (6.7)	141 (4.8)	343 (5.7)
7–	563 (18.6)	462 (15.8)	1025 (17.2)
18–	1656 (54.6)	1699 (57.9)	3355 (56.2)
35–	299 (9.9)	232 (7.9)	531 (8.9)
45–	238 (7.8)	301 (10.3)	539 (9.0)
60–	77 (2.5)	97 (3.3)	174 (2.9)
Total	3035 (100.0)	2932 (100.0)	5967 (100.0)

Table 2. Comparison of Occupations between Sexes among ILI Patients in Clinics from December 2009 to April 2010 [Case (%)]

Occupation	Male	Female	Total
Worker	324 (10.7)	176 (6.0)	500 (8.4)
Farmer	32 (1.1)	19 (0.6)	51 (0.9)
Teacher	41 (1.4)	70 (2.4)	111 (1.9)
Soldier	14 (0.5)	1 (0.03)	15 (0.3)
Student	1350 (44.5)	1094 (37.3)	2444 (41.0)
Cadre	82 (2.7)	40 (1.4)	122 (2.0)
Medical personnel	32 (1.1)	72 (2.5)	104 (1.7)
Staff	654 (21.5)	843 (28.8)	1497 (25.1)
Retired	161 (5.3)	346 (11.8)	507 (8.5)
Freelance	135 (4.4)	120 (4.1)	255 (4.3)
Other	210 (6.9)	151 (5.2)	361 (6.0)
Total	3035 (100.0)	2932 (100.0)	5967 (100.0)

Characteristics Analysis on Sex Distribution of Patients' CM Syndromes

The constituent ratio of toxic-heat invading Lung syndrome in male patients was higher than that in female patients, while the constituent ratio of wind-heat invading Lung syndrome and wind-cold tightening the exterior syndrome in female patients was relatively higher than that in male patients. The major CM syndrome distributions of H1N1 among male and female patients were different (χ^2=31.78, P=0.001, Table 3).

Characteristics Analysis on Age Distribution of Patients' CM syndromes

Statistical significances were found when comparing patients of different ages with all the major CM syndromes of influenza (χ^2=118.4, P=0.001). Analysis showed that wind-heat invading Lung syndrome had a high proportion in all age groups (>72%), and the largest proportion of toxic-heat invading Lung syndrome (13.3%) was in 18–34 aged group. The proportions of wind-cold tightening the exterior syndrome in 45–59 aged group and group beyond 60 (16.3% and 18.4%, respectively) were higher than those in other groups, which suggested that toxic-heat invading Lung syndrome might be the main syndrome in all the sexes and age groups.

Characteristics Analysis on Regional Distribution of Patients' CM syndromes

Among the patient data collected, most cases (4,305) came from southern areas. CM syndromes in different regions were compared, and the differences were statistically significant (χ^2=376.6, P=0.001, Table 4). Wind-heat invading Lung syndrome was the most prevalent (above 75.0%) in all regions except Southwest China, where wind-cold tightening the exterior syndrome (39.7%) and wind-heat invading Lung syndrome (38.8%) were both main syndromes (both 78.5%).

Characteristics Analysis on Highest Temperatures of Patients in Different Observation Points

The daily highest temperatures of all 5,967 cases were observed for 7 days since the first visit of hospital. The missing data of each day were removed when analysis. Table 5 shows that body temperatures tended to decrease gradually to normal since the 2nd day of treatment (Table 5 and Figure 1).

Characteristics Analysis on Hospital Visit Time of Patients with Different CM Syndromes

The hospital visit time of all 5,967 patients was

Table 3. Constituent Ratio of CM Differentiated Syndromes between Sexes among Flu-Like Patients in Clinics from December 2009 to April 2010 [Case (%)]

Sex	Wind-heat invading Lung	Toxic-heat invading Lung	Wind-cold tightening the exterior	Others	Total
Male	2278 (75.1)	368 (12.3)	307 (10.1)	82 (2.7)	3035 (50.9)
Female	2258 (77.0)	237 (8.1)	363 (12.4)	74 (2.5)	2932 (49.1)
Total	4536 (76.0)	605 (10.1)	670 (11.2)	156 (2.6)	5967 (100.0)

Table 4. Constituent Ratio of CM Differentiated Syndromes in Different Regions among ILI Patients in Clinics from December 2009 to April 2010 [Case (%)]

Region	Wind-heat invading Lung	Toxic-heat invading Lung	Wind-cold tightening the exterior	Others	Total
Northern China	385 (76.1)	32 (6.3)	30 (5.9)	59 (11.7)	506 (8.5)
Eastern China	678 (84.9)	43 (5.4)	74 (9.3)	4 (0.5)	799 (13.3)
Southwest China	45 (38.8)	18 (15.5)	46 (39.7)	7 (6.0)	116 (1.9)
Northwest China	105 (91.3)	4 (3.5)	5 (4.3)	1 (0.9)	115 (1.9)
Middle China	106 (84.1)	4 (3.2)	15 (11.9)	1 (0.8)	126 (2.1)
Southern China	3217 (74.7)	504 (11.7)	500 (11.6)	84 (2.0)	4305 (72.1)
Total	4536 (76.0)	605 (10.1)	670 (11.2)	156 (2.6)	5967 (100.0)

Table 5. The Highest Temperature of ILI Patients in Each Observation Point (℃)

Time point	Case	Missing data (Case)	$\bar{x} \pm s$	Median	Min	Max
Baseline	5949	18	38.3 ± 0.7	38.3	35.7	41.0
1st day	5613	354	37.5 ± 0.8	37.4	35.0	41.0
2nd day	5365	602	37.1 ± 0.6	37.0	35.2	42.0
3rd day	5102	865	36.9 ± 0.5	36.8	35.5	39.9
4th day	3596	2371	36.8 ± 0.4	36.7	35.6	39.8
5th day	1579	4388	36.8 ± 0.4	36.7	35.5	39.6
6th day	701	5266	36.7 ± 0.4	36.7	36.0	39.2
7h day	391	5576	36.7 ± 0.3	36.7	36.0	38.2
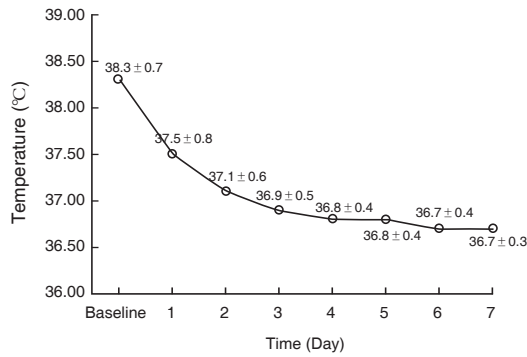
Figure 1.   Change of the Highest Temperature of ILI Patients in Each Observation Point

analyzed based on months. The proportion of January 2010 (45.4%) was the largest, but the proportion of February, 2010 once decreased to 22.2%. Table 6 indicates that majority of cases came to hospital from January to March occupied 82.5% of the total, but the least cases came to hospital was in April (5.6%). However, the percentages of patients came in December 2009 and March 2010 were relatively close to each other (Table 6).

Table 6.   Hospital Visit Time Distribution of ILI Patients

Hospital visit time	Case	Percentage (%)
December,2009	714	12.0
January,2010	2709	45.4
February, 2010	1325	22.2
March, 2010	887	14.9
April,2010	332	5.6
Total	5967	100.0

Characteristics Analysis on Prevalence of Syndromes of ILI Patients in Clinic

The major syndromes of 5,967 cases were analyzed and it was found that above 50% patients complained of fatigue, red tongue, cough, sore throat, muscle soreness, headache, yellow tongue coating, afraid of cold, thirsty, thin tongue coating, expectoration, stuffy nose, etc. (Table 7).

Table 7.   Frequency of Major Syndromes among ILI patients in clinics from December 2009 to April 2010

Syndrome	Case	Occurrence frequency (Time)	Frequency (%)
Fatigue	5967	4830	80.95
Red tongue	5967	4530	75.92
Cough	5967	4310	72.23
Sore throat	5967	4011	67.22
Muscle soreness	5967	4002	67.07
Headache	5967	3904	65.43
Yellow tongue coating	5967	3684	61.74
Afraid of old	5955	3585	60.20
Thirsty	5958	3286	55.15
Thin tongue coating	5967	3271	54.82

We also analyzed the relationship between major symptoms and disease course. Table 8 shows that the main symptoms on baseline were successively fatigue, cough, sore throat, muscular soreness, headache, aversion to cold, thirst and nasal obstruction. Then the main symptoms on the 1st day of treatment changed to be successive cough, sore throat, fatigue and nasal obstruction. The result

Table 8.   Frequency of Major Syndromes among ILI Patients in Clinics from December 2009 to April 2010 [Case (%)]

Symptom	Case					
	Baseline	1st day	2nd day	3rd day	4th day	5th day
Nasal obstruction	2870 (48.1)	2269 (38.0)	1654 (27.7)	1183 (19.8)	436 (7.3)	182 (3.1)
Cough	4310 (72.2)	3914 (65.6)	3525 (59.1)	2956 (49.5)	1810 (30.3)	874 (14.6)
Sore throat	4011 (67.2)	3135 (52.5)	2271 (38.1)	1450 (24.3)	572 (9.6)	208 (3.5)
Muscular soreness	4002 (67.1)	1899 (31.8)	899 (15.1)	507 (8.5)	109 (1.8)	37 (0.6)
Fatigue	4830 (80.9)	2520 (42.2)	1349 (22.6)	785 (13.2)	259 (4.3)	96 (1.6)
Headache	3904 (65.4)	1951 (32.7)	1033 (17.3)	623 (10.4)	155 (2.6)	62 (1.0)
Thirst	3286 (55.1)	1418 (23.8)	817 (13.7)	457 (7.9)	214 (5.0)	73 (3.6)
Conjunctival congestion	422 (7.1)	111 (1.9)	52 (0.9)	19 (0.3)	9 (0.2)	1 (0.1)
Aversion to cold	3585 (60.1)	947 (15.9)	399 (6.7)	165 (2.8)	57 (1.3)	19 (0.3)
Diarrhea	190 (3.2)	165 (2.8)	122 (2.0)	58 (1.0)	15 (0.3)	2 (0.1)
Perspiration	1563 (26.2)	943 (15.8)	507 (8.5)	297 (5.1)	129 (3.0)	52 (2.6)
Constipation	436 (7.3)	148 (2.5)	71 (1.2)	39 (0.7)	13 (0.3)	3 (0.1)
Vomiting	294 (4.9)	90 (1.5)	31 (0.5)	23 (0.4)	11 (0.3)	3 (0.1)

indicated that symptoms improved more since the 2nd day of treatment when its main symptoms changed into only cough and sore throat, and there were nearly 15% patients had cough symptoms during the whole observation time.

DISCUSSION

In this study, a prospective multi-center survey on clinical observations with 5967 influenza-like cases in 45 hospitals in China was conducted and the epidemiological characteristics of these data were initially analyzed. The results indicated that patients aged from 18–34 took the largest proportion (56.0%) among all clinic ILI patients. They were mainly students which occupied 40% of the subjects. That is to say, students and youngsters were the majority of the clinic visitors of influenza which matched the results of the previous literature reports.[1,6-14] Therefore, it is necessary to enhance the dissemination of preventive knowledge about influenza among the young population. The major clinical symptoms of ILI patients were successive fatigue, cough, headache, sore throat, muscular soreness, aversion to cold, thirst, etc. The occurrence of fatigue in ILI patients is a manifestation of vital qi deficiency in Chinese medicine, which can be traced back in the CM classical work: The *Yellow Emperor's Canon* (Huang Di Nei Jing) with the idea that vital qi can prevent infective pathogen from invasion. It was also reported in relevant literature.[1,6-16]

As for distribution of CM syndrome, the major syndrome is wind-heat invading Lung syndrome among the cases from northern, eastern, north-western, central and southern China, which counted over 75% in each region. Since the data were collected in the winter of 2009 to the spring in 2010, the wind-heat invading Lung syndrome counted unexpectedly much more than wind-cold tightening the exterior syndrome. This phenomenon could be explained by the Hostile qi theory in CM. The temperature from 2009 winter to 2010 spring was abnormally higher than the same time in past years, thus it could be considered that yang qi was excessive and unable to preserve inner the body, which led to the attack of wind-heat pathogen. Besides, there should be some other factors including virus type, living habit, body constitution of CM, and they need to be further studied.

The results also demonstrated that the constitution ratio of toxic-heat invading Lung syndrome to male patients was relatively higher than that to female patients. It was considered relevant with the difference of body constitution of CM between male and female. In CM view point, yang qi was originally sufficient in male patients, so, when yang qi was attacked by the pathogen, it was easier to change into heat. Therefore, toxic-heat invading Lung syndrome happened more in male patients.

The observation time of this study started from December 2009 to April 2010, and the analysis on hospital visit time showed that the proportion of cases in January 2010 (45.4%) was the largest. Then the cases widely decreased from February to April. During January to March, people were believed easier to be attacked by damp pathogen and suffer from febrile disease. Then April changed to another solar term, therefore the cases in April 2010 (5.6%) were much less than in other months.

The relationship between major symptoms and course of disease was also analyzed. We found that the main symptoms on baseline were successively fatigue, cough, sore throat, muscular soreness, headache, aversion to cold, thirst and nasal obstruction. Then the main symptoms on the 1st day of treatment changed to cough, sore throat, fatigue and nasal obstruction, which indicated that symptoms improved more since the 2nd day of treatment when its main symptoms changed into only cough and sore throat, and there were nearly 15% patients had cough symptoms during the whole observation time. It was probably relevant to infections that followed the flu. So the prognosis factors of patients with long-term cough after flu need to be further studied.

This study was an observation study on epidemiological characters of influenza-like cases came from 45 hospitals around China during the prevalence of H1N1. But, our study also had some limitations due to the restrictions of research conditions in each study center. One kind of important data, virological examination for all of the patients was missing here. We only hope that our study results could provide a reference for clinical integrated Chinese and Western medicine prevention and treatment of this disease.

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