

Clinical and Laboratory Profile of Febrile Respiratory Infections in General Practice

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Background: Respiratory tract infection (RTI) is a common diagnosis in the primary care setting. The aim of the study was to characterize the clinical course and laboratory manifestations of febrile RTI in Israeli adults presenting to primary care clinics.

Methods: A prospective study over a 3-month winter period in 3 urban university primary care clinics of 122 consecutive adult patients seen by their family practitioners. All participants were interviewed and had chest radiographs, tests of oxygen saturation, and blood tests.

Results: Study group included 122 adults (mean age, 44.8 ± 14.2 years; men, 38%). Fever lasted for a mean of 4.0 ± 1.7 days, and the mean number of days off work/activities was 5.3 ± 1.0 . Pneumonia was clinically suspected in 33 patients (27%), but documented in 7 (6%). Antibiotics were given to 94 patients (77%). The group of treated patients had a lower mean oxygen saturation ($P < .05$) and a higher erythrocyte sedimentation rate ($P < .05$). Blood tests were found to be abnormal, although not clinically significant, in some patients, and all resolved spontaneously.

Conclusions: RTIs are usually of short duration with a benign course where laboratory blood tests have no clinical implication. Radiographs may distinguish the 6% of patients having pneumonia from the 27% with suspected cases. (J Am Board Fam Pract 2004;17:32–7.)

Upper respiratory tract infections are common and important. Although rarely fatal, they are a source of significant morbidity and cause a considerable economic burden. Clinical presentations of sore throat do not accurately predict whether the infection is viral or bacterial, whereas throat culture and rapid antigen tests do not significantly change prescribing practice.¹ Antibiotics have only a limited place in the management of recurrent sore throat caused by group A β -hemolytic streptococcal infection.¹ Routine use of antibiotics in upper respiratory infection enhances patient belief in their effectiveness and increases the likelihood of future consultation in primary care for minor self-limiting illness.¹ In the vast majority of cases, the disease course is benign, and the principal result is tempo-

rary inactivity, work absenteeism, and health service costs.

The aim of our study is to characterize the clinical and laboratory manifestations and the clinical course of RTI in primary care clinics during a winter season.

Materials and Methods

Patients

The study group included 122 consecutive adult patients seen by their family practitioner in the 3-month period between January 1, 1997, and March 31, 1997, who met the inclusion criteria and expressed informed consent to participate in the study. Essential inclusion criteria were age above 21 years and an acute febrile illness of less than 1 week's duration (by patient's report at least 37.8°C). In addition, at least one of the following 4 complaints had to be present: cough, coryza, sore throat, or hoarseness. Women who were pregnant or who might be pregnant were excluded, as were patients known to be positive for HIV and patients who received antibiotics during the week before the study entrance.

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Israel), representing 3 different neighborhoods in the southern Israel city of Beer-Sheva, participated in the study. The Helsinki Committee of Soroka University Medical Center approved the study, and all participants gave informed consent.

Study Protocol

For each participant, a structured questionnaire was completed. The questionnaire included sociodemographic variables, complaints associated with the current illness, comorbidity and smoking habits, the period of inactivity or absence from work or study, and history of possible contacts. Blood pressure, respiratory rate, and oxygen saturation was measured in every patient, and all participants underwent a full physical examination. The practitioners were asked to assess whether the patient had follicular tonsillitis or pneumonia. Blood was drawn from all participants and sent to a central laboratory for complete blood count, erythrocyte sedimentation rate (ESR), and levels of creatinine, aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase. Throat cultures were taken from patients with a sore throat and/or suspicion of tonsillitis. Each of the patients were referred at this point for a chest radiograph (posteroanterior and lateral). Pneumonia was diagnosed only in patients in whom the radiologist determined or suspected the presence of a lung infiltrate and in whom the infiltrate disappeared or cleared significantly in the follow-up radiograph.

A telephone follow-up of symptoms was conducted at 2- to 3-day intervals. Inactivity and days off work/activities were monitored. Patients were followed up by phone interview until all symptoms cleared.

Three to 4 weeks after entering the study, the patients were invited for a follow-up visit. At this meeting, they were asked about possible continuation of RTI symptoms, and oxygen saturation was measured in the convalescence phase. Patients with abnormalities in any of the biochemical blood tests in the acute phase of the illness also had repeat blood tests at this follow-up visit. Patients with definite or suspected lung infiltrates in the acute phase chest radiograph were also referred for follow-up radiographs.

Measurement of Oxygen Saturation and Blood Tests

Oxygen saturation was measured by the Onyx finger oximeter (model 9500; (NONIN Medical, Inc., Plymouth, MN). The test was conducted on all participants at ambient air on 2 occasions (ie, at the acute and the convalescence phases of the illness). ESR was measured with the Westergren method using Vacuette syringes and pipettes (Greiner Vacuette Deutschland GmbH, Essen, Germany).

Statistical Analyses

The data were analyzed with the EPI INFO 6.01 statistical software. Continuous variables among the various groups were compared by the Student's *t* tests and discrete variables with the Mann-Whitney statistic. The presence or absence of complaints or other findings were compared among groups by the χ^2 statistic or its equivalent. Parameters measured at different times in the same individual were compared by paired *t* tests. Statistical significance was determined at $P < .05$ throughout.

Results

Forty-seven of the 122 participants (38%) were men. The mean age \pm S.D. of all participants was 44.8 ± 14.2 years (range, 21 to 78). Forty-eight percent of the patients reported that others in their close circle were also sick. Eighteen percent of the patients were current smokers. Seven percent were immunized during the previous fall for influenza, but no participant was ever given a vaccine for pneumococcus. Significant comorbidity was found in 31 patients (25%), including hypertension ($n = 17$, 14%), asthma ($n = 9$, 7%), ischemic heart disease ($n = 9$, 7%), and diabetes mellitus ($n = 3$). One patient had previous cancer and one patient had a previous splenectomy. The mean maximum oral temperature measured by patients before entering the study was 38.7°C (range 37.8°C to 40.6°C).

Table 1 presents the duration and frequency of the 4 typical RTI complaints, fever, and days off work/activities (defined as being absent from work or studies or refraining from normal daily activities for patients who neither work nor are students).

Table 2 shows the frequencies of associated complaints at the first visit. As depicted in the

Table 1. Prevalence and Duration of Fever, Typical Complaints, and Days off Work/Activities in the Various Phases of RTI among the 122 Patients

| Complaint | Prevalence (%) | Duration (days) | | | | | |
|--------------------------|----------------|------------------|-------|-----------------|-------|---------------|-------|
| | | Before 1st Visit | | After 1st Visit | | Entire Period | |
| | | Mean (SD) | Range | Mean (SD) | Range | Mean (SD) | Range |
| Fever | 100 | 2.9 (1.4) | 1-7 | 1.1 (1.3) | 0-6 | 4.0 (1.7) | 1-8 |
| Cough | 95 | 4.0 (2.0) | 1-9 | 11.9 (7.7) | 0-29 | 15.9 (8.1) | 1-35 |
| Coryza | 70 | 3.5 (1.9) | 1-8 | 3.5 (3.5) | 0-16 | 7.0 (4.0) | 1-23 |
| Sore throat | 48 | 3.6 (1.9) | 1-7 | 0.9 (1.1) | 0-4 | 4.5 (2.2) | 1-10 |
| Hoarseness | 33 | 3.3 (2.1) | 1-9 | 1.1 (1.3) | 0-5 | 4.4 (2.4) | 1-9 |
| Days off work/activities | 98 | 2.4 (1.7) | 1-7 | 2.9 (2.7) | 0-20 | 5.3 (3.0) | 0-22 |

table, 98% of the patients suffered from weakness and lethargy, 89% from headaches, and 85% from myalgias/arthralgias; thus, all patients presented with an associated nonrespiratory complaint. Gastrointestinal symptoms were found in 57 (47%) of the patients. The main findings on physical examination of the study patients are presented in Table 3.

The mean respiratory rate per minute at the first visit was 15.3 ± 2.6 (range, 12 to 30) and the mean oxygen saturation at ambient conditions was $96.4 \pm 1.3\%$ (range, 92 to 99). Eleven patients (9%) had oxygen saturation levels below 95%: 8 to 94%, 2 to 93%, and one to 92%. Only 2 of these 11 patients had pneumonia; in both, the oxygen saturation was 94%. The number of patients with abnormal mean respiratory rate was 23 (19%), and this group included all the patients with abnormal saturation

rate; thus, 99 patients (81%) had no respiratory findings.

After the initial visits, 16 patients came for one additional physician visit and 2 patients came for 2 additional examinations. Fifteen of the 16 repeat visits were a result of continued complaints. There were no new findings at these visits, and no additional tests were ordered. Throughout the entire study period, no participating patient was hospitalized.

The results of blood tests taken at the first visit are presented in Table 4. All patients with abnormal creatinine levels at first visit had normal levels when blood was tested 1 month later. Liver function tests were still abnormal at 1-month follow-up in 2 patients but returned to normal 1 month later (2 months after the first physician visit). For 62 patients (51%), there were no ab-

Table 2. Frequency of Associated Complaints in 122 Patients

| Complaint | Frequency (%) |
|-------------------------|---------------|
| Weakness and lethargy | 98 |
| Headache | 89 |
| Myalgias/arthralgias | 85 |
| Shaking chills | 53 |
| Abrupt onset of disease | 46 |
| Nausea and/or vomiting | 43 |
| Earache | 38 |
| Purulent sputum | 31 |
| Shortness of breath | 30 |
| Clear or white sputum | 16 |
| Abdominal pain | 15 |
| Diarrhea | 8 |
| Pleuritic pain | 7 |
| Bloody sputum | 3 |

Table 3. Frequency of Positive Findings on Physical Examination (n = 122)

| Finding | Frequency (%) |
|---|---------------|
| Pharyngeal erythema | 72 |
| Swollen tonsils | 19 |
| Tender maxillary/frontal sinuses | 15 |
| Rales | 14 |
| Enlarged or tender cervical lymph nodes | 13 |
| Wheezing | 12 |
| Localized reduction of breath sounds | 6 |
| Conjunctivitis | 5 |
| Tonsillar exudate | 5 |
| Use of auxiliary respiratory muscles | 2 |
| Abdomen tender to palpation | 2 |
| No respiratory findings* | 81 |

* Normal oxygen saturation and normal mean respiratory rate.

Table 4. Results of Blood Tests at First Visit (Mean and Distribution)

| Parameter | Mean (SD) | Range | Frequency (%) |
|-----------------------------------|--------------|--------------|---------------|
| WBC (/mm ³) | | | |
| Total | 7,024 (2989) | 2,700–19,000 | |
| <5,000 | | | 26 |
| 5,000–10,000* | | | 62 |
| >10,000 | | | 12 |
| Segmented (%) | 65.3 (11.8) | 30–90 | |
| Lymphocytes (%) | 21.8 (9.7) | 5–50 | |
| ESR at 60 minutes (mm) | 23.2 (18.0) | 2–110 | |
| <10 | | | 22 |
| 10–40* | | | 66 |
| >40 | | | 12 |
| Creatinine (mg/dL) | 1.0 (0.2) | 0.6–1.5 | |
| <1.2* | | | 93 |
| >1.2 | | | 7 |
| Aspartate aminotransferase (IU/L) | 22.5 (14.1) | 9–142 | |
| 0–40* | | | 93 |
| 41–100 | | | 6 |
| >100 | | | 1 |
| Alanine aminotransferase (IU/L) | 25.0 (20.2) | 4–124 | |
| 0–40* | | | 87 |
| 41–100 | | | 11 |
| >100 | | | 2 |
| Alkaline phosphatase (IU/L) | 79.2 (27.1) | 38–203 | |
| <120* | | | 93 |
| >120 | | | 7 |

* Reference range.

normal laboratory findings and their radiographs were clear.

Physicians suspected pneumonia in 33 patients (27%). However, this diagnosis was confirmed by radiograph in only 7 patients (6%), one of whom was not suspected of having pneumonia. Of this group, 2 patients had comorbid chronic illnesses, one suffered from chronic high blood pressure, and one from ischemic heart disease. Upper respiratory tract infections were diagnosed in the other 89 patients (73%).

Twenty-four patients (20%) took antibiotics for 1 to 4 days before visiting the doctor. Physicians prescribed antibiotics for 88 patients at their first visits, and 3 additional patients received antibiotics after their chest radiographs. In all, 94 patients (77%) received antibiotics during the course of their illness. Seventy-two patients received macrolides or tetracyclines, and 22 other patients received β -lactams. There was a higher rate of rales on lung auscultation among patients who received antibiotics ($P < .05$) and a

significantly higher rate of patients in whom the physician suspected pneumonia ($P < .01$). The group of treated patients had a lower mean oxygen saturation ($P < .05$) and a higher ESR ($P < .05$). No differences were found between these 2 groups in any other parameters.

All 122 patients came for the follow-up appointment at a mean of 25.1 ± 5.3 days (range, 17 to 49) after the first visit. At follow-up, all participants reported having returned to their preillness level of activity. Twenty-nine patients (24%) reported continued cough at follow-up. In 19, the cough persisted continuously from the first visit, whereas in 10 others, it recurred after a pause of 3 to 10 days.

Discussion

The high prevalence of weakness and lethargy, headaches, myalgias, and arthralgias, which were reported by almost all participants in the study, is striking. Another complaint that was more com-

mon than expected was nausea and/or vomiting. We assume that in some of the patients, vomiting was induced by cough and was not an expression of gastrointestinal involvement by the infection, particularly in light of the low rates of abdominal pain and diarrhea. Although blood tests were found to be abnormal in some patients, they were not clinically significant and all resolved spontaneously.

Pneumonia was confirmed by radiology in 6% of the patients. This rate is similar to the 5% found in a population similar to our own² and to the rate of 8% of radiologic consolidations found in another study relating to lower respiratory tract infections.³ The physician's suspicion of pneumonia was confirmed radiologically in only 18% of the cases. This rate is similar to the rate of 15% found in another study.⁴ In another study, in which we compared the physicians' presumed diagnosis with chest radiographs, results showed sensitivity of 74%, specificity of 84%, a negative predictive value of 97%, and a positive predictive value of only 27%.⁵ All 7 patients with pneumonia recovered fully without hospitalization or complications, and antibiotic therapy prescribed before the radiograph was not changed in any of these patients after the radiologic diagnosis of pneumonia. These findings lend support to the position that there may be no justification or practical therapeutic significance to routine chest radiographs in these patients, although our data does not enable us to make conclusive recommendations.

Oxygen saturation was measured for all patients in both the acute and convalescent phases of their illness. These measurements did not contribute significantly to therapeutic decisions in the patients but did show that in some of the patients, there was a significant reduction in oxygen saturation in the acute phase of the disease. These patients were not necessarily those with pneumonia by chest radiograph.

No blood test contributed in any significant way to the management decisions for these patients. This supports the common practice of not taking any blood tests in these patients. They demonstrated a broad range of results and a significant rate of abnormal test results in the acute phase of the disease that resolved spontaneously with the disease.

Most of the patients in our study were prescribed with antibiotics during the course of their disease. The rate of 77% is similar to that reported elsewhere.^{6,7} Because our study was observational and noninterventional and because the study population was not selected by a random process, we do not intend to determine whether antibiotic therapy has a beneficial effect on the course of the disease. Patients will probably recover at the same rate with or without antibiotic therapy, as supported in some articles reviewed by Verheij et al⁴ and by Rodnik and Gude.⁸ It is clear that factors other than the clinical laboratory results influence physicians to prescribe antibiotics.

Fever as a necessary, obligatory condition for inclusion in the study may be somewhat questionable because we are aware that many cases of RTI may occur without fever. On the other hand, a large spectrum of allergic conditions, many noninfectious, can be manifested by one or more of the signs that were required for inclusion in our study. Thus, the requirement of an acute febrile illness probably prevented the inclusion of noninfectious conditions. Blood tests identify significant numbers of abnormalities that have no therapeutic significance and resolve spontaneously.

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References

1. West JV. Acute upper airway infections. *Br Med Bull* 2002;61:215-30.
2. Melbye H, Straume B, Aasebo U, Dale K. Diagnosis of pneumonia in adults in general practice. Relative importance of typical symptoms and abnormal chest signs evaluated against a radiographic reference standard. *Scand J Prim Health Care* 1992;10:226-33.
3. Macfarlane JT, Colville A, Guion A, Macfarlane RM, Rose DH. Prospective study of etiology and outcome of adult lower-respiratory-tract infections in the community. *Lancet* 1993;41:511-4.
4. Melbye H, Straume B, Aasebo U, Brox J. The diagnosis of adult pneumonia in general practice. The diagnostic value of history, physical examination and some blood tests. *Scand J Prim Health Care* 1988;6: 111-7.
5. Lieberman D, Shvartzman P, Korsonsky I, Lieberman D. Diagnosis of ambulatory community-acquired pneumonia. Comparison of clinical assess-

- ment versus chest X-ray. *Scand J Prim Health Care* 2003;21:57–60.
6. Leblebicioglu H, Canbaz S, Peksen Y, Gunaydin M. Physicians' antibiotic prescribing habits for upper respiratory tract infections in Turkey. *J Chemother* 2002;14:181–4.
 7. Verheij TJM, Kaptein AA, Mulder JD. Acute bronchitis: etiology, symptoms and treatment. *Fam Pract* 1989;6:66–9.
 8. Rodnick JE, Gude JK. The use of antibiotics in acute bronchitis and acute exacerbations of chronic bronchitis. *West J Med* 1988;149:347–51.