

Pneumonias: a retrospective study in an Internal Medicine Service

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Abstract

The authors made a review of pneumonia cases admitted in an Internal Medicine Department at a Central Hospital in Oporto – Portugal, from January to December 1994. All the patients whose discharge diagnosis included the word “pneumonia” were included. The prevalence of respiratory diseases, namely pneumonia, has been recorded. They have studied the number of cases, the distribution by age and gender groups, relevant clinical data for diagnosis mentioned in the admission notes, prevalence of co-existent diseases, smoking, radiologic localization, other complementary tests (Chest X-ray, sputum cultures, bronchofibroscopy), most used antibiotic therapy and its changes, clinical outcome, average duration of hospital stay, mortality and global results.

Pneumonia was a frequent cause of admission (9.3%), mainly

male patients (63,2%) and affected females were older. Fever (67.2%) and cough (57.2%) were the clinical data most commonly found. Sputum cultures were positive in 18.2% and blood cultures in 13.6%. The right lung (39.3%) and the inferior lobes were more commonly affected. Heart failure (24.8%), diabetes mellitus (21.1%), COPD (20.2%), chronic alcoholism (14.7%) are the most common associated diseases. Smokers account for 17.2% of studied cases. Beta-lactam antibiotics alone or associated to amikacin, or erythromycin were the therapeutic choice in most cases. Global results were good with 85.2% of improvement or cure, and average time of hospital stay was 12.9 days.

Key words: pneumonia, diagnosis, coexistent diseases, antibiotic therapy-

Introduction

Pneumonia continues to be a major medical problem, not only due to the frequency and severity of its complications, but also because new microorganisms have been identified, which are profoundly altering the epidemiology of the disease. It is one of the most common causes of hospital admission, and a significant cause of morbidity and mortality.¹ In the USA, it is still the 6th highest cause of death, and it is the infection with the highest mortality rate, affecting 20% of cases that require hospitalization.^{2,3} Many of these deaths occur in patients of advanced age, but pneumonia is also a major cause of death among young people. Ascertaining its frequency, diagnosis and treatment continue to present a challenge. Pneumonia can be defined as an acute inflammatory disease of the lower airways, associated, in most cases, with “repeat” radiological signals.⁴ In only around 50% of cases can an etiological diagnosis be obtained, and it is

essential to search carefully for the causal agent in a patient with pneumonia.^{2,3} The typical signs and symptoms are not always manifested, and a wide range of pathogenic agents may be involved.

The local defenses of the respiratory tract are sufficient to eliminate most microbial aggressions, without clinical sequelae. Pneumonia occurs when the activity of the aggressive agents overrides the defense mechanisms, leading to microbial replication, inflammation and immune response.⁵ The respiratory tract is generally protected from aggressions by its mechanical and cellular defenses, and by the systemic defenses, such as the inflammatory response, specific immune responses (cellular and humoral immunity) and therapeutic interventions.⁵ Specific defects in the host defenses often predispose the individual to infections by particular etiological agents.^{5,6,7,8,9,10}

The diagnosis of pneumonia is based on the clinical history and physical examination, complemented by chest x-ray, microbiological tests (sputum, blood, bronchial secretions, bronchoalveolar lavage fluid, pleural fluid, etc.), specific serological tests, invasive techniques like transtracheal aspiration, bronchial endoscopy, lung biopsy, and even the use of recently-developed monoclonal antibodies.^{11,12,13} These techniques can enable an etiological diagnosis to be obtained more quickly in the majority of cases,

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provided a relatively well-equipped laboratory and trained technical personnel are available.¹⁴

The association between pneumonia and certain professional or recreational activities is also of particular importance. Some examples are psittacosis, Q fever, infection by *Chlamydia pneumoniae* and Legionnaire's diseases.⁶

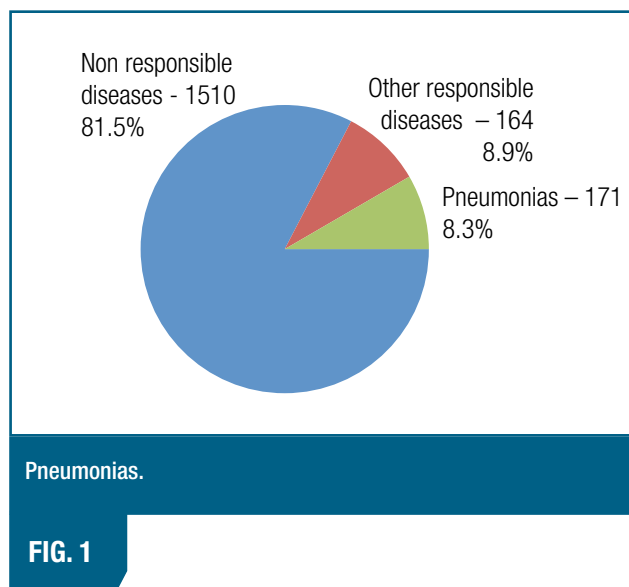
The need for hospitalization will depend, among other factors, on the severity of the disease, the existence of associated diseases and the patient's age.

The treatment of pneumonias includes general support measures and antibiotics. The most commonly indicated groups of antibiotics are beta-lactams and macrolides, aminoglycosides may be used in associations, the choice depending mainly on the patient factors and clinical situation. Immunizations have been developed with effective vaccines against a series of viral and bacterial pathogens of the respiratory tract (rubella, influenza, adenovirus, pertussis, *S. pneumoniae* and *H. influenzae*).⁵ New therapeutic opportunities are now emerging, aimed at boosting the immune defenses, and this may be particularly important in the treatment of immunosuppressed patients. Advances in molecular technology have enabled us to selectively stimulate the beneficial responses, thus, recombinant cytokines are of particular use in immunosuppressed patients.⁵ Experimental studies on humans have shown that γ -interferon, a powerful stimulator of cell phagocytosis and macrophage activation, may be effective in the prevention and treatment of opportunistic infections, being promising for the treatment of infections by *Pneumocystis carinii* and *Legionella pneumophila*.⁵ The ideal approach to the treatment of community acquired pneumonias is, therefore, changing. Numerous published investigation works show that important advances are being made in the diagnosis and treatment of pneumonias.¹⁵

The authors hope that this work will provide yet another contribution to improving our understanding and approach to this common, yet still so serious problem.

Materials and Methods

A descriptive, non-observational, retrospective study was carried out on the prevalence of pneumonias admitted to an Internal Medicine Service of the Hospital de S. João in 1994. The study is based on an analysis of the database of the Service, selecting a computer list of patients whose diagnosis on discharge (1st, 2nd



or 3rd) included the word "pneumonia". All other respiratory pathologies were not considered. The patient's hospitalization records were requested from the hospital Archive, and a protocol was designed, in which the data needed for the study were recorded.

Of all the clinical records requested from the Archive, we were provided with 122 (71.3%), which formed the basis of this study.

The Emergency Service admission forms were analyzed for clinical data such as fever, cough, sputum, dyspnea, chest pain and hemoptyses, which were recorded as present, absent, or not reported on the form.

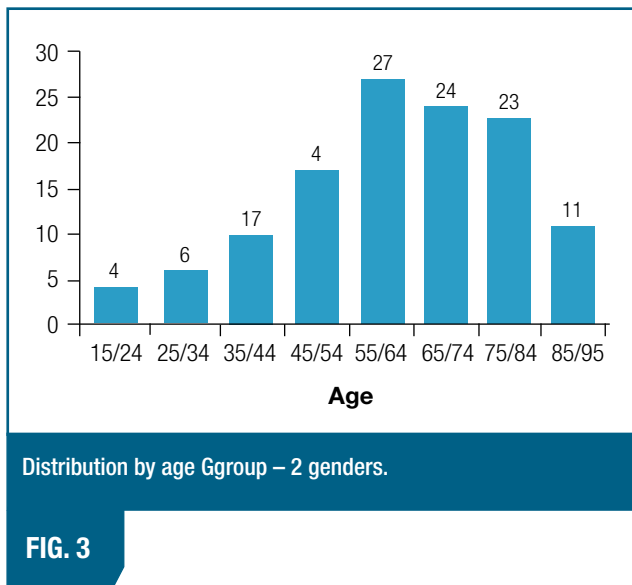
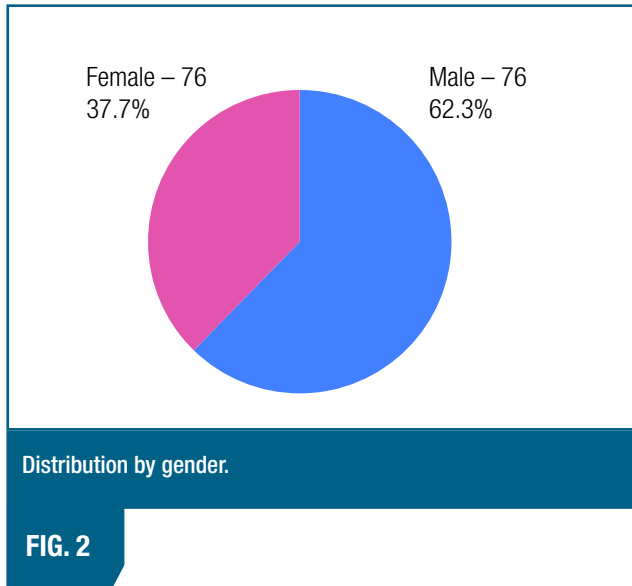
Results

In 1994, 1845 patients were admitted to the Medicine Service: 996 men and 849 women, corresponding to 54.0% and 46.0%, respectively.

335 patients (18.2%) with respiratory pathologies were identified. Of these, 171 (9.3%) had a diagnosis of pneumonia and 164 (8.9%) had other respiratory diseases (COPD, respiratory infection, pulmonary abscess, pleural effusion, tuberculosis, bronchiectasis, etc.) which were not considered in this study (Fig. 1).

Of the 122 patients whose clinical records were made available to us, pneumonia was more frequent among males, with 76 cases (62.3%), than among females, with 46 cases (37.7%) (Fig. 2).

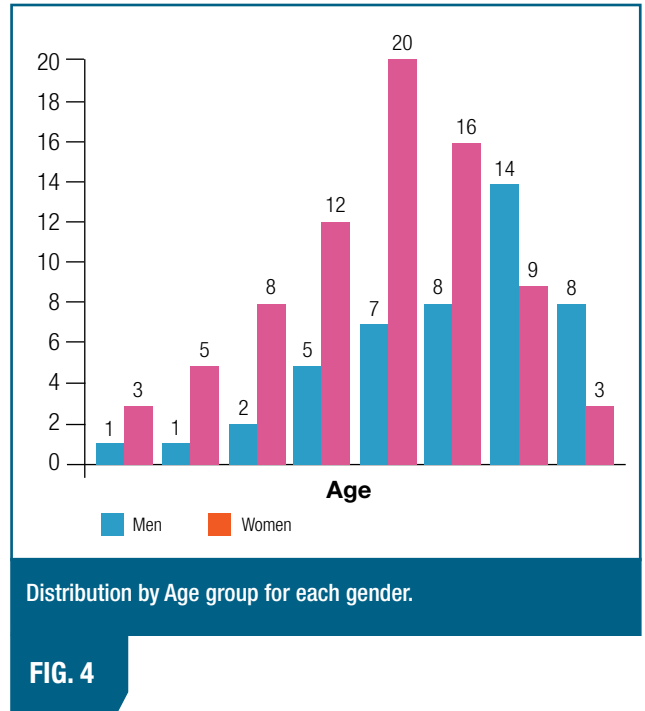
The age peak in both genders was between 55 and 64 years, with a higher incidence of pneumonias between 55 and 84 years (Fig. 3).



In men, the age peak occurred at between 55 and 64 years, and in the women, between 75 and 84 years, i.e. the disease occurred at young ages in males, than in females. From 75 years, pneumonia became more frequent among the women (Fig. 4).

The average overall age of all the patients with pneumonia was 64.9 years; 58.7 years among the men, with ages between 18 and 93 years, and 71.1 years among women, with a minimum age of 27 and a maximum age of 90 years.

The signs and symptoms most commonly reported were fever (67.2%), followed by cough (52.5%), spu-



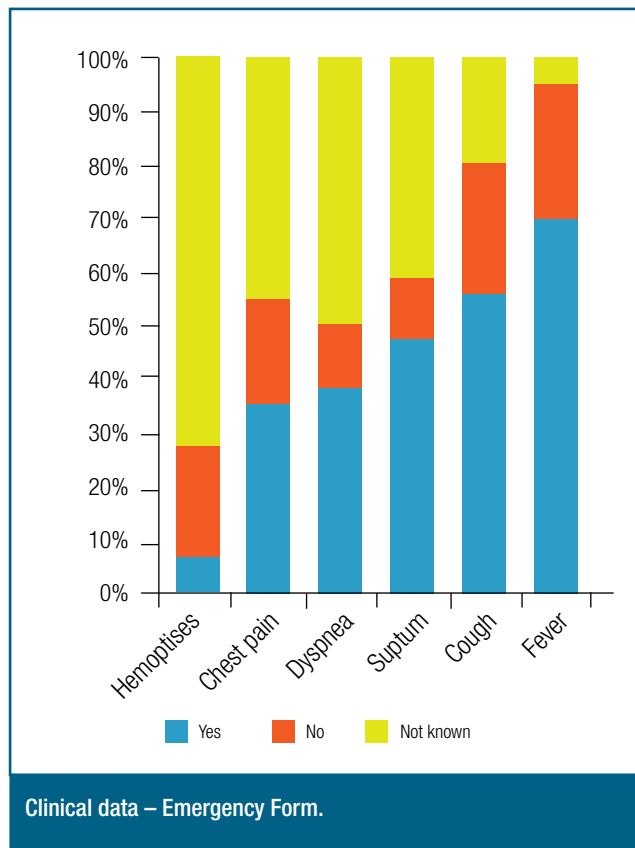
tum (45.5%), dyspnea (38.5%), chest pain (35.2%) and hemoptyses (5.7%) (Fig. 5).

There was no fever in 25.4% of the patients, and was unknown or unreported on the Emergency Service form in 7.4% of cases. Cough was absent in 27.9% and unknown in 19.6% of the patients; sputum was absent in 10.6% and not reported in 43.9% of cases. Dyspnea was absent in 10.7% and unknown in 50.8%. Chest pain was absent in 18.1% of cases and unknown in 46.7%. Hemoptyses were described in 7 cases (5.7%).

In 87 patients (71.3%), there was associated systemic pathology. Only 35 cases (28.7%) were discharged with a sole diagnosis of pneumonia. Of the associated diseases, cardiac insufficiency was the first named disease in 27 patients (24.8%), followed by diabetes mellitus in 23 patients (21.1%), chronic obstructive pulmonary disease in 22 patients (20.2%), chronic alcoholism in 16 patients (14.7%), cerebrovascular disease in 15 patients (13.8%); and neoplasias in 6 cases (5.5%).

In relation to smoking, the patient's records reported 21 smokers (17.2%), 26 non-smokers (21.3%), and smoking habit not known in 75 patients (61.5%). Individuals who smoked at least one cigarette per week were considered smokers.¹⁶

With regard to complementary diagnostic exams,



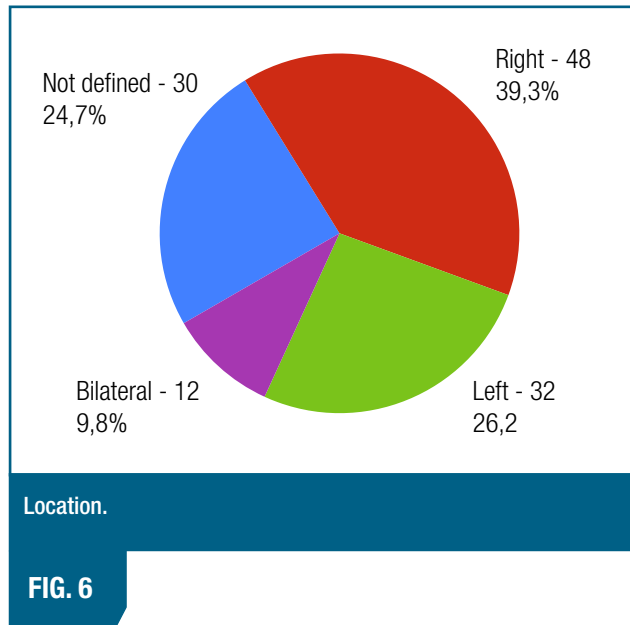
Clinical data – Emergency Form.

FIG. 5

chest x-ray was performed in 114 patients (93.4%) in the Emergency Service, and in 8 patients (6.6%) it was performed on admission. In 67 cases (58.8%), the patient's record included a summary description of the radiological image.

Microbiological examination of the expectorated sputum was carried out in 44 patients, with positive results in 8 (18.2%), negative or indeterminable results in 27 (61.3%) and unknown (result not found in the patient's record) in 9 (20.5%). *Pseudomonas aeruginosa* was isolated in the sputum in 6 patients. *Staphylococcus epidermidis* and *Citrobacter diversus* were isolated in one patient each.

Hemocultures were carried out in 44 patients (36.1%), of which 6 (13.6%) were positive, 30 (68.2%) were negative or indeterminable and 8 (18.2%) were not known. *Staphylococcus coagulase*-negative was isolated in 4 patients, *Staphylococcus coagulase*-positive in one, and *Escherichia coli* in one. No agent was isolated simultaneously in the sputum and hemocultures.



Location.

FIG. 6

Bronchofibroscopy was performed in 10 patients (8.2%). The bronchofibroscopy were carried out due to suspected bronchopulmonary neoplasia, tuberculosis with absence of Koch's bacillus in the sputum, in patients with recurrent pneumonias, and in suspected cases of bronchopulmonary mycosis or sarcoidosis. The anatomical report of the pneumonias occurred on the right in 48 cases (39.3%), on the left in 32 cases (26.2%), bilateral in 12 (9.8%) and with no defined location in 30 (24.7%) (Fig. 6).

In relation to the location in the right lung, 9 were in the lower lobe (18.8%), 5 in the upper lobe (10.4%), 4 in the mid lobe (8.3%) and no reported location in 30 patients (62.5%). Pneumonia affected the lower left lobe in 9 cases (28.1%), the upper left lobe in 1 case (3.1%), and in 22 patients (68.8%) the location was not reported.

The antibiotherapy used was very varied. The most commonly used therapeutic regimen was association with amoxicillin/clavulanic acid, followed by erythromycin and cephalosporins (Fig. 7).

The therapy initially instituted was maintained in 92 cases (75.4%), it was repeated in 21 patients (17.2%) and one or more antibiotics were added in 9 cases (7.4%). The antibiotic most frequently used in isolation was amoxicillin/clavulanic acid in 19 patients, and the association of antibiotics most prescribed was ampicillin with amikacin in 6 patients (considering cases in which therapy was maintained

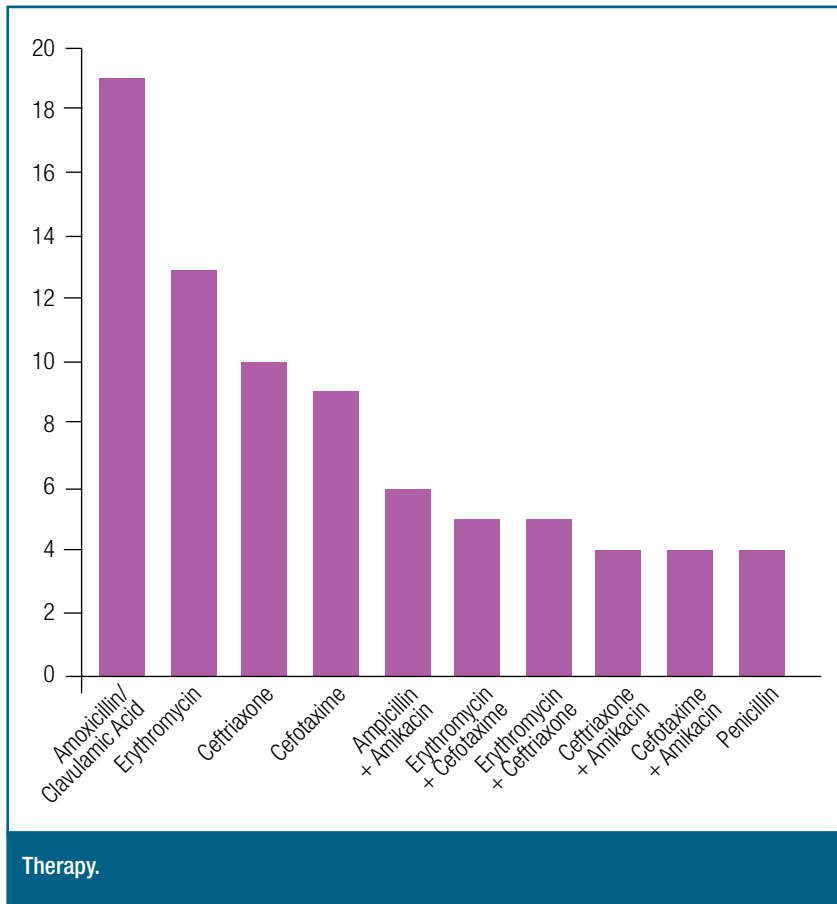


FIG. 7

from the start of hospitalization). The following were also used, but were prescribed in less than four patients: ampicillin, amoxicillin/clavulanic acid + cefotaxime, amoxicillin/clavulanic acid + amikacin, ceftazidime, ceftazidime + amikacin, cefotaxime + gentamicin, cefotaxime + flucoxacin, ceftriaxone + clindamycin, ciprofloxacin, erythromycin + amikacin, erythromycin + ceftazidime, erythromycin + penicillin G, vancomycin + amikacin, imipenem + teicoplanin, sometimes without regard for the rules of pharmacology.

In the 21 cases in which antibiotics were replaced, the most frequent replacement was amoxicillin/clavulanic acid by ceftriaxone in 14 cases, by piperacillin/tazobactam in 2 cases, and by clindamycin + amikacin in 5 cases.

In the 9 situations in which the therapy was added to, the antibiotic most frequently associated was imipenem, in 5 cases.

The average hospitalization time was 12.9 days, with periods ranging from 1 to 136 days.

The clinical evolution was favorable in the majority of cases, and 104 patients (85.2%) were discharged either improved or cured.

The morality rate was 14.8% i.e. 18 patients died. All of these had associated pathology, except for one very elderly patient, aged 87 years, in whom there was no reference to any other type of disease. The most frequent associated diseases among those who died, although with very few cases and without statistical significance, were congestive cardiac insufficiency, diabetes mellitus, chronic obstructive pulmonary disease, neoplasias, renal insufficiency, and malnutrition, and in the majority of these cases, there were associated diseases.

Discussion

Pneumonia is a common clinical situation, which is potentially fatal and can affect any age group, particularly the elderly.

Respiratory infections affect more than 40 adults per 1000 inhabitants per year, which represents around 1.5 people in Europe, of which approximately 5% will have pneumonia.^{17,18} The majority of these patients are treated in the outpatient clinic, with only more severe cases requiring hospitalization. Around 10% of hospital admissions of adults are due to infections of the lower respiratory tree, the incidence of which is higher among the elderly.^{17,19} In our study, the percentage of patients admitted for pneumonia was slightly lower (9.3%).

In recent years, besides the appearance of new pathogenic agents like *Legionella pneumophila* and *Chlamydia pneumoniae*, the main alteration occurred at the host level.²⁰ Factors like the increase in the elderly population, longer survival time of patients which chronic clinical conditions, immunosuppressant therapy and acquired immunodeficiency due to HIV infection have all contributed to the appearance of potentially pathogenic agents, previously considered

to be of little clinical significance. The appearance of *Pneumocystis carinii*, together with infections caused by mycobacteria, in patients with AIDS, requires that we gain even more experience in the future, in the treatment of these infections.²⁰

The main symptoms of pneumonia are, in general, cough, fever, sputum, chest pain, dyspnea and hemoptyses. However, these may be absent, particularly in the elderly, neutropenic patients and alcoholics, and in these cases, general symptoms, confusion and disorientation are prevalent.²¹ In our study, fever was the predominant symptom in 67.2% of cases, followed by cough in 52.5%, sputum in 45.5%, dyspnea in 38.5%, chest pain in 31.2% and hemoptyses in 5.7% of cases, similar to what is reported in the literature.²¹

Most of the patients admitted for pneumonia have associated pathology. The main risk factors are advanced age, hospitalization, viral infections, cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, cerebrovascular disease, renal insufficiency, neoplastic diseases, chronic alcoholism, smoking, malnutrition, AIDS or other immunosuppression, altered states of consciousness, general anesthesia and mechanical ventilation.²² In our study, we highlight the presence of 87 patients with associated disease (71.3%). Cardiac insufficiency was the disease most frequently found (24.8%), followed by diabetes mellitus, chronic obstructive pulmonary disease, chronic alcoholism, cerebrovascular disease, and neoplasias, which is in accordance with other studies.²³ The percentage of patients with chronic alcoholism was 14.7%, which is slightly above the average for the general population, in which around 10% of men and 3 to 55 of women develop generalized and persistent problems related to alcohol consumption, confirming that chronic alcoholism is an important risk factor.²⁴ The percentage of smokers among the patients with pneumonia was 17.2%, which is lower than in the general population.^{25,26}

In relation to the location of the pneumonias, the right lung was the most affected, in 39.3% of cases; it was more common in the lower lung lobes, a finding that is supported by other studies.^{27,28}

Microbiological examination of the expectorated sputum can yield valuable information, if the samples are properly collected. Direct examination is quick, but is only of value in less than 10% of cases. The results are affected by previous antibiotherapy and by contamination by bacteria of the oropharynx.

Also, not all patients produce sputum. In the revision carried out, diagnostic value was obtained in 8 cases of the 44 examinations carried out (18.2%), which is higher than the percentages described in the literature (12.6%).²⁸

The hemocultures should be carried out before the start of antibiotherapy, and are positive in more than 25% of patients.^{18,23} Of the 44 patients (36,1%) submitted to hemocultures, the results were positive in 6 cases (13.6%), while in 8 (18.2%), the result was unknown, as it was not stated on the patient's clinical record. There are studies in which the diagnostic value of hemocultures is as low as 4.2%.²⁸

Pneumonia by *Streptococcus pneumoniae* is the most common of the community-acquired pneumonias, and constitutes around 60% of all bacterial pneumonias¹⁹. *Escherichia coli* is an agent with epidemiological significance in hospital-acquired pneumonias, causing more than 7.5% of cases.²⁹ Around 4% of cases of pneumonia are attributed to *Staphylococcus aureus*, but this percentage increases during cold epidemics, and mortality rates are high when associated with influenza. This bacteria is the cause of around 13% of pneumonias acquired in hospital.^{29,30}

In our study, *Pseudomonas aeruginosa* was isolated in the sputum of 6 patients and *Staphylococcus epidermidis* and *Citrobacter diversus* were isolated in one patient each. In the hemoculture, *Staphylococcus coagulase-positive* and *Escherichia coli* were isolated in one patient each. It should be noted that neither *Streptococcus pneumoniae* nor *Klebsiella pneumoniae* were isolated in our study, despite the fact that these have habitually been described as the most common pathogens,^{10,31,32} a fact that may be related to the admission criteria. Patients are commonly admitted with severe pneumonias and associated pathologies, and the majority of patients with community-acquired pneumonias are treated as outpatients. The high number of cases of *Pseudomonas aeruginosa* is highlighted probably because some of these pneumonias were acquired in the hospital, and others occurred in severely sick patients, with bronchiectases, or those submitted to surgery. In relation to *Escherichia coli*, only a single case was isolated (0.81%), and it occurs more frequently among alcoholics and elderly or debilitated patients, or those who have undergone periods of antibiotics.^{33,34,35,36} In the 6 cases in which *Staphylococcus* was isolated (3.5%), the percentage is more or less in accordance

with the literature (4%).^{24,29}

Chest x-ray can help determine the probable diagnosis. Linking the x-ray image to the etiology is not always correct, as around 20% of chest x-ray images are normal. In immunosuppressed patients, the absence of an indicative image in the x-ray does not exclude the diagnosis, and in the elderly, there may be no indicative image in the first 48 hours. In our study, we only found summary descriptions of the chest x-ray results in 68 patients (58.8%), which made it difficult to correlate the x-ray image with the etiology of the pneumonia.³⁷

One of the main problems is the use of certain means of diagnosis which are mostly time-consuming and complex.^{5,14} All the costs of any invasive technique should be carefully weighed. An effort must be made to link the clinical aspects with auxiliary means of diagnosis, seeking to arrive at the etiological diagnosis.¹⁴ Bronchofibroscopy was carried out in 10 patients (8.2%) to rule out neoplasia, tuberculosis with the absence of Koch's bacillus in the sputum, in recurrent pneumonias and in cases of suspected pulmonary mycoses or sarcoidosis. Bronchofibroscopy is a good method for collecting samples in lung infections, and should be reserved for patients in which no conclusive results have been obtained though non-invasive, simpler alternative studies. Bronchial brushing, often combined with endobronchial biopsies, has been used to detect opportunistic germs in immunosuppressed patients. This technique yields good results in pneumonia by *Pneumocystis carinii*.³⁸ The therapeutic options are in accordance with the agents most commonly found, the patient's age, the presence or absence of associated disease, and the severity of the disease, and are almost always empirical.² The early administration of antibiotics is important, as some pneumonias caused by nosocomial pathogenic agents may evolve rapidly to states of septic shock, particularly in debilitated patients.

Generally, community-acquired pneumonias do not require combined antibiotherapy, except in some situations, where the aim is to obtain synergism in relation to a specific microbial agent.^{39,40,41}

Penicillin is the antibiotic of choice for pneumococci, and aminopenicillins, which are also effective against *Haemophilus influenzae*, are a good alternative. The association of amoxicillin/clavulanic acid is useful in cases that are resistant to amoxicillin and ampicillin due to the production of beta-lactamases.

The antibiotherapy used in our study was essentially empirical. Amoxicillin/clavulanic acid was the most commonly used antibiotic, in 19 patients (11.1%), and penicillin was used in 4 cases. When the symptoms suggest atypical pneumonia, the therapy of choice is a macrolide. Erythromycin was used in 13 patients (7.6%), not all with atypical pneumonias. Ceftazidime is an effective alternative for pneumonia by *Pseudomonas*. Due to the capacity of *Pseudomonas* to develop resistance to beta-lactams, the association of a second agent, usually an aminoglycoside, is recommended.⁴⁰ In our study, this was used in at least 4 patients, although other cephalosporins, like ceftriaxone and cefotaxime, were prescribed in 10 and 9 patients, respectively, while cephalosporins were the third therapeutic option. If the condition does not improve with the appropriate therapy, the patient should be reassessed, to rule out non-infections conditions, bronchial obstruction, or the presence of less common microorganisms. Hospital-acquired pneumonias almost always require associations of antibiotics, due to the existence of infections by multiple microorganisms, due to the need to widen the spectrum of activity and prevent the development of resistance.

The initial therapy is generally an association of third generation cephalosporin with an aminoglycoside, and if there is no clinical response, a third drug is associated. This may be a penicillin for Gram-positive bacteria (pneumococcus, anaerobic); vancomycin for methicillin-resistant *Staphylococcus aureus*; clindamycin for anaerobes; and co-trimoxazole or pentamidine for *Pneumocystis carinii*.^{39,40,41} In our particular case, the association most frequently used was ampicillin + amikacin, in 6 patients; only afterwards it was used ceftriaxone + amikacin and cefotaxime + amikacin in 4 patients each. It is emphasized, however, that two other associations were used, though less frequently than the latter: Erythromycin + cefotaxime and erythromycin + ceftriaxone in 5 patients each. Vancomycin and clindamycin were used in at least 4 patients to treat pneumonia by *Staphylococcus* and due to suspected anaerobes in aspiration pneumonia. Co-trimoxazole and pentamidine were not used. Fluoroquinolones are active against Gram-positive and Gram-negative bacteria, including *Pseudomonas aeruginosa*. They have weak activity against anaerobes, and are not indicated, therefore, in aspiration pneumonia. These were hardly used, only in 2 patients. In the patient infected by enteric Gram-negative

bacteria and *Staphylococcus aureus*, a wider spectrum therapy is required, and a second or third generation cephalosporin and an aminoglycoside are appropriate as initial treatment.³⁹ In certain cases, imipenem may be indicated, due to its activity for aerobes and anaerobes, whether Gram-positive or Gram-negative. Imipenem was used in only 3 patients from the start of treatment, but was the antibiotic that was most frequently added when there was no clinical response to the initial therapy (5 cases).

In cases where the initial antibiotherapy was replaced by another treatment regimen, clindamycin + amikacin and piperacillin/tazobactam were used in 5 and 2 cases, respectively, and ceftriaxone was used to replace amoxicillin/clavulanic acid in 14 cases. The latter replacement was attributed mainly to different treatment options on admission to those Emergency Services. The antibiotics used in our study were very varied, and their use is prescribed under the general guidelines for the use of antibiotics to treat pneumonias.^{39,40,41} In conclusion, the most frequently used antibiotics were beta-lactams, in isolation or associated with amikacin and erythromycin.

In relation to the clinical evolution, of the 122 patient's records consulted, 18 died, a mortality rate of 14.8%, which is considered (in the USA, this rate is as high as 20% of patients requiring hospitalization).^{2,3,42,43}

The associated diseases, in the patients who died, were congestive cardiac insufficiency, diabetes mellitus, chronic obstructive pulmonary disease, cerebrovascular disease, neoplasias, renal insufficiency, dehydration and malnutrition, which is in accordance with the literature.^{44,45,46}

The profile of pneumonia is continually changing, therefore clinics should keep up-to-date in relation to the changes in pattern of pathogenic agents, resistances to antibiotics, and the types of pneumonia, in order to find agreed strategies for use in dealing with this problem, which is so common. ■

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