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Most common aetiology of pneumonia among children hospitalized in the University Children' s Hospital in Lublin, Poland, 2010–2020

Najczęstsza etiologia zapaleń płuc wśród dzieci hospitalizowanych w Uniwersyteckim Szpitalu Dziecięcym w Lublinie w latach 2010–2020

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Abstract

Introduction and Objective. Pneumonia is defined as an acute infection of the lung parenchyma caused by various pathogens. It remains a leading cause of morbidity and mortality in the paediatric population globally. The aim of this study was to disclose most common aetiology of pneumonia among children hospitalized in the University Children's Hospital in Lublin, Poland, from 2010–2020.

Materials and method. This retrospective study included 2,250 patients in the age rage from 2–227 months, hospitalized in the Department of Paediatric Pulmonology and Rheumatology of University Children's Hospital in Lublin from 2010–2020 due to pneumonia. All necessary information were obtained from electronic medical records. According to the International Classification of Diseases Version 10 (ICD-10), patients were divided into 20 groups in terms of aetiology of pneumonia. Subsequently collected data were submitted to statistical calculations.

Results. A seasonality of pneumonia admissions was observed with predominance in the winter. Based on ICD-10 codes, the most common aetiology of pneumonia was unspecified bacterial pneumonia (J15.9) related with 30.2% of all cases. Moreover, based on IgM serology tests, Mycoplasma pneumoniae was the main identified pathogen (18.8% of all cases). Average duration of hospitalization oscillated around 7.4 days; the most common administered antibiotic was amoxicillin + clavulanic acid. Chest imaging was performed in 88.8% of patients.

Conclusions. Pneumonia dominated in the bacterial aetiology of children. Younger groups of children were more prone to the development of pneumonia. In many casus, there were observed difficulties with the identification of an exact pathogen.

Key words

children, aetiology, pneumonia, antibiotics, ICD-10, paediatrics

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Streszczenie

Wprowadzenie i cel pracy. Zapalenie płuc, definiowane jako ostra infekcja miąższu płuc o zróżnicowanej etiologii, pozostaje wiodącą przyczyną zachorowalności i śmiertelności wśród pacjentów pediatrycznych na całym świecie. Celem pracy jest przybliżenie najczęstszej etiologii zapaleń płuc wśród dzieci hospitalizowanych w Uniwersyteckim Szpitalu Dziecięcym w Lublinie w latach 2010–2020.

Materiał i metody. Badaniem retrospektywnym objęto 2250 pacjentów w wieku od 2 do 227 miesięcy, hospitalizowanych z powodu zapaleń płuc w latach 2010–2020 w Klinice Chorób Płuc i Reumatologii Dziecięcej Uniwersyteckiego Szpitalu Dziecięcego w Lublinie. Elektroniczna dokumentacja medyczna stanowiła źródło wszystkich danych dotyczących pacjentów. Zgodnie z Międzynarodową Klasyfikacją Chorób ICD-10, ze względu na etiologię zapaleń płuc, pacjenci zostali podzieleni na 20 grup. Zebrane dane posłużyły następnie do obliczeń statystycznych.

Wyniki. Zaobserwowano sezonowość zachorowalności na zapalenia płuc ze zwiększoną liczbą zakażeń w zimie. Bazując na Klasyfikacji Chorób ICD-10, stwierdzono, że najczęstszą etiologią zapaleń płuc była etiologia bakteryjna nieokreślona (rozpoznanie J15.9), leżąca u podstaw 30,2% wszystkich przypadków. Ponadto na podstawie diagnostyki serologicznej stwierdzono, że najczęściej wykrywanym patogenem związanym z rozwojem zapaleń płuc u dzieci była bakteria *Mycoplasma pneumoniae* (18,8% wszystkich przypadków). Średni czas hospitalizacji pacjentów wynosił 7,4 dnia, podczas gdy najczęściej stosowanym antybiotykiem była amoksycylina + kwas klawulanowy. Badania obrazowe klatki piersiowej wykonano u 88,8% pacjentów.

Wnioski. Wśród zapaleń płuc u dzieci dominowała etiologia bakteryjna. Młodsi pacjenci pediatryczni byli bardziej podatni na zachorowanie. W wielu przypadkach zapaleń płuc zaobserwowane zostały trudności z identyfikacją dokładnej etiologii.

Słowa kluczowe

dzieci, pediatria, etiologia, antybiotyki, zapalenie płuc, ICD-10

INTRODUCTION AND OBJECTIVE

Pneumonia is defined as an acute infection of the lung parenchyma caused by one or co-infecting pathogens, and remains a leading cause of morbidity and mortality in the paediatric population globally [1, 2, 3]. Pneumonia contributes to 1,000,000 fatal cases among children annually worldwide, with the vast majority (99%) of deaths occurring in developing countries. There is a correlation between underweight, inadequate breastfeeding, lack of immunization or air pollution and the development of pneumonia in children [4]. Other risk factors include preterm birth, low maternal education, poor access to healthcare and low socio-economic status. The course of pneumonia may be both mild and severe [3]. Cough, wheezing, hypoxaemia, tachypnoea, temperature >38.5°C, respiratory distress and central cyanosis are more severe clinical manifestations associated with worse prognosis. Other symptoms, such as temperature <38.5°C or mild dyspnoea may occur in patients suffering from clinically mild pneumonia [5, 6]. In Poland, pneumonia remains a leading cause of children hospitalization related to respiratory diseases. The prevalence of pneumonia is estimated to be 1 case per 108 children in the Polish population. There a seasonality of appearance with an increase in the incidence observable in the autumn and winter. Regarding aetiology, the most commonly isolated pathogens are *Streptococcus pneumoniae, Mycoplasma pneumoniae, and Chlamydia spp.* [7]. Because of similarities to other disorders, such as asthma, pulmonary oedema, pulmonary malignancies, and non-infective consolidative processes of the lung, other potential causes have to be ruled out [8]. Pneumonia is not only a burden for public health, but also it leads to many long distance complications. In their further life, patients are more prone to develop decreased lung function, asthma or obstructive lung disease [2].

There are many methods of pneumonia classification. Among them, the International Classification of Diseases Version 10 (ICD-10) can be distinguished, in which ICD-10 is based both on clinical features and laboratory investigation. Moreover, it contains codes for reporting different types of pneumonia. The aetiology of the disease remains diverse and wide-ranging [1]; therefore, the ICD-10 systematizes information available in electronic medical records, documents causes of mortality and morbidity presents a predictive value in monitoring the medical state of patients. It also allows statistical analyses to be performed for clinical research [9].

The aim of this study was to summarize collected patients' clinical data, to disclose the most common aetiology of pneumonia, and to systemize current knowledge regarding pneumonia among children hospitalized in the University Children's Hospital in Lublin, Poland, from 2010 – 2020, based on ICD-10 codes.

It was hypothesized that in different age groups of paediatric patients there were observable various aetiology and frequency of pneumonia.

MATERIALS AND METHOD

The retrospective study included 2,250 patients in the age range from 2–227 months old, hospitalized in the Department of Paediatric Pulmonology and Rheumatology of the University Children's Hospital in Lublin from 2010–2020 due to various clinical features of pneumonia. The interview, physical examination, treatment histories, chest imaging and information such as child's age of disease onset, duration of hospitalization and administered antibiotics, were obtained from electronic medical records. All patients fulfilled the clinical criteria of pneumonia. Taking into consideration the ICD-10, the patients were divided into 20 different groups in terms of the aetiology of pneumonia. Comparisons were carried out related to individual age groups and gender. Subsequently collected data were submitted to statistical calculations using Statistica software (version 13.3, StatSoft). Pearson's chi-squared test ($\chi 2$) was used to analyse group differences and to compare the relationships between variables.

RESULTS

In total, 2,250 patients were included in the analysis. Their ages ranged from 2 up to 227 months. Statistically, 53% (n=1189) were boys, and the average age of patients oscillated around 69± 51.7 months, median age – 50 months. Patients aged 4 years comprised the most numerous age group (17.4%); in contrast, 19-year-old patients were the least numerous (0.04%) (Fig. 1).

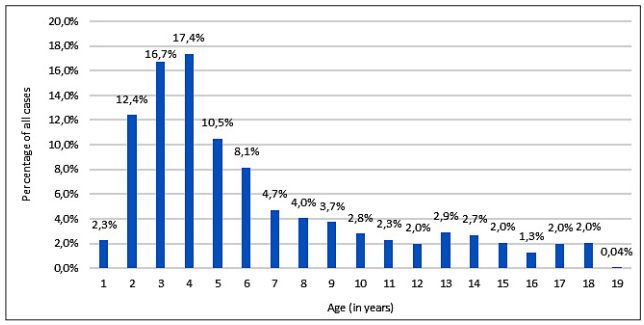

Figure 1. Percentage of patients by age

In the group of hospitalized patients included into the research, bacterial aetiology dominated in the majority of children (56.1%). The most common aetiology of pneumonia was unspecified bacterial pneumonia (J15.9) related with 30.2% of all cases. The second and the third most frequent causes were appropriately pneumonia, unspecified organism (J18.9) and pneumonia due to *Mycoplasma pneumoniae* (J15.7). Moreover, based on IgM serology tests, *Mycoplasma pneumoniae* was the main identified pathogen associated with the development of infection (18.8% of all cases) (Fig. 2).

Unidentified aetiology of pneumonia (J18.8, J18.9) presented the highest percentage of age-appropriate cases in the first year of life, while the occurrence of pneumonia due to *Streptococcus pneumoniae* (J13) and pneumonia due to *Mycoplasma pneumoniae* (J15.7) were the most abundant, respectively, in 15-year-old and 11-year-old children. Therefore, the number of unspecified cases tended to increase in younger patients, while the well-recognized aetiology of pneumonia was more characteristic for adolescents. There was observed an exception in the 19-year-old patients because this age group was represented by only 1 patient, whose aetiology (J18.9) constituted an infectious background of the whole age group [Fig. 3].

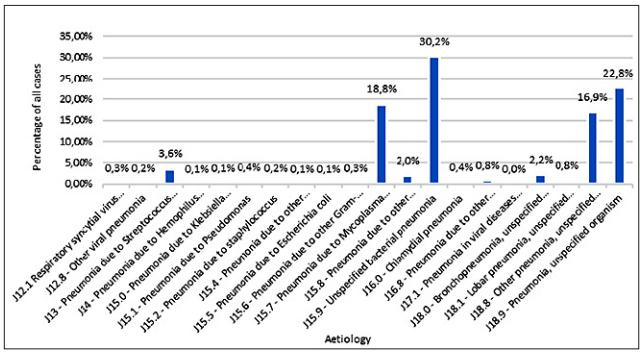

Figure 2. Aetiology of pneumonia among hospitalized patients

Approximately 82% of the total cases related with viral aetiology (J12.1, J12.8, J17.1) were observed in children under 4 years of age. However, in the older population the appearance of viral pneumonia was rare. Predominance of *Respiratory syncytial virus* pneumonia (J12.1) was noted (54.5% of all viral cases) (Fig. 4).

Atypical pneumonia caused by bacteria such as *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* (J15.7, J16.0) was diagnosed in 19.1% of all patients. Among them, the vast majority of cases were identified in children from 2–6 years old (Fig. 5).

An observable feature was the seasonality of morbidity. The pneumonia season reacheditsn apex in the winter, especially in January and February, when approximately a quarter of annual cases were noted. On the other hand, during the summer a slight decrease in the number of new cases was notable. The number of pneumonia cases in July and August was estimated at the level of 8.4% of all cases. In each and every season, unspecified bacterial pneumonia (J15.9) dominated. Different aetiologies were related with the varied months of infections' activity. For pneumonia due to *Streptococcus pneumoniae* (J13), the peak of the incidence (compared to other identified aetiologies of

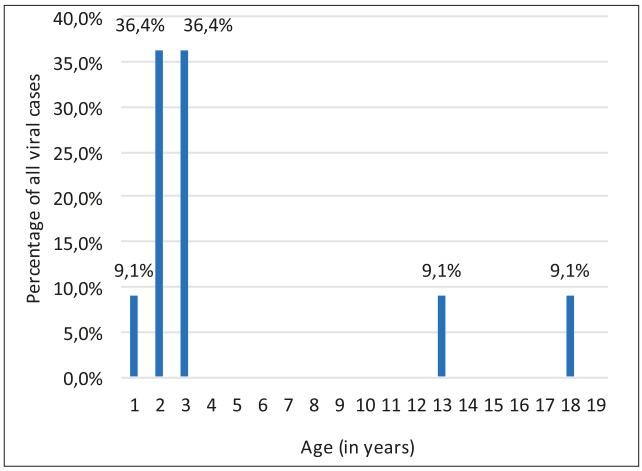

Figure 4. Viral pneumonia by age

pneumonia in proper month) was noted from September to January, for pneumonia due to *Mycoplasma pneumoniae* (J15.7), 2 separate summits were recorded, June – August and November – March, whereas for unspecified bacterial

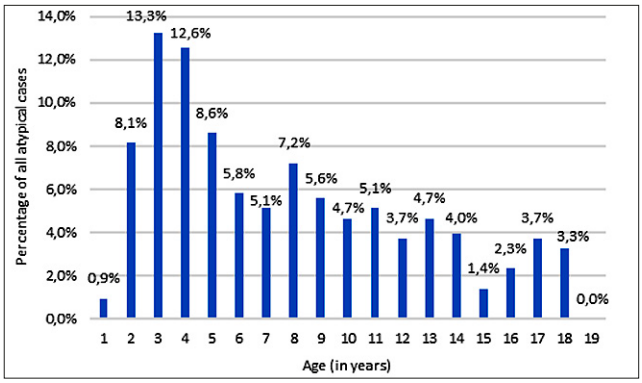

Figure 5. Atypical pneumonia by age

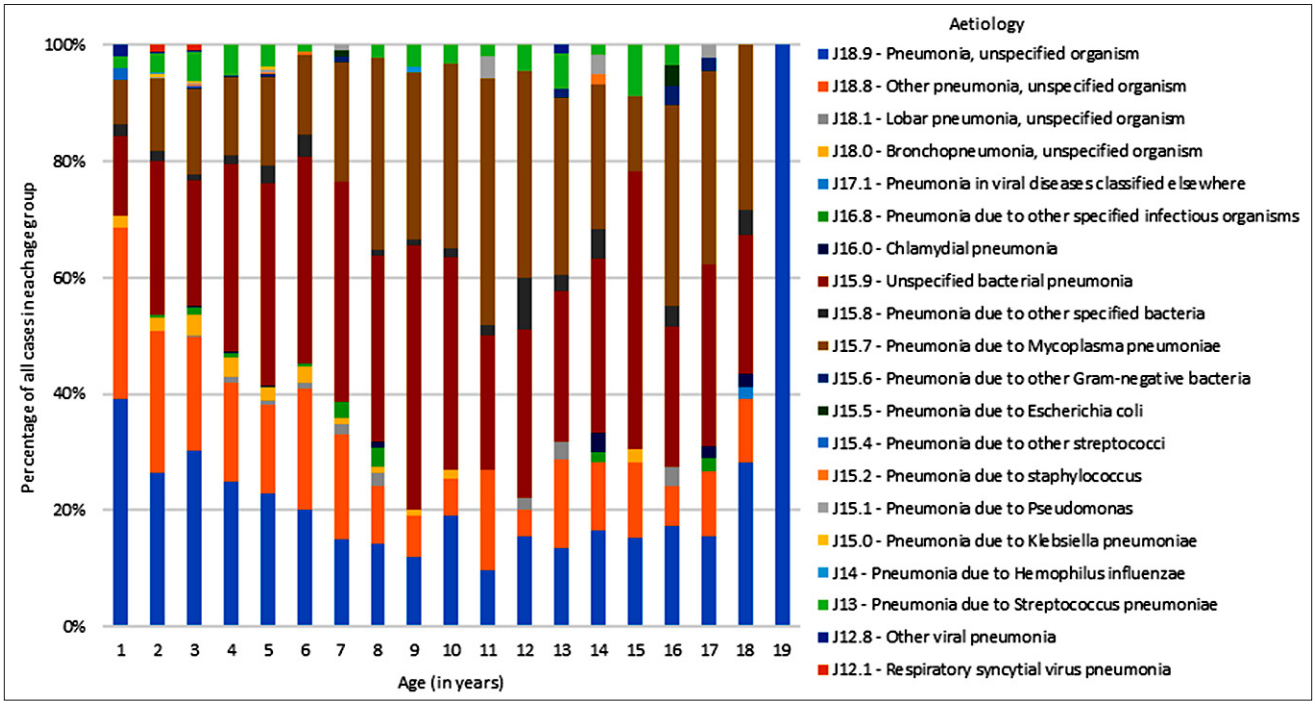

Figure 3. Percentage distribution of aetiology by age

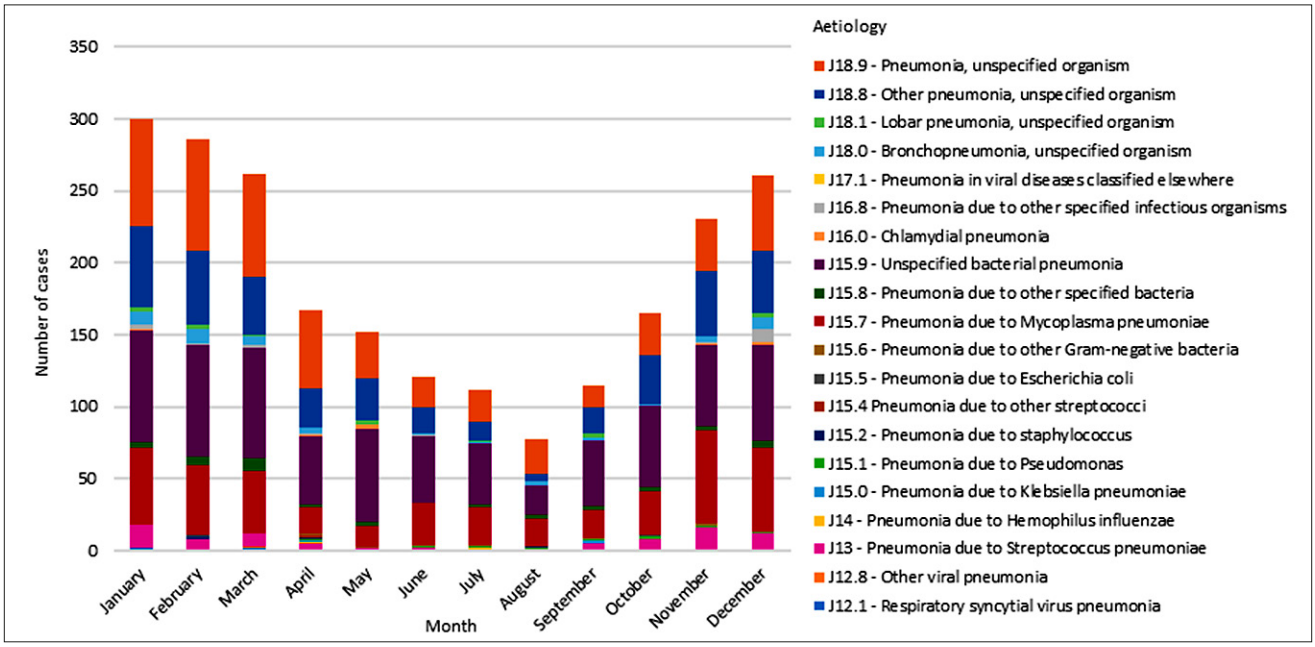

Figure 6. Seasonality of pneumonia

pneumonia (J15.9), October – May. The highest percentage of unidentified background disorders, such as both other pneumonia, unspecified organism (J18.8) and pneumonia, and unspecified organism (J18.9), was characteristic for the period October – May (Fig. 6).

The numbers of days of hospitalization of patients suffering from pneumonia was very varied. While an average duration of hospitalization was estimated at the level of 7.4 days, the longest period of time spent in hospital was 34 days, and referred to patients suffered from pneumonia in viral diseases classified elsewhere (J17.1). However, there was only 1 patient who suffered from pneumonia in viral diseases classified elsewhere (J17.1) – a 214-months- old girl with coexisting cytomegaloviral pneumonitis (B25.0); in CT (computed tomography), ground-glass opacity probably due to alveolar bleeding was observable. Other types of disorder related with prolonged hospitalization were pneumonia due to *Haemophilus influenza* (J14) and pneumonia due to other s*treptococci* (J15.4). Furthermore, the shortest length of hospital stay was 5.6 days and was characteristic for pneumonia, unspecified organism (J18.9) (Fig. 7).

Along with the older age of patients, there was observed a slight increase in the number of days spent in the hospital. The shortest hospital stay was typical for children up to 7 years of age, while prolonged hospitalization was characteristic for patients aged from 13–19 years of age (Fig. 8).

In addition, 96.8% of patients received an antibiotic therapy. The average number of administered antibiotics was 1.6. It was the highest (3.5) in the course of pneumonia due to *Haemophilus influenza* (J14), and the lowest was (0) in the course of pneumonia in viral diseases classified elsewhere (J17.1) (Fig. 9).

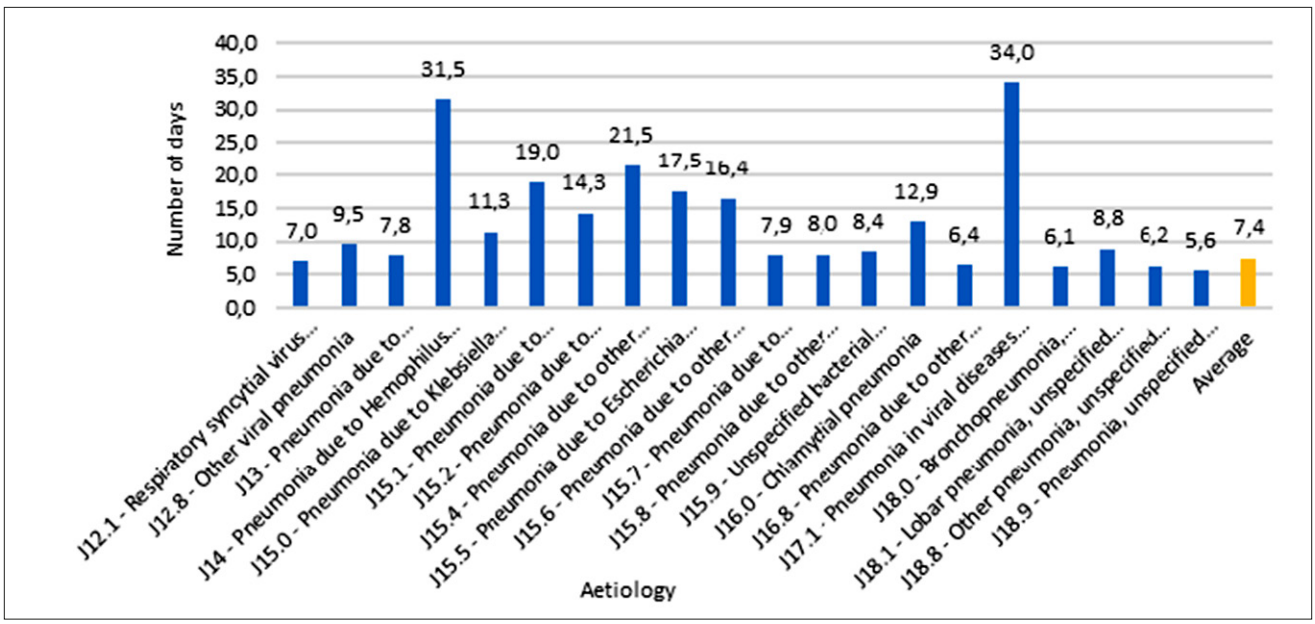

Figure 7. Length of hospital stay by aetiology

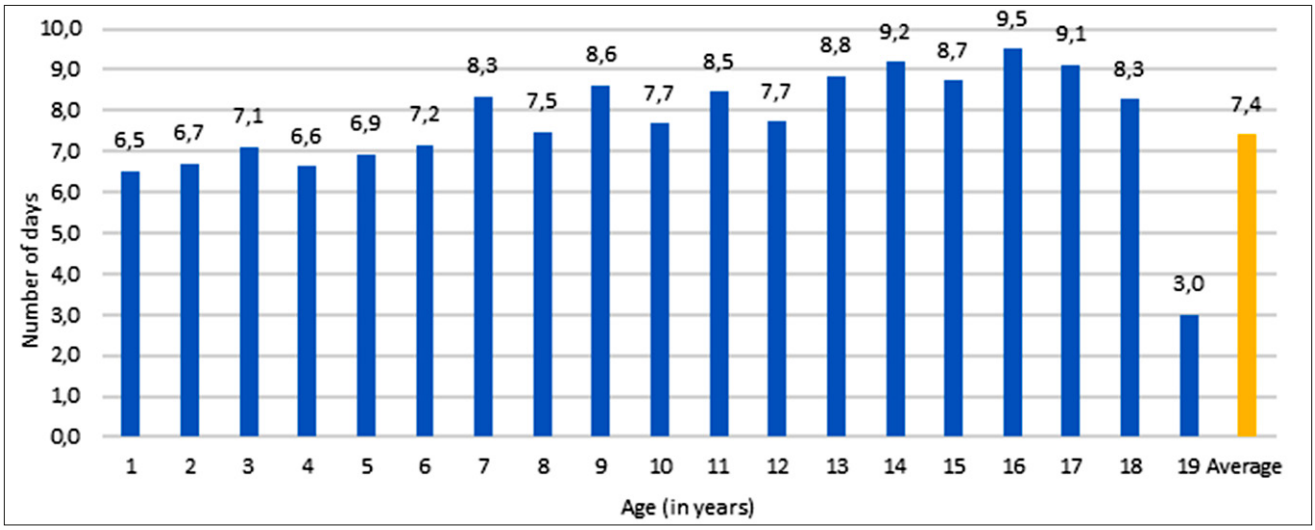

Figure 8. Length of hospital stay by age.

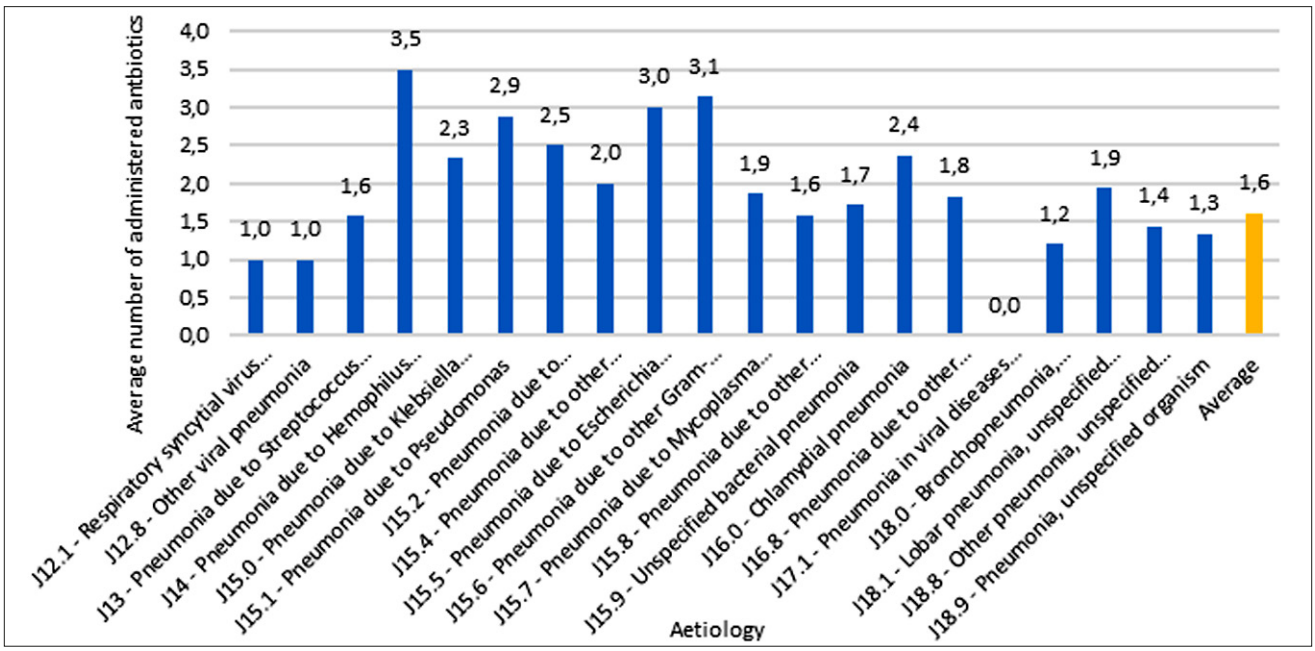

Figure 9. Average number of administered antibiotics by aetiology.

No significant correlation was observed between patient's age and number of administered antibiotics. With the exception of one patient, aged 16 years, in all age groups of patients the average number of administered antibiotic did not exceed 2 (Fig. 10).

During the therapeutic process, most frequently used

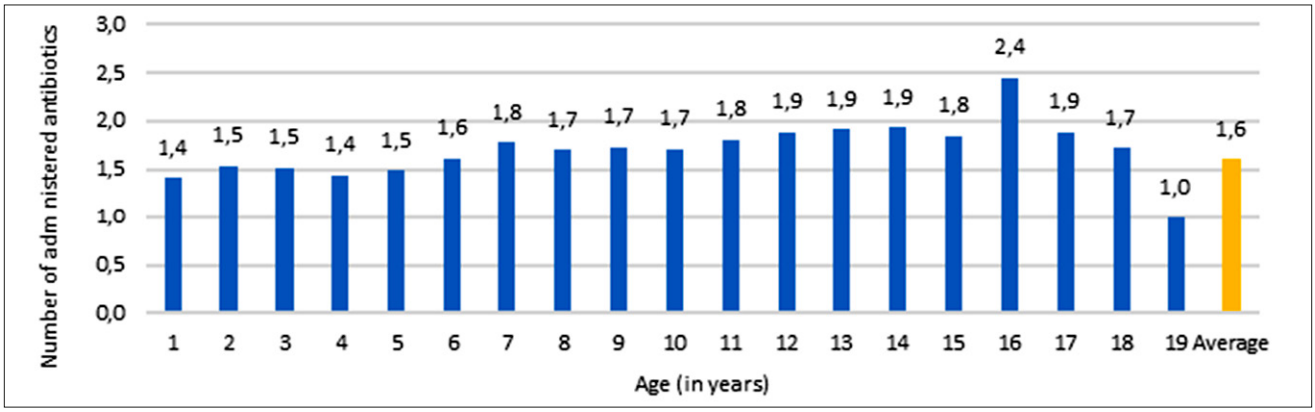

Figure 10. Average number of administered antibiotics by age

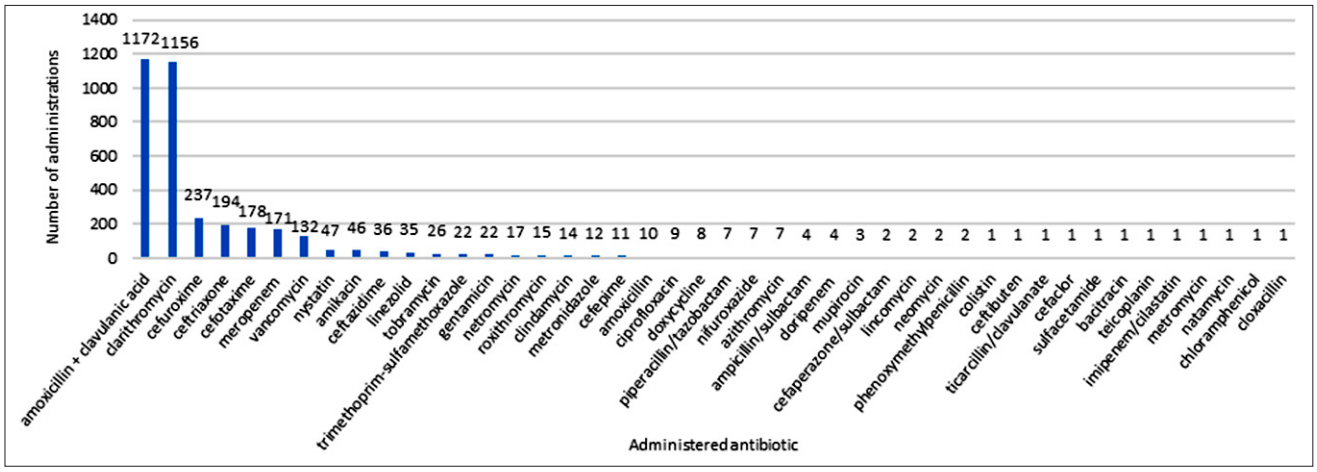

Figure 11. Administered antibiotics among hospitalized patients.

antibiotics were amoxicillin + clavulanic acid (32.4% of all taken antibiotics), clarithromycin (31.9%) and cefuroxime (6.5%) (Fig. 11).

Chest imaging was performed in 88.8% of all hospitalized patients. The most common techniques included chest X-ray in 73% of cases, and both chest X-ray and chest ultrasonography (USG) in 9.6% of cases (Fig. 12).

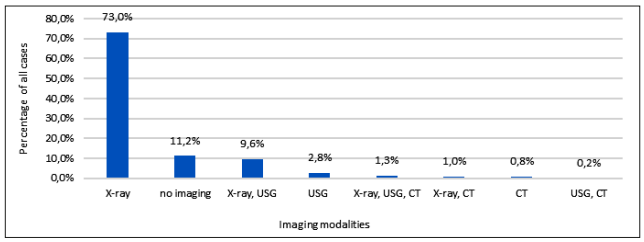

Figure 12. Imaging modalities among hospitalized patients

Imaging modalities confirmed radiological changes in all cases of examined patients. Moreover, abnormal respiratory sounds (e.g. crackles or wheeze) were observable in all children suffering from pneumonia.

DISCUSSION

Paediatric pneumonia, also known as a major 'forgotten killer of children', remains the most widespread disease in the population of children worldwide [10]. The most recent researches indicate that in the vast majority of studies, pneumonia appeares more frequently in males than females [7, 11, 12]. This analysis also showed that paediatric pneumonia presents a slight male predominance. Moreover, other investigations reveal that the male to female ratio was estimated to be 1:0.8 [13], while in the current study it was about 1:0.9.

In different researches, the average age of hospitalized patients was diverse and wide ranging. In South Korea children' s mean age was approximately 35 months, in Poland, 39 months, while in China it may be as high as 78 [7, 13, 14]. Median age of patients suffering from childhood pneumonia also depended on the characteristic of the subjects studied. It oscillated around 18 months in Columbia and even 42 months in France [15, 16]. In this research both mean (69.41 ± 51.7 months) and median age (50 months) confirmed that younger groups of children are more prone to the development of pneumonia. In similar studies there was observed a rise in number of incidences among children 1–3 years of age. Therefore, that paediatric group constituted 54.4% of total diagnosed cases, whereas in this retrospective study it oscillated around 31.4%. On the other hand, patients in the age range m 13–18 years represented the least numerous group (3.4%) [13]. However, in the current study, the age group indicated above amounted to even 24.9% of all cases.

Heterogeneity at the time of hospitalization described by different authors was observed. The average length of a hospital stay was in the range of 6–7.29 days, with the longest hospitalization among infants [7, 16, 17]. The current findings revealed that the average duration of hospitalization was around 7.4 days. In the literature, the shortest length of stay was more characteristic for the older age groups. On the other hand, in this study the longest hospital stay (9.5 days) was typical for 16-year-old patients, whereas the shortest hospitalization (6.5 days) occurred during the first year of child's life. As evidenced by research, over the years the number of hospitalization days is systematically decreasing [17]. In 1.8% of all pneumonia cases there was notable a tendency to rehospitalization within 30 days due to recurrence of the disease [7]. Treatment of both mild and moderate cases of pneumonia included not only supportive care, but also antibiotics [18]. From 83% – 98% of hospitalized paediatric patients received antibiotic therapy mainly based on oral antibiotics (81.1%) [14,19]. In this study during the therapeutic process, 97% of patients received antibiotics, in which the most frequent were: amoxicillin + clavulanic acid (32.4% of all patients took antibiotics), clarithromycin (31.9%) and cefuroxime (6.5%). According to the guidelines of the Royal College of Paediatrics and Child Health (RCPCH) in children up to 5- years-old suffering from community acquired pneumonia, the gold standard treatment includes oral amoxicillin for at least 5 days. In the case of a raised suspicion of infection caused by *Mycoplasma pneumoniae* or *Chlamydia pneumoniae*, macrolides should be prescribed. Nevertheless, intravenous antibiotics, such as penicillin/amoxicillin, amoxicillin clavulanate, cefuroxime and cefotaxime/ceftriaxone, are recommended in the hospitalization cases of severe pneumonia [20]. An abuse of antibiotics in the course of the treatment in patients with viral pneumonia is also notable. The main reasons for this phenomena are difficulties related with distinction between

the aetiology of pulmonary infection [21]. Based on the data from the United States, in the vast majority (78%) of cases of pneumonia in children the exact pathogen remained unspecified. That fact was also confirmed in the current study (the exact infectious factors in 72.8% of cases persisted undetermined).

In the paediatric population globally, viral pneumonia remained more typical and concerned the first 2 years of a child's life. After that, bacterial aetiology dominated [22]. The current results revealed a tendency to the most frequent occurrence of viral cases in patients up to 4-years-old (81.8% of all viral cases); however, in total in this age group, unidentified aetiology dominated (54.7% of all incidents).

In children aged 4–18 years, the bacterial cause of pneumonia was more numerous than any other aetiology (62.1%). Unidentified aetiology also prevailed in studies among patients suffering from childhood pneumonia in Poland. This tendency is also observable in the group of bacterial cases, in which the number of exact pathogen detection reaches about 23% of all hospitalizations, compared with 46.2% in the current analysis [7]. This situation is caused by the fact that diagnostic methods, such as specimen collection of sputum and its analysis, may be difficult in the paediatric group of patients. The main reasons for that are the relative inaccessibility of infected tissue and high risk of contamination by upper respiratory tract secretions. Lung aspirates are related with many complications, such as pneumothorax or haemoptysis, while sputum expectoration is a sampling method that may be associated with collecting problems, especially in children. Even in sputum induction there is a risk of specimen contamination [23]. Nevertheless, both in the current and other studies, in following the diagnostic process the most frequently identified organism was *Mycoplasma pneumoniae* (appropriately 65.3% and 18.8% of total cases) [14]. Similarity was also observed in fact that the other most commonly recognized pathogens were *Streptococcus pneumoniae* and *Chlamydia spp* [7]. Atypical pneumonia in children is related with pathogens such as *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae* and *Legionella pneumophila*. Due to the research, it appeared in 10–20% of all patients with diagnosed pneumonia, while in this study in 19.1% of hospitalized children [24]. Moreover, the disease more frequently affected school-aged children and adolescents, rather than infants or neonates [25, 26, 27]. As observed retrospectively, pneumonia presented a seasonality of appearance with the nadir in the summer months from June – August. Inversely, this was also related with a rise in cases in the autumn and winter seasons [12].

Similar to the current study, data showed that chest radiographs (X-ray) remains the first-line imaging examination when suspecting childhood pneumonia. Despite the fact that the low cost and broad availability provide their wide distribution, they are not indicated in ambulatory conditions and not in complicated cases. The results of chest radiographs also do not allow distinguishing viral from bacterial pneumonia. According to the national guidance from the United Kingdom and the United States, there are no recommendations for routinely performing chest radiographs in community-acquired pneumonia [28, 29, 30]. In some clinical situations, radiological changes are not observable in X-ray, but features of pneumonia may be confirmed in the more sensitive CT scan. However, CT is burdened by a higher radiation dose that may lead to many side-effects, including radiation-related cancer. It is therefore indicated to limit the frequency of using CT in the paediatric population [31]. Magnetic resonance imaging constitutes a potential alternative to CT. It is characterized by a higher security profile and similar accuracy to CT [29]. Ultrasound (USG) examination presents significant advantages in comparison with other imaging modalities due to its lower cost, immediate availability of the results, and lack of radiation. Evidence proposes USG examination as a possible first-line method in diagnosing of pneumonia in children [32]. Based on imaging modalities, however, identification of the exact aetiology remains difficult. Nevertheless, 3 radiological patterns of the disease such as focal nonsegmental or lobar pneumonia, multifocal bronchopneumonia or lobular pneumonia, and focal or diffuse 'interstitial' pneumonia, were distinguished to classify different types of disease and evaluate the clinical state of patients [33].

In view of the problems with identification of the exact pathogen, the therapy is often supported empirically with the use of broad-spectrum antibiotics. Despite the fact that this is a clinically effective treatment, it may lead to the development of antibiotic resistance; therefore, identification of the exact pathogen might be advantageous [6].

CONCLUSIONS

This study confirms that younger groups of children are more prone to the development of pneumonia. In hospitalized children with pneumonia, bacterial aetiology dominated. However, in many cases difficulties were observed with identification of the exact pathogen. Recognizing the aetiology of pneumonia in children was often challenging because of disadvantages related with respiratory sampling methods, such as non-invasive and invasive procedures. Taking the above into account, antimicrobial therapy was often administered empirically. Its benefits exceeded the potential risks, as evidenced by the fact that an increased percentage of unidentified aetiology of pneumonia had not been related either with prolonged hospitalization or growth in the average number of administered antibiotics. Nevertheless, in the future, there is a need to provide more effective non-invasive diagnostic tools to better recognize particular aetiology background of the disease. This would allow the development of more adequate treatment to the whole paediatric population, and limitation of many long-term complications. Moreover, the significant frequency of performing chest X-ray in the paediatric population prompts the consideration of using other, equally sensitive and even safer imaging modalities, such as USG.

Disclosure

The authors declare no conflict of interest.

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